Evidence report for total knee replacement plus conservative therapy versus conservative therapy alone for knee osteoarthritis

Part 1 - Scoping

Prepared by EBSCO Information Services

May 9, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

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Eric Manheimer, PhD, EBM Editor

Methods

Using an established, structured template that delineates key elements for scoping (i.e., the population, interventions, and key outcomes to consider), we collaboratively agreed with UKSH on the scope of the present evidence report. Scoping was completed on May 15, 2019.

Results – Criteria Selection for Critical Appraisal

Population:

Inclusion criteria

Adults diagnosed with knee osteoarthritis (based on clinical diagnosis or radiological evidence) and considering total knee replacement surgery

Exclusion criteria

Major exclusion criteria are previous total replacement of the same knee, need for bilateral total knee replacement, and conditions that preclude knee replacement (e.g. bacterial knee infection, certain comorbidities).

Intervention and Comparator:

Total knee replacement (followed by conservative non-surgical therapy)

Conservative (non-surgical) therapy alone (e.g., including a variety of methods such as patient advice/education, physical therapy and/or exercise, weight reduction, oral medication, and/or injections)

Outcomes:

FAQ 1: What does the treatment involve?

Include a description of the treatment or procedure, including the possible expense of surgery (as a qualitative expression) and rehabilitation following surgery. Include duration of surgery and length of stay if relevant.

Descriptive responses are acceptable, and this does not involve systematic evidence searches, critical appraisal, or evidence synthesis.

FAQ 2: Will I feel better?

Outcomes of interest are pain, symptoms, function, and quality of life.

We will also address the outcomes of having a longer-term favorable pain outcome and the possibility of reducing use of pain medication.

FAQ3: Will the treatment help me lose weight?

The outcome of interest is weight loss.

FAQ 4: Will I need surgery later?

Outcomes of interest are need for repeat surgery (especially for loss of efficacy in the longer term) among those receiving total knee replacement plus conservative care and eventual decision to have surgery among those receiving conservative care only.

FAQ 5: What are the risks?

Perioperative risks of interest – in addition to those reported in the literature – include prosthetic joint infection, mortality, blood clots, stiffness requiring brisement forcé, falls, and fracture.

In the absence of adequate sample size to assess for adverse effects in randomized trial evidence, cohort studies will be considered.

We will also include descriptive responses for key risks associated with the medication portion of conservative care (e.g., gastrointestinal bleeding with non-steroidal anti-inflammatory drugs).

FAQ 6: What are the side-effects?

Negative side effects of interest include potential need to avoid sports and activities (eg, running) that involve putting stress on the joint, surgery-related pain, and common side effects of medications.

As these are things to be aware of rather than things requiring systematic literature searches, critical appraisal, and evidence synthesis, descriptive responses will be used for most of these items; however, if evidence speaking to these outcomes is uncovered during systematic literature searches for other FAQs, we will incorporate that into our answers for this FAQ.

FAQ 7: How long does it take to recover?

Outcomes of interest are time to return to usual activity, time to return to work, and time to return to driving.

Descriptive responses are acceptable, and this does not involve systematic evidence searches, critical appraisal, or evidence synthesis.

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Part 2 - Search and Selection

Prepared by EBSCO Information Services

May 13, 2019

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Methods

First-round searching will consist of searching DynaMed Plus summaries pertinent to the topic. The search starts with DynaMed Plus because DynaMed Plus content is based on a thorough, systematic search and active literature surveillance system.

> Systematic literature surveillance (SLS) has been a cornerstone of creating DynaMed content since its inception. Currently, the SLS team works closely with members of McMaster University's Department of Health Research Methods, Evidence, and Impact to define and refine optimal search strategies, utilizing search terms for methodology and for clinical concepts (especially diagnosis and treatment) for each journal. These filters for PubMed searches are derived from PubMed Clinical Queries, McMaster University Hedges system, and DynaMed search filters and were found to capture >95% of relevant valid articles for use in DynaMed.[1]
> [1]Alper BS, Iorio A. Optimising search filters for active literature surveillance: a concordance study. Global Evidence Summit. Cape Town, South Africa; September 2017.
>
> The SLS team, in collaboration with McMaster University, continually evaluates and improves these filters to keep abreast of the ever-changing medical literature landscape. PubMed searches are performed daily. Each article is assessed by an external screener for clinical relevance, then reviewed by internal staff for both clinical relevance and validity. Any disagreements are settled by the Deputy Editor of the SLS team.
> In addition, the SLS team continually monitors the Journal source list against the list of journals catalogued in MEDLINE and existing DynaMed content to determine the set of journals that provide the highest yield for valid, clinically relevant content. As of November 2018, 507 Journals are systematically searched (see http://dynamed.com/home/content/content-sources). The journal selection threshold leads to routine adjustments to the number of journals selected.

Second-round searching will involve PubMed/MEDLINE® searches for intervention-specific systematic reviews or guidelines that involve a systematic review that are more recent than those identified in first-round searching.

Third-round searching will involve original study tracing from systematic reviews, guidelines or other relevant sources. This may be done to identify additional evidence sources if the results from the first two rounds of searching are insufficient.

Fourth-round searching will involve searches for original evidence reports. Such searching will be limited to areas considered insufficiently addressed by earlier searches, such as focused concepts published after search dates in systematic reviews.

Additional selective searching, such as tracing citations from articles found or seeking related articles, may be done for additional concepts discovered.

Additional evidence updates may also be added continuously from feedback from any source.

FAQ Summary

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Results

First-round searching – DynaMed Plus:

DynaMed Plus subsection	Relevant for FAQ(s)	Number of article citations	Number of unique references included
Total knee arthroplasty topic, clinical efficacy subtopic, pain and function subtopic (May 13, 2019)	FAQ2, FAQ3, FAQ4, FAQ5	6	1 (Skou 2015)
Total knee arthroplasty topic, preoperative decision-making subtopic, prognosis subtopic (May 13, 2019)	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6, FAQ7	20	3 (Bayliss 2017, Berstock 2018, Richardson 2019)
Total knee arthroplasty topic, perioperative management subtopic, thromboembolic prophylaxis subtopic, guidelines for thromboembolic prophylaxis subtopic (May 13, 2019)	FAQ5	2	0
Total knee arthroplasty topic, perioperative management subtopic, thromboembolic prophylaxis subtopic, need for thromboembolic prophylaxis subtopic (May 13, 2019)	FAQ5	4	0
Total knee arthroplasty topic, long-term management post-arthroplasty subtopic, evaluation for prosthetic joint infection subtopic (May 13, 2019)	FAQ5	3	0

Second-round searching – searches for intervention-specific systematic reviews:

Database	Search string	Relevant for FAQ(s)	Number of search results	Number of references included
PubMed May 13, 2019	(total knee[ti] OR knee replacement[ti] OR knee arthroplasty[ti]) AND ((long-term[tiab] OR long term[tiab] OR mid-term[tiab] OR mid term[tiab] OR persisting[tiab] OR persistent[tiab] OR enduring[tiab] OR long lasting[tiab] OR long-lasting[tiab]) AND (pain[tiab] OR function[tiab])) AND systematic[sb]	FAQ2, FAQ3	39	1 (Beswick 2012)
PubMed May 13, 2019	(total knee[ti] OR knee replacement[ti] OR knee arthroplasty[ti]) AND (duration[tiab] OR implant survival[tiab] OR revision surgery[tiab] OR repeat surgery[tiab] OR last[tiab]) AND systematic[sb]	FAQ4	67	1 (Wilson 2019)
PubMed May 13, 2019	(total knee[ti] OR knee replacement[ti] OR knee arthroplasty[ti]) AND (fall[tiab] OR falls[tiab] OR falling[tiab]) AND systematic[sb]	FAQ5	14	2 (Lo 2019, di Laura Frattura 2018)
PubMed May 13, 2019	(total knee[ti] OR knee replacement[ti] OR knee arthroplasty[ti]) AND (thromboemboli*[tiab] OR thrombotic[tiab] OR thrombosis[tiab] OR emboli*[tiab] OR infecti*[tiab] OR mortality[tiab] OR death[tiab] OR complication[tiab] OR adverse[tiab]) AND systematic[sb] AND (2018/01/01[PDAT]:3000/12/31[PDAT])	FAQ5, FAQ6	49	2 (Wilson 2019, Berstock 2018*)

* Already captured in first-round searching

Third-round searching – **study tracing from systematic reviews:**

Source	Tracing	Relevant for FAQ(s)	Number of search results	Number of references included
Not applicable				

Fourth-round searching – searches for original evidence reports:

Database	Search string	Relevant for FAQ(s)	Number of search results	Number of references included
PubMed May 13, 2019	(total knee[tiab] OR knee replacement[tiab] OR knee arthroplasty[tiab]) AND (conservative[tiab] OR non-surgical[tiab] OR nonsurgical[tiab]) AND (randomized controlled trial[pt] OR random*[tiab])	FAQ2, FAQ3, FAQ4, FAQ5, FAQ6	25	2 (Skou 2015*, Skou 2018)

* Already captured in first-round searching

Evidence report for total knee replacement plus conservative therapy

Part 3 - Critical Appraisal of Evidence Reports

Prepared by EBSCO Information Services

March 15, 2019

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Methods

For each study selected for critical appraisal, we assessed for criteria needed for Level 1 [likely reliable] evidence ratings in DynaMed's Levels of Evidence criteria in which evidence quality is labeled in 1 of 3 levels:

- **(level 1 [likely reliable] evidence)** for studies with clinical outcomes and minimal risk of bias;
- **(level 2 [mid-level] evidence)** for studies with clinical outcomes and significant methodological or statistical limitations; and
- **(level 3 [lacking direct] evidence)** for reports that do not include scientific analysis of clinical outcomes or for study types that do not include comparisons between groups.
-

The specific concepts we critically assessed are fully mapped to cover all the criteria used in GRADE. We summarized key concerns identified that reduce the certainty of evidence in categories used for GRADE methods (i.e., risks of bias, indirectness, imprecision, inconsistency, and other considerations if relevant). In the study-level summaries inconsistency assessment was applied to consistency of within-study results – this applies to consistency across related outcomes for both original studies and for systematic reviews, and also applies to consistency across studies when applied to systematic reviews.

FAQ Summary

BAYLISS 2017
Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, Cooper C, Carr AJ, Arden NK, Beard DJ, Price AJ. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. Lancet. 2017 Apr 8;389(10077):1424-1430. Epub 2017 Feb 14. PubMed

Relevant to FAQ4

- **Study design:** observational study
  - population-based data from Clinical Practice Research Datalink
    - comprised of primary care medical records of all patients attending selection of general practitioners in United Kingdom
    - representative of entire general practice population in wider UK population
  - data adjusted for all-cause mortality to generate lifetime risks of revision surgery based on age at time of primary surgery
- **Population:** patients who had undergone total knee replacement
  - This study also includes evidence for patients who had total hip replacement, but we do not consider these data further in this summary due to not being relevant for the scoped question
  - mean age 70.1 years old for knee patients
- **Intervention:** total knee replacement
- **Comparison:** not applicable

- **Study inclusion criteria:**
  - patients with joint replacement surgery from January 1, 1991 until August 10, 2011
  - aged $\geq$ 50 years at time of surgery

- **Number of studies:** Not applicable
- **Number of participants:** 54,276
- **Duration of follow-up:** mean 5.2 years; range 0 to 22.5 years; median 4.5 years

- **Certainty:** High (applies to both implant survival and lifetime risk of revision outcomes at all time points)
  - **Certainty by outcome:** Not applicable
  - **Risk of bias:** No serious concern
  - **Imprecision:** No serious concern
  - **Indirectness:** No serious concern
  - **Inconsistency:** No serious concern

- **Results:**

Implant survival at 5, 10, 15, and 20 years after total knee replacement

Years after total knee replacement	Cumulative implant survival rate (95% CI)
5	97.98% (97.84% to 98.12%)
10	96.12% (95.83% to 96.39%)
15	92.94% (92.17% to 93.64%)
20	89.69% (87.45% to 91.54%)

Lifetime risk of revision after total knee replacement by age at total knee replacement

Age at total knee replacement (years)*	Lifetime risk of revision (95% CI)**	
	Females	Males
50-54	20% (17% to 23%)	35.0% (30.9% to 39.1%)
55-59	14% (13% to 15%)	36.5% (34% to 39%)
60-64	16% (15% to 17%)	18% (17% to 19%)
65-69	6.5% (6% to 7%)	12% (11% to 13%)
70-74	5.5% (5% to 6%)	5% (4% to 6%)

*For patients having total knee replacement at aged 75, lifetime risk of revision was slightly less than 5% with similar estimates for females and males. Older than 75, risk slightly reduced and was consistent between sexes.
**Values were estimated from Figure 3 graph and are not exact, except for estimates for males aged 50-54 years old which were exactly reported in text

- mean time to revision surgery about 5 years after primary implantation in all age groups
    - 4.55 years (95% CI 4.07 to 5.02 years) for patients aged 50-59 years at initial surgery
    - 3.57 years (3.26 to 3.88 years) for patients in eighth decide at initial surgery
- consistently higher risks of revision for men and younger patients at all time points after initial surgery

BERSTOCK 2018

Berstock JR, Beswick AD, López-López JA, Whitehouse MR, Blom AW. Mortality After Total Knee Arthroplasty: A Systematic Review of Incidence, Temporal Trends, and Risk Factors. J Bone Joint Surg Am. 2018 Jun 20;100(12):1064-1070. PubMed

Relevant to FAQ5

- **Study design:** systematic review of observational studies
- **Population:** patients having primary total knee replacement
- **Intervention:** primary total knee replacement
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - reported 30- or 90-day mortality following total knee replacement
    - published from 2006 to 2016

- **Number of studies:** 37
- **Number of participants:** 1,753,449 (number of total knee replacements)
- **Duration of follow-up:** 90 days after total knee replacement

- **Certainty: Moderate**
    - **Certainty by outcome:** Not applicable – inconsistency downgrade applies to both outcomes
    - **Risk of bias:** No serious concern
    - **Imprecision:** No serious concern
    - **Indirectness:** No serious concern
    - **Inconsistency:** Serious concern

        - estimates from individual studies were heterogeneous for both 30-day and 90-day mortality outcomes

Results:

- overall mortality following total knee replacement
    - 30-day mortality 0.20% (95% CI 0.17% to 0.24%) in analysis of 24 studies including 1,753,449 total knee replacements performed from 1991 to 2014
    - 90-day mortality 0.39% (95% CI 0.32% to 0.49%) in analysis of 17 studies including 700,981 total knee replacements performed from 1991 to 2014
- cardiovascular causes were the most common cause of mortality in the 5 studies in which cause of death was reported
- mortality rates appear to be decreasing with time
    - significant temporal reduction in mortality was observed in meta-regression using median year of surgery for each study as moderator
    - meta-regression models developed by authors estimated 2015 mortality rates as follows
        - 30-day mortality: 0.10% (95% CI 0.07% to 0.14%)
        - 90-day mortality: 0.19% (95% CI 0.15% to 0.23%)

BESWICK 2012

Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. BMJ Open. 2012 Feb 22;2(1):e000435. PubMed

Relevant to FAQ2

- **Study design:** systematic review of observational studies
- **Population:** patients who had total knee replacement for treatment of osteoarthritis
    - This study also includes evidence for patients who had total hip replacement for treatment of osteoarthritis, but we do not consider these data further in this summary due to not being relevant for the scoped question
- **Intervention:** total knee replacement
- **Comparison:** not applicable

- **Study inclusion criteria:**
    - patients were unselected and representative of primary total hip or knee replacement population
    - prospective collection of data from consecutive patients
    - complete reporting of losses to follow-up
    - results classifiable as proportion of patients with different extents of pain at follow-up were reported

- **Number of studies:** 11
- **Number of participants:** 12,800
- **Duration of follow-up:** limited to between 3 months and 5 years

- duration of follow-up was restricted to between 3 months and 5 years because the systematic review authors were "...concerned with outcomes when recovery can be considered maximal and not later issues of joint loosening and revision..."
- for knee studies specifically, follow-up ranged from 3 months to 60 months

- **Certainty overall: High**
  - **Certainty by outcome:** Not applicable – only 1 outcome
  - **Risk of bias:** No serious concern if using estimates from high-quality study (see table)
    - review authors considered following 2 markers of better representativeness as indicators of study quality:
      - studies conducted at multiple centers (compared to single center studies)
      - studies with lower losses to follow-up (< 10%)
    - as indicated in table below, 1 study met both indicators of quality, 5 met only 1, and 5 met neither
  - **Imprecision:** No serious concern if using estimates from higher-quality studies
  - **Indirectness:** No serious concern
  - **Inconsistency:** No serious concern
  - **Other considerations:**
    - only 17 studies were included (6 for hip replacement, 11 for knee replacement) out of 115 studies that were otherwise eligible but did not report results classifiable as proportions of patients with different extents of pain at follow-up (typically due to 1 of following 2 reasons)
      - lack of pain outcome separate from overall outcome
      - presentation or pain results as mean only
    - small number of studies, different outcome measures reported, and different methods of analysis in studies with similar outcomes precluded meta-analysis
    - estimates varied across studies overall but were similar in the 2 studies judged highest quality

- **Results and certainty of individual studies:**

Author year; country; date of baseline	Sample size	Time point for outcome assess-ment	Number of patients with				Certainty (reasons for downgrade)
			favorable* outcome % (n/N)	uncertain† outcome % (n/N)	unfavorable‡ outcome % (n/N) without imputation§	unfavorable‡ outcome % (n/N) with imputation**	
Baker 2007; UK; 2003	9,417	12 mos (or latest available)	68.2% (6,427/9,417)	14.9% (1,407/9,417)	16.8% (1,583/9,417)	(1,583 + 237)/9,417 = 19.3% (95% CI 18.5% to 20.1%)	Moderate (downgrade due to moderate loss to follow-up)
Jones 2000; Canada; 1995-1997	292	6 mos	76.0% (222/292)	5.5% (16/292)	18.5% (54/292)	(54 + 3)/292 = 19.5% (95% CI 15.4% to 24.5%)	High
Quintana 2006; Spain; 1999-2000	792	6 mos	50.8% (402/792)	24.1% (191/792)	25.1% (199/792)	(199 + 48)/792 = 31.2%	Moderate (downgrade due to high loss to follow-up)
Nunez 2007; Spain; 2000-2001	88	36 mos	68.2% (60/88)	23.9% (21/88)	8.0% (7/88)	(7 + 2)/88 = 10.2% (95% CI 5.5% to 18.3%)	Moderate (downgrade due to not multiple center study [single center])
Stephens 2002; USA	68	6 mos	76.5% (52/68)	7.4% (5/68)	16.2% (11/68)	(11 + 1)/68 = 17.6%	Moderate (downgrade due to not multiple center study [single center])
Lundblad 2008; Sweden	69	18 mos	30.4% (21/69)	47.8% (33/69)	21.7% (15/69)	(15 + 7)/69 = 31.9%	Low (downgrade due to moderate loss to follow-up and not multiple center study [single center])

Nilsdotter 2009; Sweden; 1999-2001	102	60 mos	46.1% (47/102)	27.5% (28/102)	26.5% (27/102)	(27 + 7)/102 = 33.3%	Low (downgrade due to moderate loss to follow-up and not multiple center study [single center])
Vuorenmaa 2008; Finland	51	3 mos	66.7% (34/51)	15.7% (8/51)	17.6% (9/51)	(9 + 1)/51 = 19.6%	Low (downgrade due to moderate loss to follow-up and not multiple center study [single center])
Czurda 2010; Austria; 2003-2005	411	26 mos (mean)	66.4% (273/411)	19.7% (81/411)	13.9% (57/411)	(57 + 11)/411 = 16.5%	Low (downgrade due to moderate loss to follow-up and not multiple center study [single center])
Wylde 2011; UK; 2004-2006	1,394	41 mos (median)	31.1% (433/1,394)	54.7% (762/1,394)	14.3% (199/1,394)	(199 + 109)/1,394 = 22.1%	Low (downgrade due to high loss to follow-up and not multiple center study [single center])
Brander 2003; USA; 1998-2000	116	12 mos	84.5% (98/116)	2.6% (3/116)	12.9% (15/116)	(15 + 0)/116 = 12.9% (95% CI 8.0% to 20.2%)	Moderate (downgrade due to not multiple center study [single center])

N = Sample size of cohort, mos = months

* favorable outcome includes patients with no pain or mild pain at follow-up

† uncertain outcome includes "...all patients for whom we cannot be sure of their pain levels at follow-up. These include patients who died, had revision surgery, contralateral surgery or dislocation and were not followed up with questionnaires and those lost to follow-up. We also included as uncertain those patients with a degree of reported pain, which we could not classify as a favorable or unfavorable outcome"

‡ unfavorable outcome includes those with moderate-to-severe pain or for whom surgery had not relieved pain

§ proportion with unfavorable long-term pain outcome without imputing outcome information on patients lost to follow-up

** imputing proportion with known unfavorable long-term pain outcome to number with uncertain pain outcome

DI LAURA FRATTURA 2018
di Laura Frattura G, Filardo G, Giunchi D, Fusco A, Zaffagnini S, Candrian C. Risk of falls in patients with knee osteoarthritis undergoing total knee arthroplasty: A systematic review and best evidence synthesis. J Orthop. 2018 Aug 24;15(3):903-908. PubMed

Relevant to FAQ5

- **Study design:** systematic review of observational studies
- **Population:** knee osteoarthritis patients having total knee arthroplasty
- **Intervention:** total knee arthroplasty
    - the other systematic review summarized for the falls outcome (Lo 2019) included studies of patients having total knee arthroplasty and/or total hip arthroplasty
- **Comparison:** not applicable

- **Study inclusion criteria:** clinical reports on occurrence of falls in knee osteoarthritis patients having total knee arthroplasty
    - written in English language
    - falls defined as "unintentionally coming to rest on the ground, or at some other lower level, and not the result of a major intrinsic event such as a faint, stroke, or seizure, nor of an overwhelming external hazard such as a hit by a vehicle"
    - inclusion criteria did not require that the study assess or report pre-TKA falls prevalence, post-TKA falls prevalence, or risk factors
        - in contrast, the other systematic review that we summarized for the falls outcome (Lo 2019) only included studies "that assessed risk factors for post-operative falls" which explains why some studies (eg, Webster 2006, Swinkels 2013) included in di Laura Frattura 2018 are not included in Lo 2019 (because they did not assess risk factors, as indicated in Table 1 of di Laura Frattura 2018)
- **Number of studies:** 11
- **Number of participants:** 1,237
- **Duration of follow-up**: 12 months in 6 studies; 108 months in study with longest follow-up

- **Results**
    - fall rate was quantified in 10 out of 11 studies
        - pre-operative prevalence ranged from 23% to 63% among the 8 studies that reported it
        - post-operative prevalence among 4 studies that reported it was 12%, 17%, 22%, and 38%
        - 1 study did not report either pre-operative or post-operative prevalence
        - Because our question of interest is whether getting total knee replacement increases or decreases the fall rate beyond that due to the patients' severe OA, the only relevant studies that can address that question are the 3 studies that reported both pre-operative and post-operative prevalence of falls
            - findings of 3 studies that reported pre-operative and post-operative prevalence of falls
                - Swinkels 2009 (n = 188, 12-month follow-up): 24% pre-operative, 12% post-operative

        - Swinkels 2013 (n = 22, 9-month follow-up): 23% pre-operative, 17% post-operative
        - Tsonga 2016 (n = 68, 12-month follow-up): 63% pre-operative, 22% post-operative
    - only 1 (Swinkels 2009) found statistical correlation between surgery and changes in falls rate
        - 41% of patients considered 'fallers' stopped falling after surgery
        - 10% of 'non-fallers' became 'frequent-fallers' after surgery
    - it was assumed from context, though not explicitly stated in systematic review report, that the other 2 studies did not find a statistical correlation between surgery and changes in falls rate
- **Certainty: Very low**
    - **Certainty by outcome:** not applicable – pre vs. post-operative falls rate is only relevant outcome
    - **Risk of bias:** very serious concern (if attempting to make comparative evidence statements)
        - pre-post study design for comparative evidence statements
        - possible selective outcome reporting bias due to only 3 of 11 studies reporting both pre- and post-operative fall rate
        - it is not clear if the pre- and post- surgery fall rates can be directly compared because publication does not state that the durations of the preop and postop evaluation periods were identical
    - **Imprecision:** serious concern
        - limiting to studies that reported pre- and post-operative fall prevalence, range of pre-operative fall prevalence is 23% to 63%, and range of post-operative falls is 12% to 22%. Risk differences range from 6% to 41%.
    - **Indirectness:** no serious concern
    - **Inconsistency:** serious concern (same downgrade as for 'imprecision' and only counted once when assessing overall certainty)
        - limiting to studies that reported pre- and post-operative fall prevalence, range of pre-operative fall prevalence is 23% to 63%, and range of post-operative falls is 12% to 22%. Risk differences range from 6% to 41%.

LO 2019

Lo CWT, Tsang WWN, Yan CH, Lord SR, Hill KD, Wong AYL. Risk factors for falls in patients with total hip arthroplasty and total knee arthroplasty: a systematic review and meta-analysis. Osteoarthritis Cartilage. 2019 Apr 24. pii: S1063-4584(19)30928-8. PubMed

Relevant to FAQ5

- **Study design:** systematic review of observational studies
- **Population:** patients who had total knee arthroplasty or total hip arthroplasty
    - unilateral or bilateral for both
    - primary or revision for both
- **Intervention:** total knee arthroplasty or total hip arthroplasty
- **Comparison:** not applicable

- **Study inclusion criteria:** any study design that assessed risk factors for postop falls among patients having total knee arthroplasty or total hip arthroplasty
    - in contrast to the other systematic review that we summarized for the falls outcome (di Laura Frattura 2018), Lo 2019 only included studies "that assessed risk factors for post-operative falls" which explains why some studies (eg, Webster 2006, Swinkels 2013) included in di Laura Frattura 2018 are not included in Lo 2019

- **Number of studies:** 12
- **Number of participants:** 1,292,689
    - 1 study included 1.1 million patients
    - median number of patients per study was 295
- **Duration of follow-up:** up to 24 months after discharge

- **Results:**
    - post-total knee replacement fall incidence rates by time after surgery
        - within several days after surgery (inpatient) in 3 studies: 0.8% (this study included both knee and hip replacement patients), 1.6%, and 2.7%
        - within first month after discharge: 51.8% (this study included both knee and hip replacement patients)
        - within 12 months after discharge: 6.2%, 22.1%, 24.2%, 26.1% (this study included both knee and hip replacement patients), 38.2%, 42.6%
        - 6-18 months after discharge 32.9%
        - 12-24 months after discharge 3.1%
- **Certainty:**
    - **Certainty by outcome:**
        - inpatient fall rate – High certainty
        - fall rate up to 24 months after discharge – Very low certainty
    - **Risk of bias:** no serious concern
    - **Imprecision:**
        - inpatient fall rate – no serious concern
            - estimates were comparable, ranging from 0.8% to 2.7%
        - fall rate up to 24 months after discharge – very serious concern
            - post-operative prevalence of fall rates ranged from 3.1% to 42.6%
    - **Indirectness:**
        - inpatient fall rate – no serious concern
        - fall rate up to 24 months after discharge – serious concern
            - postoperative fall rate estimates reported for long period of follow-up time for given studies (with possible exception of study that reported rate "within first month after discharge") but the rate may differ at different time points
    - **Inconsistency:**
        - inpatient fall rate – no serious concern
        - fall rate up to 24 months after discharge – very serious concern
            - very serious concern (same downgrade as for 'imprecision' and only counted once when assessing overall certainty)
            - post-operative prevalence of fall rates ranged from 3.1% to 42.6%
- **Other considerations**: After this summary had been prepared, it had been pointed out that our primary question of interest is whether getting total knee replacement increases or decreases

the fall rate beyond that attributable to the patients' severe OA and that the only relevant studies that can address that question are those that reported both pre-operative and post-operative fall rates. Because this systematic review reported only post-operative fall rates, it was determined post hoc that it did not meet our eligibility criteria for this question and was considered unusable.

RICHARDSON 2019

Richardson SS, Schairer WW, Sculco TP, Sculco PK. Comparison of Infection Risk with Corticosteroid or Hyaluronic Acid Injection Prior to Total Knee Arthroplasty. J Bone Joint Surg Am. 2019 Jan 16;101(2):112-118. PubMed

Relevant to FAQ5

- **Study design:** observational study
- **Population:** patients having unilateral primary total knee arthroplasty selected from a United States nationwide private insurer database
- **Intervention:** total knee replacement
- **Comparison:** not applicable
    - although the overall purpose of this study was to compare periprosthetic joint infection between patients who received injections in prior year (corticosteroid or hyaluronic acid) and patients who had received no injection, we used this study to extract estimates for periprosthetic joint infection overall

- **Study inclusion criteria:**
    - patients who got both corticosteroid injections and hyaluronic injections ≤ 1 year before surgery were excluded

- **Number of studies:** not applicable
- **Number of participants:** 58,337
    - 3,249 (5.6%) received hyaluronic acid injections ≤ 1 year before surgery
    - 16,656 (28.6%) patients received corticosteroid injections ≤ 1 year before surgery
    - 38,432 (65.9%) received no injection
- **Duration of follow-up:** 6 months after surgery

- **Results and Certainty:**
    - risk of periprosthetic joint infection within 6 months after total knee arthroplasty (based on either diagnosis or related procedure)
        - 2.83% (1,649/58,337; 95% CI 2.70% to 2.96%) among total population
        - 2.74% (1,052/38,432; 95% CI 2.58% to 2.91%) among no-injection group
        - Moderate certainty of evidence
            - Downgraded for indirectness because 6-month follow-up will lead to important underestimation of deep infection incidence rates (only about 1/3 of which occur within 3 months and only about 2/3 of which occur within 2 years after index operation)

SKOU 2015
Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, Rasmussen S. A Randomized, Controlled Trial of Total Knee Replacement. N Engl J Med. 2015 Oct 22;373(17):1597-606. Erratum in: BMJ. 2019 Apr 2;365:l1032. PubMed

Relevant to FAQ2, FAQ3, FAQ4, FAQ5

- **Study design:** randomized trial
- **Population:** patients with moderate-to-severe knee osteoarthritis judged eligible for unilateral total knee replacement
    - eligibility determined by orthopedic surgeons at participating clinics
- **Intervention:** total knee replacement followed by 12 weeks of multimodal nonsurgical treatment
- **Comparison:** 12 weeks of multimodal nonsurgical treatment alone
    - delivered by physiotherapists and dietitians
    - consisted of exercise, education, dietary advice, use of insoles, and pain medication
    - consistent with international recommendations

- **Study inclusion criteria:** patients with any of following not included ("major exclusion criteria")
    - previous total replacement of same knee
    - need for bilateral total knee replacement
    - knee pain during previous week that patient rated > 60 mm on 100-mm visual-analogue scale

- **Number of studies:** 1
- **Number of participants:** 100
    - 100 is number randomized
- **Duration of follow-up:** 1 year

Improvements of ≥ 15% in $KOOS_4$ score and KOOS subscale scores from baseline to 1 year

Outcome*	Percentage with improvement of ≥ 15% in TKR group (95% CI)	Proportion with improvement of ≥ 15% in non-surgical group (95% CI)	Difference between groups in proportion with improvement of ≥ 15% (95% CI)**	Certainty (with reasons for downgrade)***
$KOOS_4$	85% (71% to 93%)	67% (53% to 79%)	17.4% (0.1% to 33.4%)	Low (risk of bias, imprecision)
KOOS subscale scores				
Pain	83% (69% to 91%)	69% (55% to 81%)	13.2% (-4.1% to 29.4%)	Low (risk of bias, imprecision)

Symptoms	85% (71% to 93%)	45% (31% to 59%)	39.9% (20.9% to 55.0%)	Moderate (risk of bias)
Quality of life	89% (76% to 96%)	69% (55% to 81%)	19.7% (3.3% to 35.0%)	Moderate (risk of bias)
Activities of daily living	89% (76% to 96%)	59% (45% to 72%)	29.9% (12.4% to 45.2%)	Moderate (risk of bias)
Sports and recreation	89% (76% to 96%)	65% (51% to 77%)	23.8% (6.9% to 39.1%)	Moderate (risk of bias)

CI, confidence interval; KOOS = Knee Injury and Osteoarthritis Outcome Score; $KOOS_4$ = summary score comprised of 4 of the 5 KOOS subscale scores (all except Sports and recreation); TKR, total knee replacement

* Based on the 46 patients in the TKR group and 49 patients in the nonsurgical group who had data available for the 12-month follow-up point

** The authors report the number needed to treat to benefit one additional person (NNTB), and although the reciprocal of the NNTB would provide the absolute risk difference, the authors appear to have used a traditional method for calculating the CI that is not as reliable as the recommended method, which has better statistical properties and can be used with any data; we therefore use the recommended approach for calculating the CI (see, for instance, Altman 2000).

*** All outcomes were downgraded for risk of bias because of lack of blinding. Although 13 patients (26%) in nonsurgical group got TKR before 1 year, we did not apply an additional risk of bias downgrade for this crossover because this amount of crossover is relatively low for a surgical trial and because the results from the per-protocol analyses at 1 year were largely consistent with those of intention-to-treat analyses (see below).

- rate of crossover from conservative therapy to total knee replacement plus conservative therapy: 13/50 (26%; 95% CI 15.9% to 39.6%)
    - Low certainty, downgrade for very serious concerns about imprecision (estimates are based on a sample of 50 people)
- use of pain medication at 1 year (any kind, on regular basis, during previous week)
    - 41% (95% CI 28% to 55%) in nonsurgical group
    - 26% (95% CI 15% to 41%) in TKR + nonsurgical group
    - difference in proportion 14.7% (95% CI -4.2% to 32.2%)
    - adjusted RR 1.57 (95% CI 0.87 to 2.85)
    - certainty downgrades for risk of bias (no blinding) and imprecision
- weight change at 1 year
    - -2.6 kg (95% CI -3.9 kg to -1.4 kg) in nonsurgical group
    - 0.1 kg (95% CI -1.5 kg to 1.7 kg) in TKR + nonsurgical group
    - difference in mean change 2.8 kg (95% CI 1.4 kg to 4.1 kg)
        - identical results for crude and adjusted analyses
    - analysis includes only patients with a body-mass index of $\geq$ 25 at baseline (43 patients in nonsurgical-treatment group and 39 patients in TKR group)
    - certainty downgrade for risk of bias (no blinding)
- serious adverse events involving index knee during 1-year study period in as-treated analysis
    - serious adverse events defined as those that
        - have the potential to compromise clinical outcome, result in disability or incapacity, or require hospital care
        - are considered to prolong hospital care, be life-threatening, or result in death
    - as-treated analysis included 49 patients who received TKR in treatment group and 13 patients who received TKA in control group
    - serious adverse events that occurred after TKR in as-treated population
        - stiffness requiring brisement forcé (manipulation of knee while patient is under anesthesia to improve range of motion) in 6.5% (4/62)

        - deep infection in 1.6% (1/62)
        - deep venous thrombosis requiring anticoagulation in 4.8% (3/62)
        - supracondylar femur fracture in 1.6% (1/62)
    - no serious adverse events occurred during TKR
    - certainty downgrades for imprecision (two downgrades due to very serious concern) for each serious adverse event listed above
- generally consistent results with per-protocol analyses
    - criteria for inclusion/exclusion
        - included patients in both groups who had attended > 75% of supervised exercise sessions
        - excluded patients
            - in nonsurgical group who underwent TKR by 12 months (n = 13)
            - in TKR group who received only nonsurgical treatment (n = 1)
    - included 25 of 49 patients in nonsurgical group (51%) and 26 of 46 patients in TKR group (57%)

SKOU 2018

Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Rasmussen S, Simonsen O. Total knee replacement and non-surgical treatment of knee osteoarthritis: 2-year outcome from two parallel randomized controlled trials. Osteoarthritis Cartilage. 2018 Sep;26(9):1170-1180. PubMed

Relevant to FAQ2, FAQ3, FAQ4, FAQ5

- **Study design:** randomized trial
    - this publication reported two-year results of two different trials, 1 of which was the Skou 2015 trial comparing addition of TKR to nonsurgical treatment alone in patients eligible for TKR
    - data specific to the 2-year results of the Skou 2015 trial could be extracted for this summary because results of the 2 trials were reported separately
- **Population:** patients with moderate-to-severe knee osteoarthritis judged eligible for unilateral total knee replacement
    - eligibility determined by orthopedic surgeons at participating clinics
- **Intervention:** total knee replacement followed by 12 weeks of multimodal nonsurgical treatment
- **Comparison:** 12 weeks of multimodal nonsurgical treatment alone
    - delivered by physiotherapists and dietitians
    - consisted of exercise, education, dietary advice, use of insoles, and pain medication
    - consistent with international recommendations

- **Study inclusion criteria:** patients with any of following not included ("major exclusion criteria")
    - previous total replacement of same knee
    - need for bilateral total knee replacement
    - knee pain during previous week that patient rated > 60 mm on 100-mm visual-analogue scale

- **Number of studies:** 1
- **Number of participants:** 100

- 100 is number randomized

- **Duration of follow-up:** 2 years

Improvements of ≥ 15% in $KOOS_4$ score and KOOS subscale scores from baseline to 2 years

Outcome*	Percentage with improvement of ≥ 15% in TKR + nonsurgical group (95% CI)	Proportion with improvement of ≥ 15% in non-surgical group (95% CI)	Difference between groups in proportion with improvement of ≥ 15% (95% CI)**	Certainty (with reasons for downgrade)***
$KOOS_4$	86% (72% to 94%)	64% (49% to 76%)	22.2% (4.2% to 38.3%)	Moderate (risk of bias)
KOOS subscale scores				
Pain	84% (69% to 92%)	70% (55% to 82%)	13.5% (-4.1% to 29.9%)	Low (risk of bias, imprecision)
Symptoms	79% (64% to 89%)	55% (41% to 69%)	23.8% (4.3% to 40.7%)	Moderate (risk of bias)
Quality of life	88% (74% to 95%)	66% (51% to 78%)	22.4% (4.9% to 38.1%)	Moderate (risk of bias)
Activities of daily living	81% (67% to 91%)	64% (49% to 76%)	17.6% (-1.0% to 34.4%)	Low (risk of bias, imprecision)
Sports and recreation	93% (80% to 98%)	66% (51% to 78%)	27.1% (10.4% to 42.1%)	Moderate (risk of bias)

CI, confidence interval; KOOS = Knee Injury and Osteoarthritis Outcome Score; $KOOS_4$ = summary score comprised of 4 of the 5 KOOS subscale scores (all except Sports and recreation); TKR, total knee replacement

* Based on the 43 patients in the TKR+nonsurgical group and 47 patients in the nonsurgical group who had data available for the 12-month follow-up point

** The authors report the number needed to treat to benefit one additional person (NNTB), and although the reciprocal of the NNTB would provide the absolute risk difference, the authors appear to have used a traditional method for calculating the CI that is not as reliable as the recommended method, which has better statistical properties and can be used with any data; we therefore use the recommended approach for calculating the CI (see, for instance, Altman 2000).

*** All outcomes were downgraded for risk of bias because of lack of blinding. Although 16 patients (32%) in nonsurgical group got TKR before 2 years, we did not apply an additional risk of bias downgrade for this crossover because this amount of crossover is relatively low for a surgical trial and because the 1-year results from the per-protocol analyses were largely consistent with those of intention-to-treat analyses.

- rate of crossover from conservative therapy to total knee replacement plus conservative therapy: 16/50 (32%; 95% CI 20.8% to 45.8%)
  - Low certainty, downgrade for very serious concerns about imprecision (estimates are based on a sample of 50 people)
- use of pain medication at 2 years (any kind, on regular basis, during previous week)
  - 49% (95% CI 35% to 63%) in nonsurgical group
  - 26% (95% CI 15% to 41%) in TKR + nonsurgical group
  - difference in proportions 23.4% (95% CI 3.3% to 40.8%)
  - RR 1.91 (95% CI 1.06 to 3.44)
  - Certainty downgrade for risk of bias (no blinding)

- weight change at 2 years
    - -2.2 kg (95% CI -3.5 kg to -0.8 kg) in nonsurgical group
    - 2.7 kg (95% CI -2.9 kg to 8.2 kg) in TKR + nonsurgical group
    - difference in mean change 4.8 kg (95% CI 2.2 kg to 7.5 kg)
    - analysis includes only patients with a body-mass index of ≥ 25 at baseline (43 patients in nonsurgical-treatment group and 39 patients in TKR group)
    - certainty downgrade for risk of bias (no blinding)
- serious adverse events involving index knee during 2-year study period in as-treated analysis
    - serious adverse events that occurred after TKR in as-treated population
        - stiffness requiring brisement forcé (manipulation of knee while patient is under anesthesia to improve range of motion) in 6.5% (4/62)
        - deep infection in 1.6% (1/62)
            - patient had three revision surgeries and ended up with prosthesis being removed and knee fused because of deep infection
        - deep venous thrombosis requiring anticoagulation in 4.8% (3/62)
    - certainty downgrades for imprecision (two downgrades due to very serious concern) for each serious adverse event listed above
    - differences in reporting of serious adverse events from Skou 2015 publication
        - Skou 2018 publication did not report the supracondylar femur fracture in 1 patient that was reported in Skou 2015 publication Table 3
        - Skou 2018 publication reported additional details about patient with deep infection that were not reported in Skou 2015 publication
- no per-protocol analyses are reported

WILSON 2019

Wilson HA, Middleton R, Abram SGF, Smith S, Alvand A, Jackson WF, Bottomley N, Hopewell S, Price AJ. Patient relevant outcomes of unicompartmental versus total knee replacement: systematic review and meta-analysis. BMJ. 2019 Feb 21;364:l352. PubMed

Relevant to FAQ4, FAQ5

- **Study design:** systematic review of randomized trials and observational studies
- **Population:** patients having total knee replacement
    - the overall purpose of this systematic review was to compare primary total knee replacement to unicompartmental knee replacement, but only total knee replacement data extracted for this summary (see “Comparison:”, below)
- **Intervention:** primary total knee replacement
    - the overall purpose of this systematic review was to compare primary total knee replacement to unicompartmental knee replacement, but only total knee replacement data extracted for this summary (see “Comparison:”, below)
- **Comparison:** not applicable
    - although the overall purpose of this systematic review was to compare outcomes between patients who received total knee replacement or unicompartmental knee replacement, we used it to extract univariate estimates for patients having total knee replacement

- **Study inclusion criteria:**

- studies published since 1997 (to focus on studies involving modern implants)
- comparing outcomes of primary total knee replacement vs. unicompartmental knee replacement in adults
- ≥ 50 patients
- follow-up of ≥ 30 days if assessing adverse event or ≥ 6 months if assessing outcome data

- **Number of studies:** 60
  - studies were divided into following three groups with separate analyses reported for each (and no analysis reported pooling all 3 groups)
    - group 1 - 5 randomized trials
    - group 2 - 12 national joint registries and national database studies
    - group 3 - 36 cohort studies
  - we restricted to group 2 studies because this group included the largest numbers of patients and therefore had greater power to estimate rate of rare adverse events (eg, mortality)
- **Number of participants:** not reported
- **Duration of follow-up:** > 30 days if assessing adverse event or > 6 months if assessing outcome data

- **Results and certainty:**

Outcome	Number of studies (TKA procedures)	Pooled incidence (95% CI)*	Certainty (downgrades)
Venous thromboembolic event†	5 (228,499)	1.23% (95% CI 0.76% to 1.82%)	High
45-day mortality	6 (696,356)	0.16% (95% CI 0.03% to 0.38%)	High
Deep infection‡	6 (250,533)	0.79% (95% CI 0.36% to 1.38%)	Moderate (indirectness§)
5-year revision	2 (149,016)	3.16% (95% CI 2.23% to 4.25%)	High
10-year revision	7 (203,212)	4.58% (95% CI 3.16% to 6.25%)	High
15-year revision	2 (132,118)	7.22% (95% CI 1.77% to 15.94%)	Moderate (inconsistency¶)

* We extracted the univariate incidence of the TKA group from each study (from forest plots comparing TKA vs. UKA) and used these to calculate a pooled incidence for each outcome (arcsine transformation with Sidik-Jonkman/Hartung-Knapp-Sidik-Jonkman (HKSJ) random effects model; use of Freeman-Turkey transformation instead of arcsine transformation yielded comparable estimates, as did use of DerSimonian-Laird random effects model instead of HKSJ random effects model).
† Follow-up time not reported, although for eligibility for inclusion in systematic review studies needed to have a follow-up of ≥ 30 days if assessing adverse event, so we did not downgrade the venous thromboembolic event outcome, because the included studies should have had sufficient follow-up period to capture venous thromboembolic events (see, for instance, Bjørnaŕ 2006 which reports that median time to presentation of DVT and PE was 20 and 12 days respectively).
‡ Classified by authors as infection that requires further intervention (ie, either revision, reoperation [debridement and implant retention], or long-term suppressive antibiotics). The follow-up time for deep infection was not specified, although for eligibility for inclusion in systematic review studies needed to have a follow-up of ≥ 30 days if assessing adverse event. Deep infection was classified under the broader outcome category 'early complications' suggesting that it does not include deep infections that occurred later.

§ Downgraded for indirectness because potential for suboptimal completeness of follow-up may lead to underestimation of deep infection incidence rates. The duration of follow-up for this outcome was not reported; however, it was grouped under broader outcome heading ‘early complications’ in Methods section, suggesting it does not include deep infections that occur in the longer-term. As noted by Jämsen 2010, about 1/3 of deep infections occur within 3 months and 2/3 within 2 years after index operation. Jämsen 2010 also makes note of the possibility that even prospective monitoring of infection may still underestimate the true risk. Considering all of this, we downgraded once.
¶ Of the 2 sources contributing to this outcome, one reported a 4.0% rate of revision and the other reported a 11.3% rate of revision.

Evidence report for total knee replacement plus conservative therapy versus conservative therapy alone for knee osteoarthritis

Part 4 - Evidence Review

Prepared by EBSCO Information Services

May 21, 2019

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Methods

For each FAQ, the key concepts (results and factors affecting certainty of the results) from the included studies that are most relevant to evidence synthesis will be summarized in Evidence Review Tables. Where evidence is very limited, or the FAQ is for descriptive summary, summary text will be provided.

Results

FAQ 1: What does the treatment involve?

Total knee replacement plus conservative therapy

Descriptive Summary

Total knee replacement (also called knee replacement surgery or total knee arthroplasty) for osteoarthritis is usually only offered to people who have not had satisfactory relief from symptoms with conservative therapy. In total knee replacement, the damaged portion of the knee joint is removed, and an artificial joint is put in its place.

A person may either be put to sleep during the operation or have an injection in the spine that numbs the lower half of the body. If the injection in the spine is used, it may be combined with sedation.

The surgeon will make a cut over the knee to allow access to the area where the surgery is performed. The cut is often about 6 to 10 inches (15 to 25 centimeters). The kneecap (patella) is moved to the side to allow the surgeon to get to the knee joint. The damaged portions of the knee joint are removed, and the artificial joint is inserted. The surgery usually lasts about 2 hours.

There is a newer method for performing total knee replacement that makes smaller cuts – about 4 to 5 inches (10 to 12 centimeters) – but this may not be available at all hospitals or performed by all surgeons.

People may be in the hospital for about 3 to 5 days, but this depends on the individual.

For a period of time after the surgery, patients are usually given medication to prevent blood clots, though recommendations are not entirely consistent. After the surgery, patients will initially walk with an assistive device (e.g., walker, crutches), and they will progressively increase the amount of weight they put on the leg with the artificial knee. Attending / performing prescribed physical therapy and exercises is very important for recovery, including after being discharged from the hospital. Some patients go to a rehabilitation facility for a short period to help ensure they stay on track with recovery. In general, assuming recovery is going well, people are often able to return to many of their normal daily activities within 3 to 6 weeks, but people may be advised to avoid any heavier tasks for up to 3 months. They may also be advised to avoid tasks that require standing for prolonged periods or bending for the first 6 weeks. Additional recovery information is provided in FAQ 7 (How long does it take to recover?).

(Cram 2012, DynaMed 2018, Foran 2015, NHS 2016, NICE 2010, NIH 2018, Mayo Clinic 2017)

Conservative therapy alone

Descriptive Summary

Non-surgical treatment for osteoarthritis of the knee may involve a number of different treatments, which should be tailored to the individual. According to the Overview and Recommendations – Management section of the DynaMed Plus topic Osteoarthritis (OA) of the knee (DynaMed Plus 2018), treatment may involve either non-pharmacologic or pharmacologic options, such as:

- Exercise therapy (including physical therapy) and weight loss (if indicated) are the mainstays of nonsurgical management of symptomatic knee OA.
  - Self-management programs are recommended for patients with knee OA (Strong recommendation); primary components of self-management programs include patient education, weight management, exercise, use of assistive/adaptive devices, and appropriate footwear.
    - Weight loss is recommended for patients with BMI ≥ 25 kg/m^2 (Strong recommendation).
    - Patients should participate in a regular (daily) exercise program (matching his or her ability) (Strong recommendation).
    - Consider the use of walking aids, assistive technology, and adaptations at home and/or work to reduce pain and increase participation in daily activities (Weak recommendation).
    - A walking cane should be used on the contralateral side.
  - Primary goals of physical therapy are improved pain, function, and joint stability.
    - Patients should receive individualized therapeutic exercise programs, with primary components including (Strong recommendation):
      - strengthening exercise
      - low-impact aerobic exercise
      - neuromuscular reeducation
      - adjunctive range of motion and stretching exercises
    - Prescribe land-based or aquatic-based therapy according to patient ability level/tolerance, preference, and local facility availability (Strong recommendation).
    - Consider adjunctive rehabilitation components, including:
      - physical modalities such as ice or heat therapy, therapeutic ultrasound, or electrical stimulation (such as transcutaneous electrical nerve stimulation [TENS] or neuromuscular electrical stimulation [NMES])
      - manual therapy (Weak recommendation)
      - nonelastic therapeutic knee taping (also called Leukotaping, McConnell taping, and patellar taping) (in patients with patellofemoral OA) (Weak recommendation)
      - valgus knee braces (in patients with medial knee OA)
    - Do not prescribe lateral wedge insoles for patients with symptomatic medial compartmental knee OA (Strong recommendation).
- Pharmacologic agents
  - In patients for whom nonpharmacologic treatments are not effective, consider acetaminophen (up to 4 g/day), a topical nonsteroidal anti-inflammatory drug (NSAID) (such as diclofenac or ketoprofen), or an oral NSAID (Weak recommendation).
  - In patients ≥ 75 years old or patients at risk for adverse effects from oral NSAIDs, use a topical NSAID such as diclofenac or ketoprofen (Strong recommendation) or consider acetaminophen (Weak recommendation).
  - Consider adding acetaminophen to NSAID treatment for symptom control.
  - Consider corticosteroid injections in patients with a knee OA flare (joint inflammation and effusion) (Weak recommendation).

- In patients with inadequate response to first-line pharmacologic agents, consider tramadol or duloxetine (Weak recommendation).
- Consider nontramadol opioids only in patients without any other medical or surgical options, and persistent symptoms (Weak recommendation).
- Consider hyaluronic acid injections (viscosupplementation) only in patients with less advanced OA who do not respond to other treatments (Weak recommendation) and who are < 65 years old.

The spread of conservative therapies noted above is broadly consistent with the composite of conservative therapies used in the randomized trial comparing total knee replacement plus conservative care vs. conservative care alone (Skou 2015, Skou 2018).

Patients who receive an injection may be advised to rest/avoid strain on the knee for a day or two after the injection (Mayo Clinic 2017, Mayo Clinic 2019).

FAQ 2: Will I feel better?

Effects of knee replacement surgery on patient symptoms can be evaluated in a randomized trial by comparing proportion of patients who improve with getting surgery vs. with not getting surgery. It can also be evaluated in a cohort study (or systematic review of these) as the proportion of patients who have an unfavorable long-term pain outcome following knee surgery. The effects of each of these evaluations are summarized separately below.

Total knee replacement (followed by conservative non-surgical therapy) vs conservative (non-surgical) therapy alone

Evidence Review Table and Descriptive Evidence Review

Only one randomized trial has compared total knee replacement vs. nonsurgical therapy alone (Skou 2015 and 2018). This trial compared unilateral total knee replacement followed by 12 weeks of guideline-based, multimodal nonsurgical treatment (including exercise, education, dietary advice, use of insoles, and pain medication) vs. 12 weeks of guideline-based, multimodal nonsurgical treatment alone in 100 patients with moderate-to-severe knee osteoarthritis. Outcomes reported included the proportion of patients in each group with improvement of ≥ 15% on pain, symptoms, activities of daily living, and quality of life and proportion using pain medications, at 1-year (Skou 2015) and 2-year (Skou 2018) follow-up times.

Skou 2015 - 1-year results

Improvements of ≥ 15% in $KOOS_4$ score and KOOS subscale scores from baseline to 1 year

Outcome*	Percentage with improvement of ≥ 15% in TKR group (95% CI)	Proportion with improvement of ≥ 15% in non-surgical group (95% CI)	Difference between groups in proportion with improvement of ≥ 15% (95% CI)	Certainty (with reasons for downgrade)**
$KOOS_4$	85% (71% to 93%)	67% (53% to 79%)	17.4% (0.1% to 33.4%)	Low (risk of bias, imprecision)
KOOS subscale scores				
Pain	83% (69% to 91%)	69% (55% to 81%)	13.2% (-4.1% to 29.4%)	Low (risk of bias, imprecision)
Symptoms	85% (71% to 93%)	45% (31% to 59%)	39.9% (20.9% to 55.0%)	Moderate (risk of bias)
Quality of life	89% (76% to 96%)	69% (55% to 81%)	19.7% (3.3% to 35.0%)	Moderate (risk of bias)
Activities of daily living	89% (76% to 96%)	59% (45% to 72%)	29.9% (12.4% to 45.2%)	Moderate (risk of bias)
Sports and recreation	89% (76% to 96%)	65% (51% to 77%)	23.8% (6.9% to 39.1%)	Moderate (risk of bias)

CI, confidence interval; KOOS = Knee Injury and Osteoarthritis Outcome Score; $KOOS_4$ = summary score comprised of 4 of the 5 KOOS subscale scores (all except Sports and recreation); TKR, total knee replacement

* Based on the 46 patients in the TKR group and 49 patients in the nonsurgical group who had data available for the 12-month follow-up point

** All outcomes were downgraded for risk of bias because of lack of blinding. Although 13 patients (26%) in nonsurgical group got TKR before 1 year, we did not apply an additional risk of bias downgrade for this crossover because this amount of crossover is relatively low for a surgical trial and because the results from the per-protocol analyses at 1 year were largely consistent with those of intention-to-treat analyses.

- **use of pain medication at 1 year (any kind, on regular basis, during previous week)**
  - 41% (95% CI 28% to 55%) in nonsurgical group
  - 26% (95% CI 15% to 41%) in TKR + nonsurgical group
  - difference in proportion 14.7% (95% CI -4.2% to 32.2%)
  - adjusted RR 1.57 (95% CI 0.87 to 2.85)
  - certainty downgrades for risk of bias (no blinding) and imprecision

Skou 2015 - 2-year results

Improvements of ≥ 15% in $KOOS_4$ score and KOOS subscale scores from baseline to 2 years

Outcome*	Percentage with improvement of ≥ 15% in TKR + nonsurgical group (95% CI)	Proportion with improvement of ≥ 15% in non-surgical group (95% CI)	Difference between groups in proportion with improvement of ≥ 15% (95% CI)	Certainty (with reasons for downgrade)**
$KOOS_4$	86% (72% to 94%)	64% (49% to 76%)	22.2% (4.2% to 38.3%)	Moderate (risk of bias)
KOOS subscale scores				
Pain	84% (69% to 92%)	70% (55% to 82%)	13.5% (-4.1% to 29.9%)	Low (risk of bias, imprecision)
Symptoms	79% (64% to 89%)	55% (41% to 69%)	23.8% (4.3% to 40.7%)	Moderate (risk of bias)
Quality of life	88% (74% to 95%)	66% (51% to 78%)	22.4% (4.9% to 38.1%)	Moderate (risk of bias)
Activities of daily living	81% (67% to 91%)	64% (49% to 76%)	17.6% (-1.0% to 34.4%)	Low (risk of bias, imprecision)
Sports and recreation	93% (80% to 98%)	66% (51% to 78%)	27.1% (10.4% to 42.1%)	Moderate (risk of bias)

CI, confidence interval; KOOS = Knee Injury and Osteoarthritis Outcome Score; $KOOS_4$ = summary score comprised of 4 of the 5 KOOS subscale scores (all except Sports and recreation); TKR, total knee replacement

* Based on the 43 patients in the TKR+nonsurgical group and 47 patients in the nonsurgical group who had data available for the 12-month follow-up point

** All outcomes were downgraded for risk of bias because of lack of blinding. Although 16 patients (32%) in nonsurgical group got TKR before 2 years, we did not apply an additional risk of bias downgrade for this crossover because this amount of crossover is relatively low for a surgical trial and because the 1-year results from the per-protocol analyses were largely consistent with those of intention-to-treat analyses.

- **use of pain medication at 2 years (any kind, on regular basis, during previous week)**
  - 49% (95% CI 35% to 63%) in nonsurgical group
  - 26% (95% CI 15% to 41%) in TKR + nonsurgical group
  - difference in proportions 23.4% (95% CI 3.3% to 40.8%)
  - RR 1.91 (95% CI 1.06 to 3.44)
  - certainty downgrades for risk of bias (no blinding) and imprecision

Total knee replacement

Evidence Review Table

A systematic review of observational studies in patients with primary total hip or knee replacement has reported results classifiable as proportion of patients with unfavorable pain outcome at follow-up from 3 months to 5 years (Beswick 2012). Among the 11 studies of total knee replacement included in this systematic review, only 1 study met both of review authors' two indicators of quality (ie, conducted at multiple centers, low loss to follow-up [< 10%]) and was thus judged High quality by the review authors. In this study, the proportion of patients with an unfavorable outcome was 19.5% (imputing proportion with known unfavorable long-term pain outcome to number with uncertain pain outcome). This proportion was comparable to the corresponding proportions in 5 other studies that were judged Moderate quality by the review authors, and it was also close to the median of these 5 studies (ie, 10.2%, 12.9%, 17.6%, 19.3%, 31.2%). The single High certainty study in Beswick 2012 only provides an estimate at the 6-month follow-up point; the 5 Moderate certainty studies provide estimates at 6 months (2 studies), 12 months (2 studies; 1 technically being 12 months or latest follow-up), and 36 months (1 study). The outcome of an unfavorable outcome at 6 months post-operatively is not necessarily the same as the outcome of an unfavorable outcome at 12 or 36 months post-operatively, and estimates for these additional timepoints are of value to patients. Therefore, in the table below, we include: the 6-month estimate from the 1 High certainty study (given a higher certainty estimate was available, we did not include 6-month estimates from the 2 Moderate certainty studies, though we note their estimates are at least broadly comparable at 17.6% and 31.2%, for a mean and median of 24.4%), the 12-month estimates from the 2 Moderate certainty studies, and the 36-month estimate from the 1 Moderate certainty study.

Author year	**Sample size**	**Time point for outcome assess-ment (months postopera tive)**	**Number of patients with**				**Certainty (reasons for downgrade)**
			favorable* outcome % (n/N)	uncertain† outcome % (n/N)	unfavorable‡ outcome % (n/N) without imputation§	unfavorable‡ outcome % (n/N) with imputation**	
Jones 2000	292	6 mos	76.0% (222/292)	5.5% (16/292)	18.5% (54/292)	19.5% (95% CI 15.4% to 24.5%)	High
Baker 2007	9,417	12 mos (or latest available)	68.2% (6,427/9,417)	14.9% (1,407/9,417)	16.8% (1,583/9,417)	19.3% (95% CI 18.5% to 20.1%)	Moderate

Brander 2003	116	12 mos	84.5% (98/116)	2.6% (3/116)	12.9% (15/116)	12.9% (95% CI 8.0% to 20.2%)	Moderate
Nunez 2007	88	36 mos	68.2% (60/88)	23.9% (21/88)	8.0% (7/88)	10.2% (95% CI 5.5% to 18.3%)	Moderate

CI, confidence interval; mos, months; N, sample size of cohort; n, number with event

* favorable outcome includes patients with no pain or mild pain at follow-up

† uncertain outcome includes "...all patients for whom we cannot be sure of their pain levels at follow-up. These include patients who died, had revision surgery, contralateral surgery or dislocation and were not followed up with questionnaires and those lost to follow-up. We also included as uncertain those patients with a degree of reported pain, which we could not classify as a favorable or unfavorable outcome"

‡ unfavorable outcome includes those with moderate-to-severe pain or for whom surgery had not relieved pain

§ proportion with unfavorable long-term pain outcome without imputing outcome information on patients lost to follow-up

** imputing proportion with known unfavorable long-term pain outcome to number with uncertain pain outcome

FAQ 3: Will the treatment help me lose weight?

Total knee replacement (followed by conservative non-surgical therapy) vs conservative (non-surgical) therapy alone

The effects of knee replacement on weight are best estimated from the results of the single randomized trial that has compared surgery vs. no surgery and reported weight as an outcome at 1-year (Skou 2015) and 2-year (Skou 2018) follow-up times.

Evidence Review Table

Comparing surgery vs. no surgery on weight change at follow-up times of 1-year (Skou 2015) and 2-years (Skou 2018)*

Follow-up	Change in TKR group (kg)	Change in nonsurgical group (kg)	Difference in mean change (kg)	Certainty (downgrade reason)
1-year	0.1 (95% CI -1.5 to 1.7)	-2.6 (95% CI -3.9 to -1.4)	2.8 (95% CI 1.4 to 4.1)	Moderate (risk of bias [no blinding])
2-year	2.7 (95% CI -2.9 to 8.2)	-2.2 (95% CI -3.5 to -0.8)	4.8 (95% CI 2.2 to 7.5)	Moderate (risk of bias [no blinding])

CI, confidence interval; TKR, total knee replacement

* Analysis on weight included only patients with a body-mass index of > 25 at baseline (39 patients in TKR group and 43 patients in nonsurgical-treatment group)

FAQ 4: Will I need surgery later?

In the randomized trial comparing surgery vs. no surgery, the need for surgery later in the non-surgery group can be estimated using the proportion who eventually got surgery over a given time period; the need for repeat surgery in the surgery group can be estimated using the proportion with surgery failure (Skou 2015; Skou 2018). These findings are summarized below under the header 'Total knee replacement (followed by conservative non-surgical therapy) vs conservative (non-surgical) therapy alone'.

The need for surgery later can also be addressed using national joint registries and national database studies that have estimated risk of revision/implant survival at various time points post-surgery as well as over a lifetime. These findings are summarized below under the header 'Total knee replacement'.

Total knee replacement (followed by conservative non-surgical therapy) vs conservative (non-surgical) therapy alone

Descriptive Evidence Review

In the randomized trial comparing surgery vs. no surgery

- among the 50 patients randomized to the no surgery group
    - 13 (26%; 95% CI 15.9% to 39.6%) had surgery before 1 year (Skou 2015)
    - 16 (32%; 95% CI 20.8% to 45.8%) had surgery before 2 years (Skou 2018)
    - certainty for both timepoints is Low (downgraded twice for imprecision due to small sample sizes)
- among the 50 patients randomized to the surgery group, 1 patient had a deep infection which required three revision surgeries and which ended up with the prosthesis being removed and knee being fused
    - certainty is Low (downgraded twice due to very serious concern about imprecision due to low event rate in a small sample size)

Total knee replacement

We found evidence from national joint registries and national database studies for the following 2 outcomes related to the question of whether a person will need surgery later: (1) cumulative implant survival at 5, 10, 15, and 20 years postoperatively (Bayliss 2017) and (2) risk of revision surgery at 5, 10, and 15 years (Wilson 2019) and over a lifetime stratified by age and gender (Bayliss 2017).

Evidence Review Tables: Cumulative implant survival from 5 years postoperatively to up to 20 years postoperatively

The study we selected to summarize and critically appraise for cumulative implant survival was a population-based study that estimated implant survival rates at up to 20 years postoperatively (Bayliss 2017).

Cumulative implant survival at 5, 10, 15, and 20 years after total knee replacement (Bayliss 2017*)

Years after total knee replacement	Cumulative implant survival rate (95% CI)	Certainty
5	97.98% (97.84% to 98.12%)	High
10	96.12% (95.83% to 96.39%)	High
15	92.94% (92.17% to 93.64%)	High
20	89.69% (87.45% to 91.54%)	High

* UK population-based study reporting on 54,276 patients who had total knee replacement from 1991 through 2011

Evidence Review Tables: Risk of revision surgery

The study we selected to critically appraise and summarize for revision surgery rates at different time points (5, 10, and 15 years) was a systematic review and meta-analysis that compared primary total vs. unicompartmental knee replacement (Wilson 2019). We mined this review for univariate revision rates from the total replacements arms of the studies included in the meta-analyses of national joint registries and national databases, and we used these extracted rates from the individual studies to calculate pooled revision rates (random-effects model) for total knee replacement for the time points of 5, 10, and 15 years after surgery.

Risk of revision surgery at 5, 10, and 15 years after total knee replacement (Wilson 2019*)

Outcome	Number of studies (TKA procedures)	Pooled incidence (95% CI)*	Certainty (downgrades)
5-year revision	2 (149,016)	3.16% (95% CI 2.23% to 4.25%)	High
10-year revision	7 (203,212)	4.58% (95% CI 3.16% to 6.25%)	High
15-year revision	2 (132,118)	7.22% (95% CI 1.77% to 15.94%)	Moderate (inconsistency**)

* We extracted the univariate incidence of the TKA group from each study (from forest plots comparing TKA vs. UKA) and used these to calculate a pooled incidence for each outcome (arcsine transformation with Sidik-Jonkman/Hartung-Knapp-Sidik-Jonkman (HKSJ) random effects model; use of Freeman-Turkey transformation instead of arcsine transformation yielded comparable estimates, as did use of DerSimonian-Laird random effects model instead of HKSJ random effects model).
** Of the 2 sources contributing to this outcome, one reported a 4.0% rate of revision and the other reported a 11.3% rate of revision.

The study we selected to summarize and critically appraise for lifetime risk of revision surgery (a measure which allows patients to easily understand their risk in the context of their predicted life expectancy) for females and males, by age at total knee replacement was a UK population-based study reporting on 54,276 patients who had knee replacement from 1991 through 2011 (Bayliss 2017).

Lifetime risk of revision surgery after total knee replacement for females and males by age at total knee replacement (Bayliss 2017)

Age at total knee replacement (years)*	**Lifetime risk of revision (95% CI)****		**Certainty**
	Females	Males	
50-54	20% (17% to 23%)	35.0% (30.9% to 39.1%)	High
55-59	14% (13% to 15%)	36.5% (34% to 39%)	High
60-64	16% (15% to 17%)	18% (17% to 19%)	High
65-69	6.5% (6% to 7%)	12% (11% to 13%)	High
70-74	5.5% (5% to 6%)	5% (4% to 6%)	High

*For patients having total knee replacement at aged 75, lifetime risk of revision was slightly less than 5% with similar estimates for females and males. Older than 75, risk slightly reduced and was consistent between sexes.
**Values were estimated from Figure 3 graph and are not exact, except for estimates for males aged 50-54 years old which were exactly reported in text

FAQ 5: What are the risks?

Total knee replacement plus conservative therapy

Risks following total knee replacement that we evaluated included prosthetic joint infection, mortality, blood clots, stiffness requiring brisement forcé, falls, and fracture. Evidence on each of these risks is summarized below.

Joint infection

Estimates of incidence of infection following total knee replacement were provided by a systematic review (Wilson 2019), a nationwide database study (Richardson 2019), and a randomized trial (Skou 2015). Key findings from each are summarized below.

Evidence Review Table: Wilson 2019

Although the overall purpose of the Wilson 2019 systematic review was to compare outcomes between patients having total knee replacement or unicompartmental knee replacement, we mined its data to calculate pooled infection incidence for patients having total knee replacement (using a comparable approach as for revision outcome, as described above).

Risk of infection after total knee replacement (Wilson 2019*)

Outcome	Number of national joint registries and national database studies (TKA procedures)	Pooled incidence (95% CI)*	Certainty (downgrades)
Deep infection**	6 (250,533)	0.79% (95% CI 0.36% to 1.38%)	Moderate (indirectness***)

* We extracted the univariate incidence of infection in the TKA group from each study (from forest plots comparing TKA vs. UKA) and used these to calculate a pooled incidence for infection (arcsine transformation with Sidik-Jonkman/Hartung-Knapp-Sidik-Jonkman (HKSJ) random effects model; use of Freeman-Turkey transformation instead of arcsine transformation yielded comparable estimates, as did use of DerSimonian-Laird random effects model instead of HKSJ random effects model).
** Classified by authors as infection that requires further intervention (ie, either revision, reoperation [debridement and implant retention], or long-term suppressive antibiotics). The follow-up time for deep infection was not specified, although for eligibility for inclusion in systematic review studies needed to have a follow-up of ≥ 30 days if assessing adverse event. Deep infection was classified under the broader outcome category 'early complications' suggesting that it does not include deep infections that occurred later.
*** Downgraded for indirectness because potential for suboptimal completeness of follow-up may lead to underestimation of deep infection incidence rates. The duration of follow-up for this outcome was not reported; however, it was grouped under broader outcome heading 'early complications' in Methods section, suggesting it does not include deep infections that occur in the longer-term. As noted by Jämsen 2010, about 1/3 of deep infections occur within 3 months and 2/3 within 2 years after index operation. Jämsen 2010 also makes note of the possibility that even prospective monitoring of infection may still underestimate the true risk. Considering all of this, we downgraded once.

Descriptive Evidence Review: Richardson 2019

This observational study reported the incidence of periprosthetic joint infection within 6 months after total knee arthroplasty among patients included in a United States nationwide private insurer database. Although the overall purpose of this study was to compare periprosthetic joint infection between patients who received injections in prior year (corticosteroid or hyaluronic acid) and patients who had received no injection, we used this study to extract univariate estimates for periprosthetic joint infection overall (separately for the total population and the no-injection group). This study was not included in

Wilson 2019 systematic review both because of its publication date of 2019 and because it was restricted to patients with total knee arthroplasty.

- risk of periprosthetic joint infection within 6 months after total knee arthroplasty
    - 2.83% (1,649/58,337; 95% CI 2.70% to 2.96%) among total population
    - 2.74% (1,052/38,432; 95% CI 2.58% to 2.91%) among no-injection group
    - Moderate certainty of evidence
        - Downgraded for indirectness because 6-month follow-up will lead to underestimation of deep infection incidence rates (only about 1/3 of which occur within 3 months and only about 2/3 of which occur within 2 years after index operation)

Descriptive Evidence Review: Skou 2015 and 2018

This randomized trial reported the incidence of deep infection at both 1 and 2 years after total knee replacement to be 1 out of 62 patients (1.6%) in as-treated analysis. This patient had three revision surgeries and ended up with prosthesis being removed and knee fused because of deep infection. The certainty of this evidence was Low because of very serious concerns about imprecision.

Mortality

Estimates of incidence of mortality following total knee replacement were provided by two systematic reviews (Berstock 2018; Wilson 2019). Key findings from each are summarized below.

Evidence Review Table: Berstock 2018

This systematic review reported the incidence of mortality at 30 days and 90 days after primary total knee replacement.

Risk of mortality after total knee replacement (Berstock 2018*)

Outcome	Number of observational studies (TKA procedures)	Pooled incidence (95% CI)*	Certainty (downgrades)
30-day mortality	24 (1,753,449)	0.20% (95% CI 0.17% to 0.24%)	Moderate (inconsistency)
90-day mortality	17 (700,981)	0.39% (95% CI 0.32% to 0.49%)	Moderate (inconsistency)

* Systematic review of observational studies published since 2006 and reporting on total knee replacements from 1991 to 2014

Evidence Review Table: Wilson 2019

Although the overall purpose of the Wilson 2019 systematic review was to compare outcomes between patients having total knee replacement or unicompartmental knee replacement, we mined its data to calculate pooled mortality incidence at 45 days after total knee replacement.

Risk of mortality after total knee replacement (Wilson 2019*)

Outcome	Number of national joint registries and national database studies (TKA procedures)	Pooled incidence (95% CI)*	Certainty (downgrades)
45-day mortality	6 (696,356)	0.16% (95% CI 0.03% to 0.38%)	High

* Systematic review reporting on total knee replacements in studies published since 1997

** We extracted the univariate incidence of mortality in the TKA group from each study (from forest plots comparing TKA vs. UKA) and used these to calculate a pooled incidence for mortality (arcsine transformation with Sidik-Jonkman/Hartung-Knapp-Sidik-Jonkman (HKSJ) random effects model; use of Freeman-Turkey transformation instead of arcsine transformation yielded comparable estimates, as did use of DerSimonian-Laird random effects model instead of HKSJ random effects).

Blood clots

Estimates of incidence of blood clots following total knee replacement were provided by a systematic review (Wilson 2019) and a randomized trial (Skou 2015). Key findings from each are summarized below.

Evidence Review Table: Wilson 2019

Although the overall purpose of the Wilson 2019 systematic review was to compare outcomes between patients having total knee replacement or unicompartmental knee replacement, we mined its data to calculate pooled incidence of venous thromboembolic events after total knee replacement.

Risk of thromboembolic events after total knee replacement (Wilson 2019*)

Outcome	Number of national joint registries and national database studies (TKA procedures)	Pooled incidence (95% CI)†	Certainty (downgrades)
Venous thromboembolic event‡	5 (228,499)	1.23% (95% CI 0.76% to 1.82%)	High

* Systematic review reporting on total knee replacements in studies published since 1997

† We extracted the univariate incidence of venous thromboembolic events in the TKA group from each study (from forest plots comparing TKA vs. UKA) and used these to calculate a pooled incidence for venous thromboembolic events (arcsine transformation with Sidik-Jonkman/Hartung-Knapp-Sidik-Jonkman (HKSJ) random effects model; use of Freeman-Turkey transformation instead of arcsine transformation yielded comparable estimates, as did use of DerSimonian-Laird random effects model instead of HKSJ random effects model).

‡Follow-up time not reported, although for eligibility for inclusion in systematic review studies needed to have a follow-up of ≥ 30 days if assessing adverse event, so we did not downgrade the venous thromboembolic event outcome, because the included studies should have had sufficient follow-up period to capture venous thromboembolic events (see, for instance, Bjørnaŕ 2006 which reports that median time to presentation of DVT and PE was 20 and 12 days respectively).

Descriptive Evidence Review: Skou 2015 and 2018

This randomized trial reported the incidence of deep venous thrombosis requiring anticoagulation after total knee replacement to be 3 out of 62 patients (4.8%) in as-treated analysis at both 1 and 2 years. The certainty of this evidence was low because of very serious concerns about imprecision.

Stiffness requiring brisement forcé

Estimate of incidence of stiffness requiring brisement forcé following total knee replacement was provided only by the randomized trial (Skou 2015).

Descriptive Evidence Review: Skou 2015 and 2018

This randomized trial reported the incidence of stiffness requiring brisement forcé to be 4 out of 62 patients (6.5%) in as-treated analysis at both 1 and 2 years. The certainty of this evidence was low because of very serious concerns about imprecision.

Falls

Because our primary question of interest is whether getting total knee replacement increases or decreases the fall rate relative to the preoperative (baseline) fall rate due to the patients' severe OA, the only relevant studies that can address that question are those that report both pre-operative and post-operative fall rates. One systematic review (di Laura Frattura 2018) included 3 studies that reported both pre-operative and post-operative prevalence of falls, summarized in table below:

Studies reporting both pre-operative and post-operative fall rates from systematic review (di Laura Frattura 2018)

Study	Number of patients	Duration of follow-up	Pre-operative fall rate	Post-operative fall rate
Swinkels 2009*	188	12 months	24%	12%
Swinkels 2013†	22	9 months	23%	17%
Tsonga 2016†	68	12 months	63%	22%

* Only Swinkels 2009 was reported to have found a statistical correlation between surgery and changes in falls rate (ie, 41% of patients considered 'fallers' stopped falling after surgery, and 10% of 'non-fallers' became 'frequent-fallers' after surgery).

† It was assumed from context, though not explicitly stated in systematic review report, that these two studies did not find a statistical correlation between surgery and changes in falls rate.

Based on the evidence from these 3 trials in the di Laura Frattura 2018 systematic review, for our study question of whether TKA changes rate of falls from preoperative (baseline) values we assigned an overall certainty rating of Very low (with downgrades due to very serious concerns about risk of bias and serious concerns about imprecision/inconsistency).

Supracondylar femur fracture

Estimate of incidence of supracondylar femur fracture following total knee replacement was provided only by the randomized trial (Skou 2015).

Descriptive Evidence Review: Skou 2015

This randomized trial reported incidence of supracondylar femur fracture in 1 out of 62 patients (1.6%) in as-treated analysis. The certainty of this evidence was low because of very serious concerns about imprecision. This outcome was not reported in Skou 2018.

Descriptive Summary

In addition to the risks outlined above pertaining to total knee replacement, risks associated with medications that might be used are noted in the section on conservative therapy.

Conservative therapy alone

Descriptive Summary

It depends on the specific treatment(s) used.

Although serious risks may be uncommon, risks with medication may include the following:

- NSAIDs can cause bleeding, which is sometimes serious
- tramadol and opioids can be addictive
- duloxetine can cause changes in thoughts or behavior and can be associated with withdrawal symptoms if suddenly stopped
- injections can lead to infection or bleeding; corticosteroid injections specifically may cause weakening of tendons, possibly contributing to or causing a tear

Acetaminophen/paracetamol does not typically have serious risks when taken as directed.

You can discuss possible risks in more detail with your health care professional.

(DynaMed Plus 2018, Mayo Clinic 2017, Mayo Clinic 2019)

FAQ 6: What are the side effects?

Total knee replacement plus conservative therapy

Descriptive Summary

It is normal to have some pain after surgery, and it may feel worse at night or with activity. This can last up to several weeks and is part of the knee healing. You will be given pain medicine for any pain you experience from the surgery. Some people also report feeling fatigued for a short period of time after surgery. This is also normal, because having total knee replacement is a major operation. People also usually have swelling in the area, and it may take up to three months for this to start going away. It may take up to a year for swelling to go away completely. You may also have to avoid certain activities that place stress on the knee (this is addressed in further detail in FAQ 7: How long does it take to recover?).

(See FAQ 1 for references.)

In addition to the side effects of surgery, side effects of conservative therapy are noted below.

Conservative therapy alone

Descriptive Summary

It depends on the treatment(s) used.

Side effects may include:

- Acetaminophen/paracetamol: does not typically cause side effects
- NSAIDs: upset stomach and heart burn
- Tramadol and opioids: fatigue, dizziness, constipation, and upset stomach
- Duloxetine: fatigue, dizziness, dry mouth, constipation or diarrhea, headache, and upset stomach
- Injections: typically tolerated well, but some may have bruising, swelling, or skin irritation

You can discuss side effects in more detail with your health care professional.

(DynaMed Plus 2018, Mayo Clinic 2017, Mayo Clinic 2018)

FAQ 7: How long does it take to recover?

Total knee replacement plus conservative therapy

Descriptive Summary

Attending / performing prescribed physical therapy and exercises is very important for recovery, including after being discharged from the hospital. In general, assuming recovery is going well, people are often able to return to many of their normal daily activities within 3 to 6 weeks, but people may be advised to avoid any heavier tasks for up to 3 months. They may also be advised to avoid tasks that require standing for prolonged periods or bending for the first 6 weeks.

For resuming specific activities, the following are general timelines people might be able to expect, but these are overall approximations, and all timelines should be tailored to the specific patient:

- Walking without assistive devices: around 6 weeks
- Driving: once the person is able to bend the knee enough to get in and out of the car and operate it safely; this may be as early as 3 weeks, but may take up to 12 weeks
- Returning to work: this depends on the job a person has, but people can usually return to work within 6 to 12 weeks
- Sexual activity: within about 6 to 8 weeks as long as vigorous sex and kneeling positions are avoided
- Sports: low-impact activities (such as walking, golf, biking, swimming) may be possible after about 6 weeks, but high-impact activities (such as jogging, tennis, or contact or jumping sports) should be avoided until the surgeon says it is okay to do these kinds of activities

Fully recovering from surgery may take up to a year, or in some cases 2 years.

(See FAQ 1 for references)

Conservative therapy alone

Descriptive Summary

There is no recovery period when using conservative therapy alone, aside from patients possibly being advised to rest/avoid strain on the knee for a day or two after the injection. (See FAQ 1 for references.)

Evidence report for total knee replacement plus conservative therapy versus conservative therapy alone for knee osteoarthritis

Part 5 - Evidence Synthesis

Prepared by EBSCO Information Services

May 23, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

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Methods

Evidence synthesis process

Synthesis methods will be based on the most appropriate methods matching the available evidence. We will systematically consider synthesis methods with the following questions:

Is it useful and appropriate to present the synthesis of evidence results as a single result as the best representation of the body of evidence?

State "Yes" or "No". Provide justification if "No".

If "Yes", leave the statement below that reads "If 'Yes', what method is the best approach?" and select the best method from those listed. Delete everything else. If another method not listed is deemed appropriate, provide justification.

If "No", leave the statement below that reads "If 'No', what method is best to represent the evidence synthesis?" and select the best method from those listed. Delete everything else. If another method not listed is deemed appropriate, provide justification.

If "Yes", what method is the best approach?

Pick one of the following and justify:

(1) meta-analysis already done

(2) meta-analysis created from the evidence results

(3) median of sufficiently-valid results, stating cutoff for validity

(4) median of all results

If "No", what method is best to represent the evidence synthesis?

Pick one of the following and justify:

(1) range of all results

(2) range of sufficiently valid results

(3) descriptive summary without quantitative representation (e.g., consistency in direction, but inconsistency in magnitude)

(4) statement of inconsistency too limiting for single synthesized conclusion

Where evidence is very limited, or the FAQ is for descriptive summary, such that summary text was provided instead of Evidence Review Tables, the Descriptive Evidence Summary will be noted.

Results

FAQ 1: What does the treatment involve?

Total knee replacement surgery plus conservative therapy

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

Total knee replacement (also called knee replacement surgery or total knee arthroplasty) for osteoarthritis is usually only offered to people who have not had satisfactory relief from symptoms with conservative therapy. In total knee replacement, the damaged portion of the knee joint is removed, and an artificial joint is put in its place.

A person may either be put to sleep during the operation or have an injection in the spine that numbs the lower half of the body. If the injection in the spine is used, it may be combined with sedation.

The surgeon will make a cut over the knee to allow access to the area where the surgery is performed. The cut is often about 6 to 10 inches (15 to 25 centimeters). The kneecap (patella) is moved to the side to allow the surgeon to get to the knee joint. The damaged portions of the knee joint are removed, and the artificial joint is inserted. The surgery usually lasts about 2 hours.

There is a newer method for performing total knee replacement that makes smaller cuts – about 4 to 5 inches (10 to 12 centimeters) – but this may not be available at all hospitals or performed by all surgeons.

People may be in the hospital for about 3 to 5 days, but this depends on the individual.

For a period of time after the surgery, patients are usually given medication to prevent blood clots, though recommendations are not entirely consistent. After the surgery, patients will initially walk with an assistive device (e.g., walker, crutches), and they will progressively increase the amount of weight they put on the leg with the artificial knee. Attending / performing prescribed physical therapy and exercises is very important for recovery, including after being discharged from the hospital. Some patients go to a rehabilitation facility for a short period to help ensure they stay on track with recovery. In general, assuming recovery is going well, people are often able to return to many of their normal daily activities within 3 to 6 weeks, but people may be advised to avoid any heavier tasks for up to 3 months. They may also be advised to avoid tasks that require standing for prolonged periods or bending for the first 6 weeks. Additional recovery information is provided in FAQ 7 (How long does it take to recover?).

(Cram 2012, DynaMed 2018, Foran 2015, NHS 2016, NICE 2010, NIH 2018, Mayo Clinic 2017)

Conservative (non-surgical) treatment alone

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

Non-surgical treatment for osteoarthritis of the knee may involve a number of different treatments, which should be tailored to the individual. Treatment may involve non-pharmacologic and pharmacologic options, such as:

- Non-pharmacologic options: exercise, physical therapy, heat or ice applied to the knee, weight loss (if indicated), assistive walking devices (e.g., cane, walker), and self-management programs/patient education (including appropriate footwear)
- Pharmacologic treatments may include:
  - Oral medications: acetaminophen/paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), duloxetine, tramadol, non-tramadol opioids
  - Topical medication: topical NSAIDs
  - Injections: corticosteroids or hyaluronic acid

(DynaMed 2018, Skou 2015, Skou 2018)

Patients who receive an injection may be advised to rest/avoid strain on the knee for a day or two after the injection (Mayo Clinic 2017, Mayo Clinic 2019).

FAQ 2: Will I feel better?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	1 (Skou 2015)
Second-round (Systematic review searches)	39	1 (Beswick 2012)
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	25	1 (Skou 2018)

Part 3 Critical Appraisal:

Certainty	Systematic reviews	Randomized trials	Other article types
High	Beswick 2012 (for unfavorable outcome at 6 months of follow-up)*		
Moderate	Beswick 2012 (for unfavorable outcome at 12 and 36 months of follow-up)*	Skou 2015 (KOOS subscales for symptoms, ADLs, and S&R)** Skou 2018 ($KOOS_4$ composite score and KOOS subscales for symptoms, QoL, and S&R)**	
Low		Skou 2015 ($KOOS_4$ composite score and KOOS subscales for pain and QoL)** Skou 2018 (KOOS subscales for pain and ADLs)**	
Very low			
Unusable			
Not applicable			

ADLs, activities of daily living; KOOS, Knee Injury and Osteoarthritis Outcome Score; $KOOS_4$ = summary score comprised of 4 of the 5 KOOS subscale scores (all except sports and recreation); QoL, quality of life; S&R, sports and recreation

*Beswick 2012 only provides estimates for outcomes following total knee replacement (it does not provide comparative estimates for total knee replacement plus conservative therapy vs. conservative therapy alone). For Beswick 2012, we focus on moderate and high certainty estimates. For the 6-month follow-up point, we do not include the 2 moderate certainty estimates with this duration of follow-up (point estimates of 17.6% and 31.2%).

**Skou 2015 and 2018 provide comparative data for total knee replacement plus conservative therapy vs. conservative therapy alone. By virtue of having these two arms, Skou 2015 and 2018 also provide univariate estimates for both groups.

Part 4 Results for FAQ2: Will I feel better?

Effects of knee replacement surgery on patients' symptoms can be evaluated in 1) a randomized trial by comparing proportion of patients who improve or require pain medication with surgery vs. no surgery; and 2) a cohort study (or systematic review of these) as the proportion of patients who have an unfavorable long-term pain outcome following surgery. The effects of each of these evaluations are summarized separately below.

Randomized trial comparing surgery vs. no surgery on proportion who improved and proportion who required pain medication at 1-year and 2-year follow-up times

Only one randomized trial has compared total knee replacement vs. nonsurgical therapy alone (Skou 2015 [1-year follow-up primary publication] and 2018 [2-year follow-up]). It compared unilateral total knee replacement followed by 12 weeks of guideline-based, multimodal nonsurgical treatment (including exercise, education, dietary advice, use of insoles, and pain medication) vs. 12 weeks of guideline-based, multimodal nonsurgical treatment alone in 100 patients with moderate-to-severe knee osteoarthritis. The relevant 1-year and 2-year outcomes are summarized below.

Improvements of ≥ 15% in $KOOS_4$ score and KOOS subscale scores from baseline at 1 year and 2 years after surgery

Outcome*	Percentage with improvement of ≥ 15% in TKR group (95% CI)	Proportion with improvement of ≥ 15% in non-surgical group (95% CI)	Difference between groups in proportion with improvement of ≥ 15% (95% CI)	Certainty (with reasons for downgrade)**
1-year results (Skou 2015)				
$KOOS_4$	85% (71% to 93%)	67% (53% to 79%)	17.4% (0.1% to 33.4%)	Low (risk of bias, imprecision)
KOOS subscale scores				
Pain	83% (69% to 91%)	69% (55% to 81%)	13.2% (-4.1% to 29.4%)	Low (risk of bias, imprecision)
Symptoms	85% (71% to 93%)	45% (31% to 59%)	39.9% (20.9% to 55.0%)	Moderate (risk of bias)
Quality of life	89% (76% to 96%)	69% (55% to 81%)	19.7% (3.3% to 35.0%)	Moderate (risk of bias)
Activities of daily living	89% (76% to 96%)	59% (45% to 72%)	29.9% (12.4% to 45.2%)	Moderate (risk of bias)
Sports and recreation	89% (76% to 96%)	65% (51% to 77%)	23.8% (6.9% to 39.1%)	Moderate (risk of bias)
2-year results (Skou 2018)				
$KOOS_4$	86% (72% to 94%)	64% (49% to 76%)	22.2% (4.2% to 38.3%)	Moderate (risk of bias)
KOOS subscale scores				

Pain	84% (69% to 92%)	70% (55% to 82%)	13.5% (-4.1% to 29.9%)	Low (risk of bias, imprecision)
Symptoms	79% (64% to 89%)	55% (41% to 69%)	23.8% (4.3% to 40.7%)	Moderate (risk of bias)
Quality of life	88% (74% to 95%)	66% (51% to 78%)	22.4% (4.9% to 38.1%)	Moderate (risk of bias)
Activities of daily living	81% (67% to 91%)	64% (49% to 76%)	17.6% (-1.0% to 34.4%)	Low (risk of bias, imprecision)
Sports and recreation	93% (80% to 98%)	66% (51% to 78%)	27.1% (10.4% to 42.1%)	Moderate (risk of bias)

CI, confidence interval; KOOS = Knee Injury and Osteoarthritis Outcome Score; $KOOS_4$ = summary score comprised of 4 of the 5 KOOS subscale scores (all except Sports and recreation); TKR, total knee replacement

* 1-year results are based on the 46 patients in the TKR group and 49 patients in the nonsurgical group who had data available at 1 year; 2-year results are based on the 43 patients in the TKR group and 47 patients in the nonsurgical group who had data available at 2 years

** All outcomes were downgraded for risk of bias because of lack of blinding. Although 13 patients (26%) in nonsurgical group got TKR before 1 year and 16 patients (32%) before year 2, we did not apply an additional risk of bias downgrade for this crossover because this amount of crossover is relatively low for a surgical trial and because the results from the per-protocol analyses at 1 year were largely consistent with those of intention-to-treat analyses.

- **use of pain medication (any kind, on regular basis, during previous week)**
  - at 1 year (Skou 2015)
    - 41% (95% CI 28% to 55%) in nonsurgical group
    - 26% (95% CI 15% to 41%) in TKR group
    - difference in proportion 14.7% (95% CI -4.2% to 32.2%)
    - adjusted RR 1.57 (95% CI 0.87 to 2.85)
    - Low certainty, downgrades for risk of bias (no blinding) and imprecision
  - at 2 years (Skou 2018)
    - 49% (95% CI 35% to 63%) in nonsurgical group
    - 26% (95% CI 15% to 41%) in TKR group
    - difference in proportions 23.4% (95% CI 3.3% to 40.8%)
    - RR 1.91 (95% CI 1.06 to 3.44)
    - Low certainty, downgrades for risk of bias (no blinding) and imprecision

Systematic review of cohort studies evaluating proportion of patients who have an unfavorable long-term pain outcome following knee surgery

A systematic review of observational studies in patients with primary total hip or knee replacement has reported results classifiable as proportion of patients with unfavorable pain outcome at follow-up from 3 months to 5 years (Beswick 2012). Among the 11 studies of total knee replacement included in this systematic review, only 1 met both of the review authors' two indicators of quality (ie, conducted at multiple centers, and low loss to follow-up [< 10%]) and was thus judged high quality by the review authors. In this study, the proportion of patients with an unfavorable outcome at 6 months was 19.5% (imputing proportion with known unfavorable long-term pain outcome to number with uncertain pain outcome). Because this single high certainty study only provides an estimate at the 6-month follow-up point, the 5 moderate certainty studies were also assessed. Two of these also reported estimates at 6-months and these estimates were broadly comparable to that of the high-certainty study (ie, 17.6% and 31.2%, for a mean and median of 24.4%). Three moderate certainty studies provided estimates at later follow-up times (12 months in two studies and 36 months in one).

Proportion with unfavorable long-term pain outcome following TKA (Beswick 2012)

Author year	Sample size	Time point for outcome assess-ment	Number of patients with				Certainty (reasons for downgrade)
			favorable* outcome %	uncertain† outcome %	unfavorable‡ outcome % without imputation§	unfavorable‡ outcome % with imputation**	
Jones 2000	292	6 mos	76.0%	5.5%	18.5%	19.5% (95% CI 15.4% to 24.5%)	High
Baker 2007	9,417	12 mos (or latest available)	68.2%	14.9%	16.8%	19.3% (95% CI 18.5% to 20.1%)	Moderate
Brander 2003	116	12 mos	84.5%	2.6%	12.9%	12.9% (95% CI 8.0% to 20.2%)	Moderate
Nunez 2007	88	36 mos	68.2%	23.9%	8.0%	10.2% (95% CI 5.5% to 18.3%)	Moderate

CI, confidence interval; mos, months; N, sample size of cohort; n, number with event
* favorable outcome includes patients with no pain or mild pain at follow-up
† uncertain outcome includes "...all patients for whom we cannot be sure of their pain levels at follow-up. These include patients who died, had revision surgery, contralateral surgery or dislocation and were not followed up with questionnaires and those lost to follow-up. We also included as uncertain those patients with a degree of reported pain, which we could not classify as a favorable or unfavorable outcome"
‡ unfavorable outcome includes those with moderate-to-severe pain or for whom surgery had not relieved pain
§ proportion with unfavorable long-term pain outcome without imputing outcome information on patients lost to follow-up
** imputing proportion with known unfavorable long-term pain outcome to number with uncertain pain outcome

Evidence Synthesis Process for FAQ2: Will I feel better?

Is it useful and appropriate to present the synthesis of evidence results as a single result as the best representation of the body of evidence?

No. Two different outcomes are most relevant for the global question of "Will I feel better?" (including pain, symptoms, function, and quality of life). The outcome of ≥15% improvement in $KOOS_4$ (from Skou 2015 and 2018) and the outcome of favorable outcome (converted from unfavorable outcome from Beswick 2012) are comparable in magnitude but not clearly appropriate to combine for a single quantitative estimate. We also report on use of pain medication (only reported in Skou 2015 and 2018), as this was a separately-scoped outcome.

- Skou 2015 and 2018: comparing total knee replacement followed by multimodal nonsurgical treatment (12 weeks) vs. multimodal nonsurgical treatment alone
    - at 1-year follow-up

        - improvement of ≥15%
            - overall $KOOS_4$ measure (includes pain, symptoms, quality of life, and activities of daily living)
                - 85% (95% CI 71% to 93%) for surgery group
                - 67% (95% CI 53% to 79%) for no surgery group
                - difference in proportions, 17.4% (95% CI 0.1% to 33.4%)
                - Low certainty
        - use of pain medication (any kind, on regular basis, during previous week)
            - 41% (95% CI 28% to 55%) for no surgery group
            - 26% (95% CI 15% to 41%) for surgery group
            - difference in proportions, 14.7% (95% CI -4.2% to 32.2%)
            - Low certainty
    - at 2-year follow-up
        - improvement of ≥15%
            - overall $KOOS_4$ measure (includes pain, symptoms, quality of life, and activities of daily living)
                - 86% (72% to 94%) for surgery group
                - 64% (49% to 76%) for no surgery group
                - difference in proportions, 22.2% (95% CI 4.2% to 38.3%)
                - Moderate certainty
        - use of pain medication (any kind, on regular basis, during previous week)
            - 49% (95% CI 35% to 63%) in no surgery group
            - 26% (95% CI 15% to 41%) in surgery group
            - difference in proportions, 23.4% (95% CI 3.3% to 40.8%)
            - Low certainty
- Beswick 2012: assessing long-term unfavorable outcome after total knee replacement surgery
    - Jones 2000, 6 months of follow-up: 19.5% (95% CI 15.4% to 24.5%), High certainty
    - Baker 2007, 12 months (or latest) of follow-up: 19.3% (95% CI 18.5% to 20.1%), Moderate certainty
    - Brander 2003, 12 months of follow-up: 12.9% (95% CI 8.0% to 20.2%), Moderate certainty
    - Nunez 2007, 36 months of follow-up: 10.2% (95% CI 5.5% to 18.3%), Moderate certainty

Global synthesis: Improvement in pain/symptoms

The 6-month results from Beswick 2012 suggest 80.5% (95% CI 75.5% to 84.6%) of patients having knee replacement surgery have a favorable outcome. These results are broadly comparable to three estimates at follow-up points from 12 to 36 months: 80.7% (95% CI 79.9% to 81.5%), 87.1% (95% CI 79.7% to 92%), and 89.8% (95% CI 81.7% to 94.5%). The mean and median of the point estimates are 84.5% and 83.9%, respectively.

These estimates are comparable with the results in Skou 2015 and 2018, in which 85% (71% to 93%) and 86% (72% to 94%) of those in the surgery group had ≥15% improvement at 1 and 2 years, respectively. This was in comparison to 67% (53% to 79%) and 64% (49% to 76%) in the non-surgical group at 1 and 2 years, respectively.

Overall, the lowest and highest probabilities of a "favorable outcome" or "feeling better" come from Beswick 2012 at 6 months of follow-up (80.5%) and 36 months of follow-up (89.8%), but the mean and median estimates from Beswick 2012 (84.5% and 83.9%) are sufficiently comparable to the estimates from Skou 2015/2018 (85% to 86%) that we use the Skou 2015/2018 for representative results. Accordingly, as the Skou 2015 and 2018 results were over 1 and 2 years, respectively, and as these estimates were comparable at both timeframes, we adopt the simple timeframe of "over 2 years" for reporting purposes (in line with IPDAS criteria for reporting timeframes).

Out of 100 people who have total knee replacement surgery, about 85 to 86 (85% to 86%) may have improvement in their pain, symptoms, function, and/or quality of life over 2 years. (Moderate certainty)

Out of 100 people who are treated without surgery, about 64 to 67 (64% to 67%) may have improvement in their pain, symptoms, function, and/or quality of life over 2 years. (Moderate certainty)

Global synthesis: Use of pain medication

For the outcome of use of pain medication, only Skou 2015 and 2018 report results. For the surgical group, 26% reported using pain medication at both the 1- and 2-year follow-up points, whereas for the non-surgical group, 41% and 49% reported using pain medication at the 1- and 2-year follow-up points, respectively. The difference in proportions at 1 year did not reach conventional statistical significance, the difference at 2 years did, and we note the difference in proportions are comparable overall. We consider it reasonable to report the absolute rates in each group as a single estimate for the surgical group (only one estimate available) and as a range of sufficiently-valid results for the non-surgical group (41% to 49%).

Out of 100 people who have total knee replacement surgery, about 26 (26%) may use pain medication of some kind to help with their symptoms. (Low certainty)

Out of 100 people who are treated without surgery, about 41 to 49 (41% to 49%) may use pain medication of some kind to help with their symptoms. (Low certainty)

FAQ 3: Will the treatment help me lose weight?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	1 (Skou 2015)
Second-round (Systematic review searches)	39	0
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	25	1 (Skou 2018)

Part 3 Critical Appraisal:

Certainty	**Systematic reviews**	**Randomized trials**	**Other article types**
High			
Moderate		Skou 2015, Skou 2018	
Low			
Very low			
Unusable			
Not applicable			

Part 4 Results for FAQ3:

The effects of knee replacement on weight are best estimated from the results of the single randomized trial that has compared surgery vs. no surgery and reported weight as an outcome at 1-year (Skou 2015) and 2-year (Skou 2018) follow-up times.

Evidence Review Table

Comparing surgery vs. no surgery on weight change at follow-up times of 1-year (Skou 2015) and 2-years (Skou 2018)*

Follow-up	Change in TKR group (kg)	Change in nonsurgical group (kg)	Difference in mean change (kg)	Certainty (downgrade reason)
1-year	0.1 (95% CI -1.5 to 1.7)	-2.6 (95% CI -3.9 to -1.4)	2.8 (95% CI 1.4 to 4.1)	Moderate (risk of bias [no blinding])
2-year	2.7 (95% CI -2.9 to 8.2)	-2.2 (95% CI -3.5 to -0.8)	4.8 (95% CI 2.2 to 7.5)	Moderate (risk of bias [no blinding])

CI, confidence interval; TKR, total knee replacement
* Analysis on weight included only patients with a body-mass index of > 25 at baseline (39 patients in TKR group and 43 patients in nonsurgical-treatment group)

Evidence Synthesis Process for FAQ3:

Is it useful and appropriate to present the synthesis of evidence results as a single result as the best representation of the body of evidence?

Yes. We concluded on the one randomized trial that compared surgery vs. no surgery and reported moderate certainty evidence on body weight outcome at 1-year and 2-year follow-up times.

The most reliable evidence available suggests that patients who have total knee replacement may gain weight at 1 year and 2 years after surgery (compared to a no surgery group):

- difference at 1 year 2.8 kg (95% CI 1.4 to 4.1 kg)
- difference at 2 years 4.8 kg (95% CI 2.2 to 7.5 kg)

Imperial system

Weight loss is possible with a good diet and exercise regardless of what treatment a person receives. People who have total knee replacement surgery in addition to conservative therapy may have some worsening in their weight over one to two years compared to those who use conservative therapy alone. They may gain more or lose less weight (about 6 to 11 pounds) compared to those who use conservative therapy alone. (Moderate certainty)

Weight loss is possible with a good diet and exercise regardless of what treatment a person receives. People who use conservative therapy alone may have some improvement in their weight over one to two years compared to those who have total knee replacement surgery in addition to conservative therapy. They may lose more or gain less weight (about 6 to 11 pounds) compared to those who have total knee replacement surgery in addition to conservative therapy. (Moderate certainty)

Metric system

Weight loss is possible with a good diet and exercise regardless of what treatment a person receives. People who have total knee replacement surgery in addition to conservative therapy may have some worsening in their weight over one to two years compared to those who use conservative therapy alone. They may gain more or lose less weight (about 3 to 5 kilograms) compared to those who use conservative therapy alone. (Moderate certainty)

Weight loss is possible with a good diet and exercise regardless of what treatment a person receives. People who use conservative therapy alone may have some improvement in their weight over one to two years compared to those who have total knee replacement surgery in addition to conservative therapy. They may lose more or gain less weight (about 3 to 5 kilograms) compared to those who have total knee replacement surgery in addition to conservative therapy. (Moderate certainty)

Another way of saying this

Weight loss is possible with a good diet and exercise regardless of what treatment you receive. Compared to people who have total knee replacement in addition to conservative therapy, people using conservative therapy alone may be more likely to lose weight or keep their weight stable over one to two years. (Moderate certainty)

Weight loss is possible with a good diet and exercise regardless of what treatment you receive. Compared to people who use conservative therapy alone, people who have total knee replacement in addition to conservative therapy may be less likely to lose weight or keep their weight stable over one to two years. (Moderate certainty)

FAQ 4: Will I need surgery later?

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	26	2 (Skou 2015, Bayliss 2017)
Second-round (Systematic review searches)	67	1 (Wilson 2019)
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	25	1 (Skou 2018)

Part 3 Critical Appraisal:

Certainty	**Systematic reviews**	**Randomized trials**	**Other article types**
High	Wilson 2019 (5- and 10-year revision rates)		Bayliss 2017
Moderate	Wilson 2019 (15-year revision rate)		
Low		Skou 2015, Skou 2018	
Very low			
Unusable			
Not applicable			

Part 4 Results for FAQ4: Will I need surgery later?

Need for surgery later among total knee replacement surgery patients can be best evaluated as the proportion of patients who require revision surgery at different follow-up times and over a lifetime based on national joint registries and national database studies and/or systematic review and meta-analyses of these.

Need for surgery later among patients deemed eligible for total knee replacement surgery but having only conservative treatment initially can be best evaluated as the proportion of patients in a randomized trial who were assigned to conservative treatment (alone, without surgery) but who got surgery at 1-year (Skou 2015) and 2-year (Skou 2018) follow-up.

Total knee replacement surgery

Part 4 Results for cumulative implant survival from 5 years postoperatively to up to 20 years postoperatively

Two studies used population-based data sources to estimate revision surgery rates at 5-year intervals following surgery up to 20 years (Bayliss 2017; Wilson 2019). The table below summaries their results.

Risk of revision surgery at 5, 10, 15, and 20 years after total knee replacement (Bayliss 2017; Wilson 2019)*

Years after total knee replacement	Author year	surgery revision rate % (95% CI)	Certainty
5	Bayliss 2017	2.02% (1.88% to 2.16%)	High
	Wilson 2019	3.16% (2.23% to 4.25%)	High
10	Bayliss 2017	3.88% (3.61% to 4.17%)	High
	Wilson 2019	4.58% (3.16% to 6.25%)	High
15	Bayliss 2017	7.06% (6.36% to 7.83%)	High
	Wilson 2019	7.22% (1.77% to 15.94%)	Moderate (inconsistency)
20	Bayliss 2017	10.31% (8.46% to 12.55%)	High

* The large registry study of Bayliss 2017 is presented separately, as it was not included in the Wilson 2019 systematic review. Wilson 2019 sought to compare unicompartmental knee arthroplasty vs. total knee arthroplasty (TKA), so studies had to provide evidence for both to be included. Bayliss 2017 only included people who had undergone TKA (or total hip arthroplasty, but we do not consider those data in this evidence report). We converted the implant survival rates in Bayliss 2017 to the rate of revision to facilitate comparison to the results from Wilson 2019. For Wilson 2019, we extracted univariate estimates for the TKA groups and meta-analyzed those estimates.

Evidence Synthesis Process for cumulative implant survival from 5 years postoperatively to up to 20 years postoperatively

Is it useful and appropriate to present the synthesis of evidence results as a combined, single result as the best representation of the body of evidence?

Yes, for the follow-up point of 20 years after total knee replacement. At 20 years of follow-up, only Bayliss 2017 reported revision rates.

No for the follow-up points of 5, 10, and 15 years after total knee replacement (we instead use a range of sufficiently-valid results). At the other follow-up periods, both studies reported on revision rates. For 5 and 10 years, the evidence is of High certainty from both studies. For 15 years, the evidence is of High and Moderate certainty from Bayliss 2017 and Wilson 2019, respectively, but we note Wilson 2019 was downgraded to Moderate certainty due to inconsistency in the meta-analysis, and this downgrade could not apply for the outcome of interest for Bayliss 2017; additionally, the estimates from these 2 sources for the 15-year point are comparable (about 7%).

Out of 100 people who have total knee replacement surgery:

- **2 to 3 (2% to 3%) may have another surgery 5 years after their first surgery**
- **4 to 5 (4% to 5%) may have another surgery 10 years after their first surgery**
- **7 (7%) may have another surgery 15 years after their first surgery**
- **10 (10%) may have another surgery 20 years after their first surgery**

(High certainty)

Part 4 Results for lifetime risk of revision surgery

The UK population-based study (Bayliss 2017) reported lifetime risk of revision surgery, an outcome that allows patients to easily understand their risk in the context of their predicted life expectancy. Lifetime risk of revision surgery by age at surgery and gender are reported below.

Lifetime risk of revision surgery after total knee replacement for females and males by age at total knee replacement (Bayliss 2017)

Age at total knee replacement (years)*	**Lifetime risk of revision (95% CI)**		**Certainty**
	Females	Males	
50-54	20% (17% to 23%)	35.0% (30.9% to 39.1%)	High
55-59	14% (13% to 15%)	36.5% (34% to 39%)	High
60-64	16% (15% to 17%)	18% (17% to 19%)	High
65-69	6.5% (6% to 7%)	12% (11% to 13%)	High
70-74	5.5% (5% to 6%)	5% (4% to 6%)	High

*For patients having total knee replacement at aged 75, lifetime risk of revision was slightly less than 5% with similar estimates for females and males. Older than 75, risk slightly reduced and was consistent between sexes.

Is it useful and appropriate to present the synthesis of evidence results as a single result as the best representation of the body of evidence?

No. Providing a synthesis statement for the above findings beyond what is presented in the table was deemed inappropriate due to the difference in estimates and providing such age- or sex-specific estimates is beyond the scope of this work. However, we provide these estimates in Part 5 as we consider them potentially informative for individualized estimates based on age at total knee replacement and sex.

Conservative (non-surgical) treatment alone

Part 4 Results for FAQ4: Will I need surgery later? Risk of initial surgery among patients deemed eligible for surgery but initially having only conservative treatment

Descriptive Evidence Review

Proportion of 50 patients randomized to no surgery group who got surgery (Low certainty):

- at 1-year follow-up 26% (95% CI, 15.9% to 39.6%) (Skou 2015)
- at 2-year follow-up 32% (95% CI, 20.8% to 45.8%) (Skou 2018)

Evidence Synthesis Process for FAQ4

Is it useful and appropriate to present the synthesis of evidence results as a single result as the best representation of the body of evidence?

Yes. Only a single estimate was available at 1-year (Skou 2015) and 2-year (Skou 2018) follow-up times which each provide Low certainty evidence for the rate of delayed surgery in the control group.

Out of 100 people who have conservative (non-surgical) treatment:

- **about 26 (26%) may have surgery within 1 year**
- **about 32 (32%) may have surgery within 2 years**

(Low certainty)

FAQ 5: What are the risks?

Total knee replacement

Pre-Synthesis Efforts:

Part 2 Search:

	Number of articles evaluated	Number of unique articles selected for evaluation
First-round (DynaMed Plus)	35	3 (Skou 2015, Berstock 2018, Richardson 2019)
Second-round (Systematic review searches)	63	3 (Wilson 2019, Lo 2019, di Laura Frattura 2018)
Third-round (Original study tracing)	Not applicable	
Fourth-round (Original article searches)	25	1 (Skou 2018)

Part 3 Critical Appraisal:

Certainty	**Systematic reviews**	**Randomized trials**	**Other article types**
High	Wilson 2019 (venous thrombotic event, 45-day mortality)		
Moderate	Berstock 2018, Wilson 2019 (deep infection)		Richardson 2019
Low		Skou 2015, Skou 2018	
Very low	di Laura Frattura 2018		
Unusable	Lo 2019*		
Not applicable			

*This systematic review only provided rates of falls post-operatively, but this precludes inference regarding fall rate without surgery/pre-operatively. The other systematic review of falls (di Laura Frattura 2018) permits comparative inference, albeit only with Very low certainty.

Part 4 Results for FAQ5:

Risks of total knee replacement were provided by multiple sources: 3 systematic reviews (Berstock 2018, di Laura Frattura 2018, and Wilson 2019), 2 randomized, controlled trials (Skou 2015, Skou 2018), and a large cohort study (Richardson 2019).

These sources provided evidence for the outcomes of deep/prosthetic joint infection (Richardson 2019, Skou 2015, Skou 2018, Wilson 2019), mortality (Berstock 2018, Wilson 2019), venous thromboembolic events (Skou 2015, Skou 2018, Wilson 2019), stiffness of the knee requiring brisement forcé (manipulation of the knee while the patient is anesthetized to improve the range of motion of the knee; Skou 2015, Skou 2018), supracondylar femur and fracture (Skou 2015, Skou 2018), falls (di Laura Frattura 2018).

Source **Study type; sample size for outcome**	**Key findings and follow-up**	**Certainty**
Deep/prosthetic joint infection		
Wilson 2019 Systematic review; 6 national joint registries and national database studies totaling 250,533 TKRs	deep infection: 0.79% (95% CI 0.36% to 1.38%) all studies had to have ≥30 days of follow-up, but follow-up otherwise not specified	Moderate
Richardson 2019 Cohort study; 58,337 people (not included in Wilson 2019)	periprosthetic joint infection: • 2.83% (95% CI 2.70% to 2.96%) in overall cohort • 2.74% (95% CI 2.58% to 2.91%) among those without injections in the prior year • these rates are not meaningfully different, so we use the overall cohort hereafter follow-up was 6 months	Moderate
Skou 2015, Skou 2018 Randomized trial; 62 patients in as-treated analysis	At 1 year, 1 patient (1.6%) had deep infection. By the 2-year follow-up, there were no additional cases of infection, but the aforementioned case had required 3 revision surgeries and eventual removal of the prosthesis with knee fusion.	Low
Mortality		
Berstock 2018	• 30-day mortality: 0.20% (95% CI 0.17% to 0.24%) • 90-day mortality: 0.39% (95% CI 0.32% to 0.49%)	Moderate

<table>
<tr><td>Systematic review; 24 observational studies totaling 1,753,449 TKRs (30-day mortality), 17 observational studies totaling 700,981 TKRs (90-day mortality)</td><td></td><td></td></tr>
<tr><td>Wilson 2019

Systematic review; 6 national joint registries and national database studies totaling 696,356 TKRs</td><td>45-day mortality: 0.16% (95% CI 0.03% to 0.38%)</td><td>Moderate</td></tr>
<tr><td colspan="3">VTE</td></tr>
<tr><td>Wilson 2019

Systematic review; 5 national joint registries and national database studies totaling 228,499 TKRs</td><td>VTE: 1.23% (95% CI 0.76% to 1.82%)

all studies had to have ≥30 days, but follow-up otherwise not specified</td><td>High</td></tr>
<tr><td>Skou 2015, Skou 2018

Randomized trial; 62 patients in as-treated analysis</td><td>At 1 year, DVT had occurred in 3 out of 62 patients (4.8%); no change by 2 years</td><td>Low</td></tr>
<tr><td colspan="3">Stiffness requiring brisement forcé</td></tr>
<tr><td>Skou 2015, Skou 2018

Randomized trial; 62 patients in as-treated analysis</td><td>At 1 year, 4 out of 62 patients (6.5%) had stiffness requiring brisement forcé (manipulation of knee while patient is under anesthesia to improve range of motion); no change by 2 years</td><td>Low</td></tr>
<tr><td colspan="3">Supracondylar femur fracture</td></tr>
<tr><td>Skou 2015

Randomized trial; 62 patients in as-treated analysis</td><td>At 1 year, 1 out of 62 patients (1.6%) had supracondylar femur fracture; this outcome was not reported at 2 years</td><td>Low</td></tr>
<tr><td colspan="3">Falls</td></tr>
<tr><td>di Laura Frattura 2018

Systematic review; 3 pre-post design studies totaling 278 patients</td><td><table><tr><td>Study, sample size</td><td>Follow-up</td><td>Pre-operative rate</td><td>Post-operative rate</td></tr><tr><td>Swinkels 2009, n = 188</td><td>12 months</td><td>24%</td><td>12%</td></tr><tr><td>Swinkels 2013, n = 22</td><td>9 months</td><td>23%</td><td>17%</td></tr><tr><td>Tsonga 2016 n = 68</td><td>12 months</td><td>63%</td><td>22%</td></tr></table></td><td>Very low</td></tr>
</table>

CI, confidence interval; DVT, deep venous thrombosis; TKR, total knee replacement; VTE, venous thromboembolic event

Evidence Synthesis Process for FAQ5:

Outcome	**Single result best representation?**	**Synthesis method and synthesis**
Deep/prosthetic joint infection	No. There are two Moderate certainty estimates: Wilson 2019 (0.79%; 95% CI 0.36% to 1.38%) and Richardson 2019 (overall cohort: 2.83%, 95% CI 2.70% to 2.96%; estimates for cohort without injections in the prior year were comparable). Although one could perhaps consider pooling the results from Richardson 2019 with the results from Wilson 2019, we note one of our concerns was possible underestimation of infection rates, so we favor reporting the results as a range of sufficiently-valid estimates – which would give an upper bound of the range of "up to 3%" – instead of pooling.	Range of sufficiently-valid estimates: **Out of 100 people who have total knee replacement surgery, up to 3 (up to 3%) may have an infection.** (Moderate certainty)
Mortality	Yes. Estimates of mortality at 30 days (Berstock 2018; 0.20%, 95% CI 0.17% to 0.24%), 45 days (Wilson 2019; 0.16%, 95% CI 0.03% to 0.38%), and 90 days (Berstock 2018; 0.39%, 95% CI 0.32% to 0.49%) are all comparable at <0.5%. However, none of these estimates permit inference into how these mortality rates might compare to those who do *not* receive total knee replacement surgery.	Meta-analyses already done and created from evidence results **Out of 100 people who have total knee replacement surgery, fewer than 1 (<1%) die, but research is not clear how this compares to people who do not have surgery.** (Moderate certainty)
VTE	Yes. There is one High certainty estimate for this outcome, based on a systematic review (Wilson 2019): 1.23% (95% CI 0.76% to 1.82%). (The other estimate is the Low certainty estimate from Skou 2015 and 2018, based on 3 events among 62 participants. We consider this inappropriate for evidence synthesis in light of Higher certainty results giving a different estimate.)	Meta-analysis created from evidence results **Out of 100 people who have total knee replacement surgery, about 1 (1%) may have a blood clot.** (High certainty) **You may be given medication for a period of**

		time after surgery to help prevent this.
Stiffness requiring brisement forcé	Yes. Only Skou 2015 and 2018 reported on this outcome, with 4 out of 62 patients (6.5%) experiencing this outcome. Given the use of a "per 100" denominator, "about 6 to 7" per 100 will be reported, because 4/62 = 6.45% (which was rounded to 6.5% for single decimal place reporting).	Other: Single primary study **Out of 100 people who have total knee replacement surgery, about 6 to 7 (6% to 7%) may get stiffness in the knee that has to be fixed by moving the knee while the person is under anesthesia.** (Low certainty)
Supracondylar femur fracture	Yes. Only Skou 2015 reported on this outcome. At 1 year, 1 out of 62 patients (1.6%) experienced this outcome, and this outcome was not reported at 2 years.	Other: Single primary study **Out of 100 people who have total knee replacement surgery, about 2 (2%) may have a fracture of part of their knee due to the surgery.** (Low certainty)
Falls		
di Laura Frattura 2018 Systematic review; 3 pre-post design studies totaling 278 patients	No. The di Laura Fattura 2018 systematic review provides Very low certainty evidence of a possible reduction in falls with total knee replacement surgery, based on 3 primary studies totaling 278 people. The range of fall rates among the pre-operative group is 23% to 63%, and this offers an estimate of the rate of falling among those who opt for conservative therapy alone. The range of fall rates among the post-operative group is 12% to 22%, and this offers an estimate of the rate of falling among those who opt for total knee replacement plus conservative therapy. There is considerable imprecision/inconsistency in the individual estimates, so pooling is considered inappropriate. We also note we favor reporting a range rather than a median due to the Very low certainty of the evidence, as the median of the results could imply precision or certainty beyond that which we actually possess.	Range of sufficiently-valid estimates **Out of 100 people who have total knee replacement surgery, 12 to 22 (12% to 22%) may have a fall.** **Out of 100 people who have treatment without surgery, 23 to 63 (23% to 63%) may have a fall.** (Very low certainty)

Conservative (non-surgical) treatment alone

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

It depends on the specific treatment(s) used.

Although serious risks may be uncommon, risks with medication may include the following:

- **Acetaminophen/paracetamol: does not typically have serious risks when taken as directed**
- **NSAIDs: bleeding, which is sometimes serious**
- **tramadol and opioids: can be addictive, withdrawal symptoms if suddenly stopped**
- **duloxetine: changes in thoughts or behavior, withdrawal symptoms if suddenly stopped**
- **injections: infection or bleeding; corticosteroid injections may cause weakening of tendons, possibly contributing to or causing a tear**

You can discuss possible risks in more detail with your health care professional.

(DynaMed Plus 2018, Mayo Clinic 2017, Mayo Clinic 2019)

See also the estimate for risk of falls on the immediately-preceding pages, suggesting that out of 1,000 people who have treatment without surgery, 230 to 630 (23% to 63%) may have a fall. (di Laura Frattura 2018).

FAQ 6: What are the side effects?

Total knee replacement plus conservative therapy

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

It is normal to have some pain after surgery, and it may feel worse at night or with activity. This can last up to several weeks and is part of the knee healing. You will be given pain medicine to help with any pain from the surgery. Some people may feel tired for a short period of time after surgery. This is also normal, because having total knee replacement is a major surgery. People also usually have swelling in the area, and it may take up to three months for this to start going away. It may take up to a year for swelling to go away completely.

You may also have to avoid certain activities that place stress on the knee (this is addressed in further detail in FAQ 7: How long does it take to recover?).

(See FAQ 1 for references.)

In addition to the side effects of surgery, side effects of conservative therapy also apply. (These are noted below.)

Conservative (non-surgical) treatment alone

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

It depends on the treatment(s) used.

Side effects may include:

- **Acetaminophen/paracetamol: does not typically cause side effects**
- **NSAIDs: upset stomach and heartburn**
- **Tramadol and opioids: fatigue, dizziness, constipation, upset stomach**
- **Duloxetine: fatigue, dizziness, dry mouth, constipation or diarrhea, headache, upset stomach**
- **Injections: typically tolerated well, but some may have bruising, swelling, or skin irritation**

You can discuss side effects in more detail with your health care professional.

(DynaMed Plus 2018, Mayo Clinic 2017, Mayo Clinic 2018)

FAQ 7: How long does it take to recover?

Total knee replacement plus conservative therapy

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

Attending / performing prescribed physical therapy and exercises is very important for recovery, including after being discharged from the hospital. In general, assuming recovery is going well, people are often able to return to many of their normal daily activities within 3 to 6 weeks, but people may be advised to avoid any heavier tasks for up to 3 months. They may also be advised to avoid tasks that require standing for prolonged periods or bending for the first 6 weeks.

For resuming specific activities, the following are general timelines people might be able to expect, but these are overall approximations, and all timelines should be tailored to the specific patient:

- Walking without assistive devices: around 6 weeks
- Driving: once the person is able to bend the knee enough to get in and out of the car and operate it safely; this may be as early as 3 weeks, but may take up to 12 weeks
- Returning to work: this depends on the job a person has, but people can usually return to work within 6 to 12 weeks
- Sexual activity: within about 6 to 8 weeks as long as vigorous sex and kneeling positions are avoided
- Sports: low-impact activities (such as walking, golf, biking, swimming) may be possible after about 6 weeks, but high-impact activities (such as jogging, tennis, or contact or jumping sports) should be avoided until the surgeon says it is okay to do these kinds of activities

Fully recovering from surgery may take up to a year, or in some cases 2 years.

Doing the physical therapy and exercises as prescribed is very important to make sure you get the most out of your knee replacement surgery. People are often able to return to most normal activities within 3 to 6 weeks, but activities that place more strain on the knee may not be possible for 12 weeks or longer. People may be able to:

- **walk without assistance by 6 weeks**
- **drive as early as 3 weeks (but it may take up to 12 weeks)**
- **return to work within 6 to 12 weeks**
- **have sex within 6 to 8 weeks**
- **play sports that are easy on the knee (walking, golf, biking, or swimming) in about 6 weeks**

Fully recovering from surgery may take up to a year. In some cases, it may take up to 2 years.
Your healthcare professional will give you more detail on recovery timelines tailored to you.

(See FAQ 1 for references)

Conservative (non-surgical) treatment alone

Pre-Synthesis Efforts: Not applicable

Descriptive Summary

Conservative treatment does not usually need a recovery period, other than patients possibly being advised to rest/avoid strain on the knee for a day or two if given an injection into the knee.

(See FAQ 1 for references.)

Evidence report for total knee replacement plus conservative therapy versus conservative therapy alone for knee osteoarthritis

Reference list

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May 21, 2019

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ALTMAN 2000
Altman D, Machin D, Bryant T, Gardner M. Statistics with Confidence, 2nd ed. 2000. BMJ Books.

BAYLISS 2017
Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, Cooper C, Carr AJ, Arden NK, Beard DJ, Price AJ. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. Lancet. 2017 Apr 8;389(10077):1424-1430. Epub 2017 Feb 14. PubMed

BERSTOCK 2018
Berstock JR, Beswick AD, López-López JA, Whitehouse MR, Blom AW. Mortality After Total Knee Arthroplasty: A Systematic Review of Incidence, Temporal Trends, and Risk Factors. J Bone Joint Surg Am. 2018 Jun 20;100(12):1064-1070. PubMed

BESWICK 2012
Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. BMJ Open. 2012 Feb 22;2(1):e000435. PubMed

BJØRNAŘ 2006
Bjørnarå BT, Gudmundsen TE, Dahl OE. Frequency and timing of clinical venous thromboembolism after major joint surgery. J Bone Joint Surg Br. 2006 Mar;88(3):386-91. PubMed

CRAM 2012
Cram P, Lu X, Kates SL, Singh JA, Li Y, Wolf BR. Total knee arthroplasty volume, utilization, and outcomes among Medicare beneficiaries, 1991-2010. JAMA. 2012 Sep 26;308(12):1227-36. PubMed

DI LAURA FRATTURA 2018
di Laura Frattura G, Filardo G, Giunchi D, Fusco A, Zaffagnini S, Candrian C. Risk of falls in patients with knee osteoarthritis undergoing total knee arthroplasty: A systematic review and best evidence synthesis. J Orthop. 2018 Aug 24;15(3):903-908. PubMed

DYNAMED 2018
DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T360995, Total knee arthroplasty; [updated 2018 Dec 01, cited 2019 May 21]. Available from https://www.dynamed.com/topics/dmp~AN~T360995. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T905974, Venous thromboembolism (VTE) prophylaxis for orthopedic surgery patients; [updated 2018 Nov 30, cited 2019 May 23]. Available from https://www.dynamed.com/topics/dmp~AN~T905974. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T116897, Osteoarthritis (OA) of the knee; [updated 2018 Nov 30, cited 2019 May 21]. Available from https://www.dynamed.com/topics/dmp~AN~T116897. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T232955, Duloxetine; [updated 2018 Nov 30, cited 2019 May 21]. Available from https://www.dynamed.com/topics/dmp~AN~T232955. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T233023, Acetaminophen; [updated 2018 Nov 30, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T233023. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T233086, Ibuprofen; [updated 2018 Nov 30, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T233086. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T233025, Naproxen; [updated 2018 Nov 30, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T233025. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T233475, Tramadol; [updated 2018 Nov 30, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T233475. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T233026, Hydrocodone; [updated 2018 Nov 30, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T233026. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T907747, Hydrocodone/Acetaminophen; [updated 2018 Nov 06, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T907747. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T233077, Oxycodone; [updated 2018 Nov 30, cited place 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T233077. Registration and login required.

DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. T361112, Opioids for chronic noncancer pain; [updated 2018 Dec 04, cited 2019 Apr 09]. Available from https://www.dynamed.com/topics/dmp~AN~T361112. Registration and login required.

FORAN 2015
Foran JRH. Total Knee Replacement. American Academy of Orthopedic Surgeons. Last reviewed/updated August 2015. Accessed May 21, 2019. Available at https://orthoinfo.aaos.org/en/treatment/total-knee-replacement/.

JÄMSEN 2010
Jämsen E, Furnes O, Engesaeter LB, Konttinen YT, Odgaard A, Stefánsdóttir A, Lidgren L. Prevention of deep infection in joint replacement surgery. Acta Orthop. 2010 Dec;81(6):660-6. doi: 10.3109/17453674.2010.537805. Review. PubMed

LO 2019
Lo CWT, Tsang WWN, Yan CH, Lord SR, Hill KD, Wong AYL. Risk factors for falls in patients with total hip arthroplasty and total knee arthroplasty: a systematic review and meta-analysis. Osteoarthritis Cartilage. 2019 Apr 24. pii: S1063-4584(19)30928-8. PubMed

NHS 2016
National Health Service. Knee replacement: Overview. Last reviewed/updated July 25, 2016. Accessed May 21, 2019. Available at https://www.nhs.uk/conditions/knee-replacement/.

National Health Service. Knee replacement: How it is performed. Last reviewed/updated July 25, 2016. Accessed May 21, 2019. Available at https://www.nhs.uk/conditions/knee-replacement/what-happens/.

National Health Service. Knee replacement: Risks. Last reviewed/updated July 25, 2016. Accessed May 21, 2019. Available at https://www.nhs.uk/conditions/knee-replacement/risks/.

National Health Service. Knee replacement: Recovery. Last reviewed/updated July 25, 2016. Accessed May 21, 2019. Available at https://www.nhs.uk/conditions/knee-replacement/recovery/.

NICE 2010
National Institute for Health and Care Excellence. Mini-incision surgery for total knee replacement. Interventional procedures guidance [IPG345]. May 2010. Accessed May 21, 2019. Available at https://www.nice.org.uk/guidance/ipg345.

NIH 2018
National Institutes of Health, US National Library of Medicine. Knee joint replacement. Medline Plus Medical Encyclopedia. Last reviewed/updated August 15, 2018. Accessed May 21, 2019. Available at https://medlineplus.gov/ency/article/002974.htm.

MAYO CLINIC 2019
Mayo Clinic. Hyaluronic Acid (Injection Route). Last reviewed/updated February 2019. Accessed May 21, 2019. Available at https://www.mayoclinic.org/drugs-supplements/hyaluronic-acid-injection-route/description/drg-20074557.

MAYO CLINIC 2017
Mayo Clinic. Knee replacement. Last reviewed/updated December 29, 2017. Accessed May 21, 2019. Available at https://www.mayoclinic.org/tests-procedures/knee-replacement/about/pac-20385276.

Mayo Clinic. Cortisone shots. Last reviewed/updated December 30, 2017. Accessed May 21, 2019. Available at https://www.mayoclinic.org/tests-procedures/cortisone-shots/about/pac-20384794.

RICHARDSON 2019
Richardson SS, Schairer WW, Sculco TP, Sculco PK. Comparison of Infection Risk with Corticosteroid or Hyaluronic Acid Injection Prior to Total Knee Arthroplasty. J Bone Joint Surg Am. 2019 Jan 16;101(2):112-118. PubMed

SKOU 2015
Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, Rasmussen S. A Randomized, Controlled Trial of Total Knee Replacement. N Engl J Med. 2015 Oct 22;373(17):1597-606. Erratum in: BMJ. 2019 Apr 2;365:l1032. PubMed

SKOU 2018
Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Rasmussen S, Simonsen O. Total knee replacement and non-surgical treatment of knee osteoarthritis: 2-year outcome from two parallel randomized controlled trials. Osteoarthritis Cartilage. 2018 Sep;26(9):1170-1180. PubMed

WILSON 2019
Wilson HA, Middleton R, Abram SGF, Smith S, Alvand A, Jackson WF, Bottomley N, Hopewell S, Price AJ. Patient relevant outcomes of unicompartmental versus total knee replacement: systematic review and meta-analysis. BMJ. 2019 Feb 21;364:l352. PubMed