

## Predictors of persistent postsurgical pain following total knee arthroplasty: A protocol for systematic review and meta-analysis

Vahid Ashoorion<sup>a,b</sup>, Behnam Sadeghirad<sup>a,c</sup>, Li Wang <sup>a,d</sup>, Anthony Adili<sup>e,f</sup>, Rachel Couban<sup>a</sup>, Gordon Guyatt<sup>c,e</sup>, and Jason Busse <sup>a,c,d,e</sup>

<sup>a</sup>The Michael G. DeGrootte Institute for Pain Research and Care, McMaster University, Ontario, Canada; <sup>b</sup>Isfahan Medical Education Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran; <sup>c</sup>Department of Health Research Methods, Evidence, and Impact, McMaster University, Ontario, Canada; <sup>d</sup>Department of Anesthesia, McMaster University, Ontario, Canada; <sup>e</sup>The Michael G. DeGrootte Centre for Medicinal Cannabis Research, McMaster University, Ontario, Canada; <sup>f</sup>Department of Surgery, McMaster University, Ontario, Canada

### ABSTRACT

**Background:** Total knee arthroplasty (TKA) is a commonly performed procedure, primarily when knee joints have been damaged by progressive arthritis; however, over 20% of surgical patients develop persistent postsurgical pain (PPSP). We plan to conduct a systematic review and meta-analysis of factors associated with the development of PPSP following TKA.

**Methods:** We will include peer-reviewed cohort or case-control studies that explore, in an adjusted model, factors associated with the development of PPSP after TKA. We will identify eligible studies, in any language, by a systematic search of MEDLINE, EMBASE, CINAHL, AMED, Scopus, SPORTDiscus, and PsycINFO, from inception of each database. Pairs of reviewers will, independently and in duplicate, screen titles and abstracts of identified citations, review the full texts of potentially eligible studies, and extract information from eligible studies. When possible, we will pool estimates of association for all independent variables reported by more than one study and report both an adjusted odds ratio and the absolute risk increase and associated 95% confidence intervals (Cis). We will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to summarize the quality of evidence for all meta-analyses as high, moderate, low, or very low.

**Discussion:** Our results will facilitate identification of patients at risk for the development of PPSP following TKA, highlight promising predictors for further study, and help guide the design of interventional studies to improve prognosis of high-risk patients.

### RÉSUMÉ

**Contexte:** L'arthroplastie complète du genou est une intervention communément réalisée, principalement lorsque les articulations des genoux ont été endommagées par l'arthrite dégénérative; toutefois, plus de 20 % des patients ayant été opérés développent de la douleur postopératoire persistante. Nous comptons effectuer une revue systématique et une méta-analyse des facteurs associés au développement de la douleur postopératoire persistante après une arthroplastie complète du genou.

**Méthodes:** Nous inclurons les études de cohorte ou les études cas-témoins examinées par des pairs qui explorent, dans un modèle ajusté, les facteurs associés au développement de la douleur postopératoire persistante après une arthroplastie complète du genou. Nous recenserons les études admissibles, peu importe la langue dans laquelle elle sont écrites, en faisant une recherche systématique dans MEDLINE, EMBASE, CINAHL, AMED, Scopus, SPORTDiscus et PsycINFO, depuis les tout débuts de chaque base de données. Des paires d'examineurs passeront en revue les titres et les résumés des citations répertoriées de manière indépendante et en double, puis ils examineront les textes complets des études potentiellement admissibles et en extraîtront l'information. Lorsque possible, nous ferons une estimation globale de l'association pour toutes les variables indépendantes rapportées par plus d'une étude et rapporterons les rapports de cote ajustés, ainsi que l'augmentation du risque absolu et les IC à 95 % associés. Nous utiliserons l'approche GRADE pour résumer la qualité des données probantes pour toutes les méta-analyses, afin de déterminer si elle est élevée, modérée, faible ou très faible.

**Discussion:** Nos résultats faciliteront le repérage des patients à risque de développer de la douleur postopératoire persistante après une arthroplastie complète du genou, mettront en

### ARTICLE HISTORY

Received 4 March 2019

Revised 11 April 2019

Accepted 1 May 2019

### KEYWORDS

knee replacement; chronic pain; risk factors; prognosis; meta-analysis

**CONTACT** Vahid Ashoorion  [ashooriv@mcmaster.ca](mailto:ashooriv@mcmaster.ca)  The Michael G. DeGrootte Institute for Pain Research and Care, McMaster University, 1280 Main St. West, Hamilton, Ontario, L8S 4K1, Canada.

**Systematic review registration:** The protocol has been registered at the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42018065943).

 Supplemental data for the article can be accessed on the [publisher's website](#)

© 2019 The Author(s). Published with license by Taylor & Francis Group, LLC.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

lumière les prédicteurs prometteurs pour de futures et contribuerot à orienter la conception d'études interventionnelles afin d'améliorer le pronostic des patients à haut risque.

## Introduction

Total knee arthroplasty (TKA) is one of the most common orthopedic surgeries performed worldwide, primarily for patients with advanced osteoarthritis who have failed nonoperative treatment.<sup>1,2</sup> In 2016, more than 67 000 patients underwent TKA in Canada.<sup>3</sup> The prevalence of osteoarthritis is increasing, due to higher rates of obesity and increasing life expectancy in Western societies,<sup>4</sup> and from 2005 to 2030 the number of TKAs performed in the United States is expected to grow by more than six times.<sup>5</sup>

Pain is the primary reason for patients to undergo knee replacement with the expectation that surgery will provide relief<sup>6</sup>; however, more than 20% of patients develop persistent postsurgical pain (PPSP), with higher rates associated with revision surgery.<sup>7–10</sup> Moreover, despite advances in surgical technology and perioperative anesthetic management, the incidence of PPSP after TKA surgery has not decreased.<sup>11</sup>

We found eight reviews that have explored predictors of PPSP following TKA, of which three were narrative<sup>12–14</sup> and five were systematic reviews<sup>15–19</sup> (Table 1). The systematic reviews all had important limitations, including outdated searches and failure to evaluate the overall quality of evidence.<sup>14–19</sup> The two systematic reviews that reported meta-analyses ignored nonsignificant risk factors when the measures of association were not reported, which risks overestimating the magnitude of associations. Statistical pooling in both reviews was problematic. One review used Fisher's *Z* effect size for pooling estimates of

association from a variety of statistical tests (i.e., correlation, *t* test, analysis of variance, chi-square, linear regression, and logistic regression).<sup>14</sup> Interpretation of results pooled using Fisher's *Z* is nonintuitive, and pooling estimates from a variety of statistical analyses with different properties is inappropriate. The other review that provided pooled estimates only looked at procedural and surgical techniques as predictors of anterior knee pain following primary TKA, combined both unadjusted and adjusted estimates of association, and pooled treatment effects from randomized controlled trials with measures of association from observational studies.<sup>19</sup> We propose to conduct a new systematic review and meta-analysis of observational studies to identify predictors of PPSP following TKA that addresses limitations of prior reviews.

## Methods

### Standardized reporting

We registered our protocol with PROSPERO (CRD42018065943) and will follow the Meta-analysis of Observational Studies in Epidemiology Statement for reporting of our systematic review.<sup>20</sup>

### Data sources and search strategy

We will systematically search MEDLINE, EMBASE, CINAHL, AMED, Scopus, SPORTDiscus, and PsycINFO, from inception of each database, without any language restriction. An experienced medical

**Table 1.** Characteristics of prior systematic reviews on predictors of PPSP after TKA.

Citation	Eligible study designs	Search period	Databases searched	Assessed risk of bias	Assessed overall certainty in evidence	Type of synthesis
Harmelink et al. <sup>15</sup>	Observational studies	January 2000 and January 2016	EMBASE and MEDLINE	Yes	Yes	Narrative
Vissers et al. <sup>16</sup>	Observational studies with at least 6 weeks' follow-up (included both total knee and total hip arthroplasty)	From database inception to January 2011	MEDLINE and EMBASE	Yes	No	Narrative
Wylde et al. <sup>17</sup>	Cohort studies	From database inception to October 2016	MEDLINE, EMBASE and PsycINFO	Yes	No	Narrative
Lewis et al. <sup>18</sup>	Cohort, case-control, or cross-sectional studies	From 1980 to December 2012	MEDLINE, EBSCO, Scopus, CINAHL, SPORTDiscus, and AMED	Yes	No	Pooled adjusted and nonadjusted measures of association
Duan et al. <sup>19</sup>	RCTs or observational studies	From database inception to July 25, 2017	MEDLINE, EMBASE, and Cochrane Central	Yes	No	Pooled adjusted and crude odds ratios from RCTs and observational studies

PPSP = persistent postsurgical pain; TKA = total knee arthroplasty; RCT = randomized controlled trial.

librarian (R.C.) has developed search strategies for each database (Appendix). We will review reference lists from eligible studies and related reviews for additional potentially eligible studies.

### **Eligibility criteria and study selection**

We will include peer-reviewed cohort and case-control studies that enroll adults (18 years or older) who undergo TKA and investigate, in an adjusted analysis, risk factors for PPSP after TKA. Studies will be ineligible if their predictive models include significant associations with variables collected after baseline, because the association may be a result of PPSP. When study populations overlap by more than 50% among eligible articles, we will include only the study with the largest sample size and longest follow-up. We will exclude conference abstracts.

Pairs of reviewers will screen the titles, abstract, and full-text articles of potentially eligible studies, independently and in duplicate. Reviewers will, when necessary, resolve disagreements by discussion or by consultation with an adjudicator. We will use online systematic review software (Distiller SR, Evidence Partners [Internet]. Ottawa (ON), Canada; <https://www.evidencepartners.com/products/distillersr-systematic-review-software/>) to facilitate literature screening and prepare a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram to illustrate the flow of studies through the selection process.

### **Data extraction**

Pairs of reviewers, working independently and in duplicate, will extract relevant information from all eligible studies. Before starting data abstraction, we will conduct calibration exercises to ensure consistency between reviewers. We will use piloted, standardized forms to extract the following information: (1) study characteristics (e.g., authors, publication year, country of origin, funding source); (2) study population characteristics (e.g., sample size, age, sex distribution, underlying condition leading to TKA, measure of disease severity, opioid use prior to surgery); (3) surgical procedure (e.g., unilateral or bilateral, primary or revision surgery, cemented, type of prosthesis); (4) risk of bias and statistical analysis approaches; and (5) measures of association with PPSP for all independent risk factors explored in an adjusted model.

When a study reports more than one regression model, we will use the model with the largest population, longest follow-up, or largest number of risk factors. When studies report the dependent variable

(PPSP) as both a dichotomous outcome (e.g., presence or absence of PPSP) using logistic regression and as a continuous outcome (e.g., pain score) using linear regression, we will use the results from the logistic regression model. All disagreements on data extraction will be resolved through discussion. We will contact authors for clarification of eligibility or missing data.

### **Risk of bias assessment**

We will use the following criteria from the *Users' Guides to the Medical Literature* to assess the risk of bias: (1) representativeness of study population; (2) validity of outcome assessment; (3) proportion of missing data and loss to follow-up ( $\geq 20\%$  will be considered high risk of bias); and (4) whether predictive models are appropriately adjusted.<sup>21</sup> We define a model as appropriately adjusted when it includes age, sex, and a measure of disease severity (e.g., pain intensity, type of injury, grade of osteoarthritis). We will assess whether the adjusted model was data driven (only those with significant associations in bivariate analysis were entered in the final model) or theory driven (all risk factors of interest were entered).

### **Data synthesis**

We will assess interrater agreement of full-text screening with the kappa statistic.<sup>22</sup> We will report intensity of PPSP across studies as the median and interquartile range, after converting all pain scales to a 10-cm visual analogue scale.<sup>23,24</sup> For continuous predictors that are entered as categorical variables in the regression model (i.e., multiple odds ratios [ORs] reported for one variable), we will assume linearity and that the associations across categories are independent of each other and calculate the OR and 95% confidence interval (CI) for each category using Bucher's approach and combine ORs using the inverse variance method to produce a single OR for the predictor.<sup>25,26</sup> In studies that excluded predictors from their final adjusted analysis due to nonsignificant association in univariate or bivariate analysis or the adjusted OR and its 95% CI were not reported due to nonsignificant association in final adjusted model, we will use an OR of 1 and impute the associated variance using the hot deck approach to avoid overestimation of association.<sup>26,27</sup>

We will pool all independent factors assessed for an association with PPSP that are reported by more than one study as an OR and associated 95% CI and calculate the absolute risk increase. We will estimate the baseline risk for PPSP after TKA using the lowest rate of PPSP from the study eligible for review with the

largest sample size among studies at low risk of bias. When the measure of association is reported as relative risk, we will convert it to an OR using the reported baseline risk in the reference or unexposed group (participants without the risk factor).<sup>28</sup> We will use DerSimonian-Laird random effects models for all meta-analyses.<sup>29</sup> We will assess publication bias by visual assessment of funnel plots and Egger's test when at least ten studies are included in a meta-analysis.<sup>30,31</sup>

If pooling is not possible, we will explore the consistency of association between pooled results and studies reporting the same predictors that could not be pooled. We will define nonpoolable predictors as promising if they meet the following criteria: (1) a statistically significant association with PPSP of  $P \leq 0.01$ , (2) a large magnitude of association ( $OR \geq 2.0$ ), and (3) a sample size of at least 500 patients. Data analysis will be performed using STATA software (Version 15.1).

### **Subgroup analyses, metaregression, and sensitivity analyses**

Statistical tests of heterogeneity can be misleading when estimates of precision are very narrow due to large sample sizes; thus, we will evaluate heterogeneity for all pooled estimates through visual inspection of forest plots.<sup>32</sup> We will explore four a priori hypotheses to explain variability between studies, assuming a larger association with PPSP with the following study characteristics: (1) longer duration of follow-up, (2) higher threshold for PPSP (e.g., moderate to severe pain vs. no to mild pain), (3) larger proportion of patients lost to follow-up, and (4) greater risk of bias on a criterion-by-criterion basis. In addition, we will conduct a subgroup analysis exploring studies that adjusted for preoperative pain vs. those adjusted with another measure of disease severity (e.g., grade of Osteoarthritis (OA)), and if we find a significant subgroup effect we will prioritize pooled measures of association from studies that adjusted for pain severity. We will conduct subgroup analyses only if each subgroup contains three or more studies and explore for subgroup effects with a test of interaction.<sup>33</sup> We will examine the effect of imputing data for nonsignificant predictors and converting categorical data for patient age to continuous data in a sensitivity analysis.

### **Certainty of evidence**

We will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the certainty of evidence as high,

moderate, low, or very low, based on risk of bias, inconsistency, indirectness, imprecision, and publication bias.<sup>34</sup> Once we have established the baseline risk of PPSP after TKA, we will estimate the absolute increase in risk for both modifiable and nonmodifiable factors that would alter clinical decision making and rate down for imprecision if the 95% CI associated with the risk difference includes this threshold.

## **Discussion**

Due to the large volume of TKAs performed each year and the high rate of patients who develop PPSP, there is an urgent need for a high-quality systematic review to identify factors associated with the development of persistent pain. Modifiable factors that show large associations have the potential to be directly targeted to reduce the rate of PPSP after TKA. Moreover, patients who present with important nonmodifiable factors may benefit from nonspecific interventions. Either scenario would help direct clinical trials to establish the effectiveness of promising strategies.

Our proposed review has several strengths in relation to prior reviews. First, we will update the search. Second, we will pool similar predictors across studies and optimize interpretability by reporting measures of association in both relative and absolute measures. Third, we will incorporate nonsignificant predictors into our meta-analyses by imputing measures of association when they are not reported to avoid overestimating the strength of associations. Fourth, we will assess the overall certainty of evidence using the GRADE approach.

A potential limitation is the quality and comprehensiveness of reporting in the primary literature. We may find that nonmodifiable factors, such as disease severity or surgical approaches, have been commonly explored for their association with PPSP after TKA, whereas modifiable factors, such as anxiety or coping abilities, have not. The findings of our review will help inform patients considering TKA about their prognosis and identify key areas for future research.

## **Acknowledgments**

Appreciation is extended to the Michael G. DeGroot Institute for Pain Research and Care, McMaster University for support of Vahid Ashoorion to lead this systematic review as a part of his postdoctoral research.

## **Disclosure statement**

No potential conflict of interest was reported by the authors.

## Funding

This work was supported by the Michael G. DeGroot Institute for Pain Research and Care.

## ORCID

Li Wang  <http://orcid.org/0000-0003-1585-8846>

Jason Busse  <http://orcid.org/0000-0002-0178-8712>

## References

- Singh JA, Lewallen DG. Cerebrovascular disease is associated with outcomes after total knee arthroplasty: A U.S. Total Joint Registry Study. *2012*;1(3):233–45.
- Singh JA, Lewallen DG. Medical and psychological comorbidity predicts poor pain outcomes after total knee arthroplasty. *Rheumatol (United Kingdom)*. *2013*;52:916–23.
- Canadian Institute for Health Information. Hip and knee replacements in Canada, 2016–2017. [Internet]. *2018* [accessed 2019 Apr 11]. <https://www.cihi.ca/sites/default/files/document/cjrr-annual-report-2018-en.pdf>
- Dowsey MM, Nikpour M, Dieppe P, Choong PFM, Singh JA, O'Byrne MM, Colligan RC, Lewallen DG, Riddle DL, Wade JB, et al. Associations between pre-operative radiographic changes and outcomes after total knee joint replacement for osteoarthritis. *Clin Orthop Relat Res*. [Internet]. *2010*;15(5):804–12 [accessed 2016 Dec 9]. <http://www.ncbi.nlm.nih.gov/pubmed/21239114>.
- Singh JA, Gabriel SE, Lewallen DG. Higher body mass index is not associated with worse pain outcomes after primary or revision total knee arthroplasty. *J Arthroplasty*. [Internet]. *2011* Apr;26(3):366–374.e1 [accessed 2016 Dec 9]. <http://linkinghub.elsevier.com/retrieve/pii/S0883540310001464>.
- 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*. [Internet]. *2012* Feb 22;2(1):e000435 [accessed 2018 Dec 6]. <http://www.ncbi.nlm.nih.gov/pubmed/22357571>.
- Baker PN, Van Der Meulen JH, Lewsey J, Gregg PJ. The role of pain and function in determining patient satisfaction after total knee replacement data from the national joint registry for england and wales. *J Bone Jt Surg [Br]*. [Internet]. *2007*;89(7):893–900. [accessed 2016 Dec 9]. <http://www.bjj.boneandjoint.org.uk/content/89-B/7/893.short>.
- Brander VA, Stulberg SD, Adams AD, Harden RN, Bruehl S, Stanos SP, Houle T. Predicting total knee replacement pain: a prospective, observational study. *Clin Orthop Relat Res*. *2003* Dec 04. *2003*;416:27–36. doi:10.1097/01.blo.0000092983.12414.e9.
- Burke LE, Ma J, Azar KMJ, Bennett GG, Peterson ED, Zheng Y, Riley W, Stephens J, Shah SH, Suffoletto B, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: A scientific statement from the American heart association. *Circulation*. *2015*;132:1157–213. accessed <http://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed13&AN=2015395729>.
- Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. *Pain* [Internet]. *2011* Mar;152(3):566–72 [accessed 2016 Dec 9]. <http://www.ncbi.nlm.nih.gov/pubmed/21239114>.
- Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* [Internet]. *2006*;367: 1618–25 [accessed 2016 Dec 9]. <http://linkinghub.elsevier.com/retrieve/pii/S014067360668700X>.
- Chodór P, Kruczyński J. Predicting persistent unclear pain following primary total knee arthroplasty. *Ortop Traumatol Rehabil*. [Internet]. *2016* Nov 30;18(6):527–36 [accessed 2018 Dec 10]. <http://www.ortopedia.com.pl/abstracted.php?level=5&ICID=1230507>.
- Kim DH, Pearson-Chauhan KM, McCarthy RJ, Buvanendran A. Predictive factors for developing chronic pain after total knee arthroplasty. *J Arthroplasty*. [Internet]. *2018* Nov;33(11):3372–78 [accessed 2018 Dec 10]. <https://linkinghub.elsevier.com/retrieve/pii/S0883540318306715>.
- Lavand'homme P, Thienpont E. Pain after total knee arthroplasty: a narrative review focusing on the stratification of patients at risk for persistent pain. *Bone Joint J*. [Internet]. *2015* Oct;97–B(10 Suppl A):45–48 [accessed 2016 Jan 5]. <http://www.ncbi.nlm.nih.gov/pubmed/26430086>.
- Harmelink KEM, Zeegers AVCM, Hulleger W, Hoogboom TJ, Nijhuis-van der Sanden MWG, Staal JB. Are there prognostic factors for one-year outcome after total knee arthroplasty? A systematic review. *J Arthroplasty*. [Internet]. *2017* Dec;32(12):3840–3853.e1 [accessed 2018 Dec 10]. <https://linkinghub.elsevier.com/retrieve/pii/S0883540317305946>.
- Vissers MM, Bussmann JB, Verhaar JAN, Busschbach JJV, Bierma-Zeinstra SMA, Reijman M. Psychological factors affecting the outcome of total hip and knee arthroplasty: A systematic review. *Semin Arthritis Rheum*. [Internet]. *2012* Feb;41(4):576–88 [accessed 2018 Dec 10]. <https://linkinghub.elsevier.com/retrieve/pii/S0049017211001971>.
- Wylde V, Beswick AD, Dennis J, Gooberman-Hill R. Post-operative patient-related risk factors for chronic pain after total knee replacement: a systematic review. *BMJ Open*. [Internet]. *2017* Nov 3;7(11):e018105 [accessed 2018 Dec 10]. <http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2017-018105>.
- Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. *Br J Anaesth*. [Internet]. *2015*;114(4):551–61. [accessed 2016 Jan 5 Apr1]. <http://bja.oxfordjournals.org/lookup/doi/10.1093/bja/aeu441>
- Duan G, Liu C, Lin W, Shao J, Fu K, Niu Y, Wang F. Different factors conduct anterior knee pain following primary total knee arthroplasty: A systematic review and meta-analysis. *J Arthroplasty*. [Internet]. *2018* Jun;33(6):1962–1971.e3 [accessed 2018 Dec 14]. <http://www.ncbi.nlm.nih.gov/pubmed/29398258>.

20. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* [Internet]. 2000 Apr 19;283(15):2008–12 [accessed 2019 Feb 11]. <http://www.ncbi.nlm.nih.gov/pubmed/10789670>.
21. Randolph A, Cook DJ, Guyatt GH. Prognosis. In: Guyatt GH, Rennie D, Meade MO, Cook DJ editors. *Users' guides to the medical literature*. 3rd. New York (Chicago, San Francisco, Athens, London, Toronto): McGraw Hill; 2015. p. 421–30.
22. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* [Internet]. 1977 Mar;33(1):159–74 [accessed 2016 Dec 9]. <http://www.ncbi.nlm.nih.gov/pubmed/843571>.
23. Thorlund K, Walter SD, Johnston BC, Furukawa TA, Guyatt GH. Pooling health-related quality of life outcomes in meta-analysis—a tutorial and review of methods for enhancing interpretability. *Res Synth Methods*. [Internet]. 2011 Sep 1;2(3):188–203 [accessed 2019 Apr 9]. doi:<http://doi.wiley.com/10.1002/jrsm.46>.
24. Johnston BC, Patrick DL, Thorlund K, Busse JW, da Costa BR, Schünemann HJ, Guyatt GH. Patient-reported outcomes in meta-analyses –part 2: methods for improving interpretability for decision-makers. *Health Qual Life Outcomes*. [Internet]. 2013 Dec 21;11(1):211 [accessed 2019 Apr 9]. <http://www.ncbi.nlm.nih.gov/pubmed/24359184>.
25. Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol*. [Internet]. 1997 Jun;50(6):683–91 [accessed 2019 Feb 20]. <http://www.ncbi.nlm.nih.gov/pubmed/9250266>.
26. Wang L, Guyatt GH, Kennedy SA, Mha BR, Bhsc HYK, Mbbs AK, Chang Y, Craigie S, Dc CPBDA, Couban RJ, et al. Predictors of persistent pain after breast cancer surgery: a systematic review and meta-analysis of observational studies. *Can Med Assoc J*. 2016 July 11;188:1–10. doi:10.1503/cmaj.151276.
27. Andridge RR, Little RJA. A review of hot deck imputation for survey non-response. *Int Stat Rev*. [Internet]. 2010 Apr;78(1):40–64 [accessed 2018 Dec 11]. <http://www.ncbi.nlm.nih.gov/pubmed/21743766>.
28. Wang Z. Converting odds ratio to relative risk in cohort studies with partial data information. *J Stat Softw*. [Internet]. 2013;55(5):1–11. [accessed 2019 Feb 19 Oct22]. <http://www.jstatsoft.org/v55/i05/>
29. Murad H, Montori V, Ioannidis J, Prasad K, Cook D, Guyatt GH. 2015. Fixed-effects and random-effects models. In: Guyatt GH, Rennie D, Meade M, Cook DJ, editors. *Users' guides to the medical literature: A manual for evidence-based clinical practice*. 3rd ed. New York, Toronto: McGraw Hill; 2015;507–14.
30. Higgins J, Thomas J, Li T, Page M, Welch V, Cumpston M, Chandler J, Mellor L. *Cochrane handbook for systematic reviews of interventions | cochrane training* [Internet] accessed. 2018 Dec 15 <https://training.cochrane.org/handbook>.
31. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, McGinn T, Hayden J, Williams K, Shea B. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. *BMJ*. [Internet]. 2015 Mar 16;350(mar16 7):h870–h870 [accessed 2018 Dec 15]. <http://www.ncbi.nlm.nih.gov/pubmed/25775931>.
32. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I 2 in assessing heterogeneity may mislead. *BMC Med Res Methodol*. [Internet]. 2008 Dec 27;8(1):79 [accessed 2019 Feb 11]. <http://www.ncbi.nlm.nih.gov/pubmed/19036172>.
33. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ*. [Internet]. 2003 Jan 25;326(7382):219 [accessed 2019 Apr 9]. <http://www.ncbi.nlm.nih.gov/pubmed/12543843>.
34. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, McGinn T, Hayden J, Williams K, Shea B, et al. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. *BMJ*. [Internet]. 2015;350(mar16 7):h870–h870. [accessed 2016 Dec 9]. <http://www.bmj.com/cgi/doi/10.1136/bmj.h870>.