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Is patellar resurfacing superior to patellar retention in primary TKA? A systematic review of overlapping meta-analyses --Manuscript Draft--

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Abstract:	Purpose: The need of patellar resurfacing in total knee arthroplasty (TKA) is a subject of debate. This systematic review of overlapping meta-analyses aimed to assess and analyze current evidence regarding patellar resurfacing and non-resurfacing in TKA. Methods: A systematic literature search was performed in March 2017 in PubMed, CINHAL and Cochrane Library. Inclusion criteria were meta-analysis of randomized controlled trials that compared TKA with and without patellar resurfacing considering as outcomes re-operations rate, complications, anterior knee pain, functional scores. The quality of meta-analyses was evaluated with AMSTAR score and the most relevant meta-analysis was determined by applying the Jadad algorithm. Results: Ten meta-analyses, published between 2005 and 2015, were included in the systematic review. Two studies found a significantly increased Knee Society Score (KSS) in the resurfacing group. According to four meta-analyses, anterior knee pain incidence was lower in resurfacing group. Six of the included studies described a greater risk of re-intervention in the non-resurfacing groups. The overall quality of included studies was moderate. The most relevant meta-analysis reported no differences in functional scores and incidence of anterior knee pain between the groups. Conclusions: Comparable outcomes were found when comparing patellar resurfacing and non-resurfacing in TKA. The higher risk of re-operations after non-resurfacing should be interpreted with caution due to the methodological limitations of the meta-analyses regarding search criteria, heterogeneity and the inherent bias of easier indication to reoperation when the patella is not resurfaced.

Suggested Reviewers:	
	Patella; Arthroplasty, Replacement, Knee; Patellar resurfacing; patellofemoral; Meta-analysis; Review; knee

Is patellar resurfacing superior to patellar retention in primary TKA? A systematic review of overlapping meta-analyses

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Level of Evidence: Level II, systematic review of meta-analyses

Introduction

The need of resurfacing the patella in total knee arthroplasty (TKA) is an unresolved controversy. There are three different possible approaches: systematic resurfacing, selective resurfacing and systematic non-resurfacing [49]. Systematic resurfacing is supposed to be effective in reducing reoperation rate, postoperative anterior knee pain and improving knee function [26]. Advocates of systematic non-resurfacing claim lesser intra-operative complications, decreased surgical time and similar clinical results [48]. General indications for selective resurfacing have been reported in literature, however there are still no universally accepted guidelines [2, 35, 49]. In order to resolve this issue, a number of studies have been published, including randomized controlled trials (RCTs) and high level quality studies [5, 10, 11, 16, 24, 25]. The results of these studies have been addressed in several meta-analyses in the past few years, without reaching definitive conclusions and with results that are somehow controversial, especially regarding anterior knee pain and functional scores [3, 12, 17, 20, 29, 39, 41, 42, 44, 45]. Systematic reviews of meta-analyses within the same topic have been conducted in order to present and investigate similar controversies on rotator cuff tears, anterior cruciate ligament reconstruction and Achilles tendon rupture [30, 47, 59-61]. The Jadad algorithm [22] has been employed to "select the most relevant and valid of the conflicting reviews". The algorithm is based on the evaluation of the question asked by the various meta-analyses, the similarity of included trials and their quality, the selection criteria and the quality of data synthesis and statistical analysis.

To our knowledge, there is no systematic review of overlapping meta-analyses investigating the relative effects between patellar resurfacing and non-resurfacing during TKA. The objective of the present study was to perform a systematic review of overlapping meta-analyses regarding patellar resurfacing versus non-resurfacing during TKA, in order to answer the following questions: (1) Is patellar resurfacing superior to non-resurfacing regarding clinical outcomes such as anterior knee pain or universally recognized knee scores?; (2) Is revision rate superior in patellar resurfacing or

non-resurfacing?; (3) Are infection rates or mechanical complications more frequent in the resurfacing group?; (4) Which is the most relevant and valid meta-analysis on patellar resurfacing vs non resurfacing according to the Jadad algorithm?

Material and Methods

Search strategy and inclusion criteria:

Present study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [31] guidelines. A systematic literature search was performed by two independent investigators on March 2017 in the databases of PubMed, CINHAL and Cochrane Library. The search was further complemented with screening of the website *clinicaltrials.gov*. The keywords used were "patella*", combined with "TKA" OR "total knee replacement" OR "total knee prosthesis" OR "total knee arthroplasty" AND "meta-analysis". No language restrictions were applied. The references of the included studies were manually checked to find any relevant meta-analyses missed by the electronic search. The titles and abstracts were first reviewed, and the full texts were acquired if the information was not sufficient to determine eligibility. Disagreements were settled by discussion, and the senior author was consulted when necessary.

The inclusion criteria of the present systematic review were: meta-analysis of RCTs or quasi-randomized controlled trials; comparison between the outcomes of TKA with patellar resurfacing or non-resurfacing; investigation of at least one main outcome such as reoperations, complications, anterior knee pain, functional scores. Narrative reviews, systematic reviews without meta-analysis,

A piloted form was designed for data extraction prior to study start and two investigators independently extracted the following information from each meta-analysis: first author, journal, year of

meetings abstract and correspondences were excluded.

publication, databases for search and date of search, primary study design, the number of RCTs included. Details of methodology such as level of evidence, software used, use of execution of subgroup analysis, sensitivity analysis, meta-regression or evaluation of publication bias were collected as well. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) [19] guidelines were applied during data extraction. This is a common, sensible and transparent approach to grade quality (or certainty) of evidence and strength of recommendations in scientific literature. Finally, the results from each meta-analysis were extracted and the heterogeneity of outcomes was assessed.

Quality evaluation:

The quality of the included meta-analyses was evaluated by the Oxford Levels of Evidence [58, 62]. A Level I meta-analysis was defined by including Level I RCTs; a level II meta-analysis was defined by including at least one quasi-randomized study (with inadequate randomization) or low-quality RCTs (e.g. <80% follow-up rate). Additionally, A Measurement Tool to Assess Systematic Reviews (AMSTAR)[52] was applied. The AMSTAR has been widely used to evaluate the quality of systematic reviews [30, 47, 59-61]. This is an eleven items score, ranging from a minimum of zero to a maximum of eleven points, indicating the highest quality. The quality of the meta-analyses was independently evaluated by two authors. Potential disagreements between authors were settled by discussion, and the senior author was consulted if necessary.

Application of Jadad decision algorithm:

The Jadad algorithm was applied to evaluate outcomes and quality parameters of the meta-analyses that only included RCTs [22]. The Jadad Decision Algorithm was designed based on following questions: (1) Do the meta-analyses ask the same question? (2) Do the meta-analyses include the same studies? (3) Do the meta-analyses containing the same trials have the same methodological

quality? (4) Do the discordant meta-analyses including different trials use the same selection criteria? This method has been already employed to offer treatment recommendations among meta-analyses with discordant conclusions [30, 47, 59-61]. The algorithm was independently applied by three authors, who reached a consensus regarding which meta-analysis offered the best available evidence.

The meta-analysis of the highest quality was selected based on the following factors: publication status and methodology of the primary studies, language restrictions and the analysis of data on individual patients. Concerning the publication characteristics, the included meta-analyses were published over an extended period of time; thus, more recent meta-analyses were preferred to less recent once.

Results

The initial search yielded a total of 484 results. After duplicate removal, 428 papers were screened. Of these, 418 studies were excluded because not meeting the inclusion criteria. Finally, 10 meta-analyses were included in the final systematic review [3, 12, 17, 20, 29, 39, 41, 42, 44, 45] (Figure 1). The included meta-analyses were published between 2005 and 2015, and included a different number of RCTs, ranging from 10 RCTs in the meta-analysis by Fu et. al to 18 RCTs in the one published by Pavlou et al. (Table 4). In total, 35 individual studies, published between 1983 and 2012, were included in the eligible meta-analyses [1, 4-11, 14-18, 21, 23-25, 27, 28, 32-34, 36-38, 40, 43, 46, 50, 51, 53-57], and two studies were included in all 10 meta-analyses (Table 5). All meta-analyses were found in the Pubmed database, nine in the Cochrane Library and six in the Embase database. One meta-analysis was found in the database of unpublished studies (Es. clinical-trial.org) and four meta-analyses applied language restriction (Table 6). The most frequently used software for data analysis in included meta-analyses was RevMan (Open source software, Cochrane collaboration). The results of each meta-analysis are depicted in Figure 3.

Quality appraisal

Three meta-analyses included both RCTs and quasi-randomized controlled trials, however, all meta-analyses were determined as level of evidence II due to the low quality of several of the included RCTs. Four meta-analyses did not perform any form of quality appraisal of the included RCTs, while only two meta-analyses used the PRISMA guidelines and no one reported the evidence according to the GRADE guidelines (Table 1). The result of AMSTAR score ranged from 3 to 9, with none of the meta-analyses presenting a-priori design (Table 2).

All the meta-analyses reported some entity of heterogeneity for at least one of the investigated outcomes. Four studies performed a sensitivity analysis, three studies performed a subgroup analysis, one performed a meta-regression and four investigated publication bias. The outcome with the lowest heterogeneity was the risk of re-operation, either in general or related to patello-femoral problems. The outcomes with higher heterogeneity were the anterior knee pain and the Knee Society Score (KSS) function score (Table 3). The study by He et Al. was the only to perform a subgroup analysis based on study quality according to the Detsky scale [13]. Finally, the study by He et al. was selected as the meta-analysis offering the best current evidence (Figure 2)

Subjective outcomes:

<u>Functional scores</u>: Concerning postoperative scores, all meta-analyses analyzed different scales for reporting of clinical outcomes. The majority of the meta-analyses did not find any significant differences in functional scores between patellar resurfacing and non-resurfacing. Two studies found a significantly increased KSS score in the resurfacing group compared to the non-resurfacing. No differences concerning subjective satisfaction were found when analyzed in three articles (29, 39, 45).

<u>Pain</u>: All meta-analyses included anterior knee pain as one of the main outcomes. According to four meta-analyses, the incidence of anterior knee pain was lower in the resurfacing group. In the re-

maining six articles, no statistically significance was found. Two meta-analyses specifically evaluated knee pain scores and one analyzed the visual analogue scale (VAS) without finding any significant difference. Stair climbing pain was significantly reduced in the resurfacing group in one meta-analysis.

Reoperations:

Six of the included studies concluded a greater risk of re-intervention in the non-resurfacing group. Four studies described a greater risk of re-operation specifically related to patello-femoral problems. No meta-analysis clearly addressed the non patello-femoral related risk of re-intervention. No article reported a lower risk for reoperation with the patellar non-resurfacing approach.

Complications:

<u>Complications related to patello-femoral joint</u>: Considering general complications related to patella-femoral problems, one study found that patellar resurfacing led to significantly less complications compared to non-resurfacing. One study reported no significant difference, and the other studies did not report data on this topic.

<u>Others</u>: According to two meta-analyses there were no difference in risk of infection between the groups. One meta-analysis addressed both post-operative patellar tilt and patellar shift without finding any significant difference between the groups.

Results of Jadad Decision Algorithm:

The meta-analysis by He et al., [20] was selected as the study of the highest quality according to the Jadad algorithm. This study did not find differences in KSS score and KSS function, incidence of anterior knee pain and pain scale according to the Standardized Mean Difference (SMD) between patellar resurfacing and non-resurfacing. Risk of re-operation was higher after non-resurfacing, however, when the authors considered only high quality RCTs, no differences were reported.

Discussion

The aim of this study was to perform a systematic review of overlapping meta-analyses on clinical and functional outcomes of patellar resurfacing compared with non-resurfacing in order to identify and evaluate controversies among meta-analyses of this topic. It was shown that a majority of the meta-analyses unanimously reported equivalent results after patellar resurfacing compared with non-resurfacing in terms of functional scores and complication rates, however, an increased risk of reoperation after patellar non-resurfacing was reported. Across all outcomes that this review examined, non-resurfacing of the patella never demonstrated a superior outcome compared with patellar resurfacing.

The first aim of this study was to evaluate if clinical outcomes such as anterior knee pain or validated knee scores, such as the KSS, differ between resurfacing and non-resurfacing of the patella. Although two meta-analyses reported superior clinical scores in favor of the resurfacing group, the mean differences compared with the non-resurfacing group were trivial and not clinically meaningful. Moreover, strict conclusion making regarding the superiority of one technique over the other was aggravated by the high statistical heterogeneity of these outcomes. Several confounding factors could in fact jeopardize a valid evaluation of such outcomes, e.g. the use of different evaluation scales for clinical outcome. It should be noted that, despite this, not all the studies performed a sensitivity analysis or a publication bias evaluation to address the problem of heterogeneity of these outcomes. Only Pavlou et al. [44] performed a separate analysis of clinical scores in the patellar resurfacing groups considering if the total knee arthroplasty had a patellar-friendly or non patellar-friendly design, based on shape, position and depth of the trochlear groove. However, this analysis did not showed superior outcomes when patellar-friendly TKA designs, which were claimed to improve the extensor mechanism function, were used [44]. With regard to post-operative anterior knee pain, four meta-analyses reported less pain after patellar resurfacing compared to non-resurfacing,

while six studies found no difference in anterior knee pain between the two techniques. This heterogeneity in the result of post-operative pain among the studies could be related to the large number of possible factors causing residual anterior knee pain after TKA and how pain was evaluated. For example, pain related to stair climbing was evaluated in one meta-analysis, which reported superior results in favor of the resurfacing group. However, since only one meta-analysis included this information and this specific task for evaluation of pain, the data is insufficient for evidence making in this topic.

The rate of re-intervention for patellar resurfacing compared with non-resurfacing was another main aspect for investigation in this review. Interestingly, the outcome of re-intervention rate was the most unanimously reported among included studies. The study by Parvizi et al. [42], was the only not to report a significant difference in re-intervention rate between the techniques. In all other studies, a lower risk for reoperation was reported after patellar resurfacing compared with non-resurfacing. Furthermore, the heterogeneity reported for this outcome was low which strengthen the reliability of the results. Additionally, several meta-analyses performed a subgroup analysis to specifically investigate the re-operation rates of patellar resurfacing and non-resurfacing groups. Pakos et al. and Li et al. [29, 41], analyzed the studies based on the follow-up time and reported a significant increase of re-operation after patellar non-resurfacing in studies with more than five years of follow-up, a result not seen in studies with less than five years follow-up. The authors explained this finding by proposing that complications tend to appear in the long-term, after the third or fourth post-operative year. The higher incidence of re-operation in the non-resurfacing group may also be explained by the lesser invasiveness that a selective patellar resurfacing surgery is associated with, compared with the more complex surgery required if re-operation is necessary for indications other than performing a patellar resurfacing, which might be the case in patients who received patellar resurfacing at the index TKA. Thus, it is possible that the higher re-operation rates in the non-resurfacing group is related to a selection bias, since surgeons likely are more prone to perform a secondary surgery for patellar resurfacing in this group.

Present review also aimed to investigate if the infection rate or mechanical complications, such as patellar tilt and shift, were higher after patellar resurfacing compared with non-resurfacing. The infection rate did not differ between the groups in any of the meta-analyses, which reflects that the longer operative time commonly associated with patellar resurfacing does not affect the risk of infection. The statistical heterogeneity for this outcome was low, however, since the infection rate after TKA is generally low, small sample sizes might bias this outcome due to imprecision. The clinical indication for patellar resurfacing in TKA continue to be a subject for debate, especially in regard to how this may influence subsequent anterior knee pain and functional scores [35, 49]. Generally, surgeons are of different opinions and may advocate a systematic performance of resurfacing, selective resurfacing or systematic non-resurfacing, since no universally accepted guidelines exist. One of the most effective approaches for evaluation of current evidence in scientific literature is still to perform meta-analyses. Nevertheless, it is important to ascertain adequate knowledge of both clinical interpretation and statistical performance of such an analysis in order to conduct a meta-analysis of high quality. Previous meta-analyses on patellar resurfacing in TKA have many times reported conflicting results although the same pool of papers have been analyzed [3, 12, 17, 20, 29, 39, 41, 42, 44, 45] which indicates that the methodological aspects for performance of a meta-analysis are challenging. In this review, specific scores were applied to evaluate the quality of included meta-analyses in order to identify the studies of the highest quality. According to the Jadad algorithm [22], the article by He et al. [20] was found to be most valid and relevant based on its methodological quality. This meta-analysis reflected the general results presented above, since it reported a ssignificantly reduced risk of re-operation after patellar resurfacing (p= 0.03) and similar clinical outcomes of the two techniques. However, it should be underlined that when a subgroup of seven high quality RCTs was analyzed by He et al. [20], no evidence regarding superiority of patellar resurfacing in terms of re-operation risk was found. Possible explanations for that could be either the reduction of confounding factors following a higher quality of the included studies, or to the reduction of statistical power due to the smaller sample size.

This study has a number of limitations and the main limitation relies on its design. It represents a systematical and critical evaluation of studies that summarize the evidence from RCTs using statistical artifacts. Therefore, no novel data are provided by this study. A secondary structural limitation is the impossibility to pool the results of the various meta-analysis, allowing only a descriptive presentation of the data and an arbitrary selection of the most reliable findings. The database choice, the inclusion of unpublished studies or the application of language restriction were not consistent among the various meta-analyses and the high statistical heterogeneity of the outcomes contributed to the inconsistency of the results.

Conclusion

This evaluation of meta-analyses of clinical and functional outcomes after patellar resurfacing and non-resurfacing showed comparable results between the two techniques. The generally higher risk of reoperations after non-resurfacing should be interpreted with caution due to the methodological limitations of the meta-analyses regarding search criteria, heterogeneity, quality of the included RCTs and the inherent bias of easier indication to reoperation when the patella is not resurfaced at the index TKA.

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Figure legends:

Figure 1: PRISMA flow-chart for the selection of the included studies

Figure 2: Jadad algorithm for the selection of the best quality of evidence

Figure 3: Summary table of the outcomes of the included meta-analyses

Tables legends:

Table 1: Methodological information of the included meta-analyses (RCT, randomized controlled

trial; PF, patello-femoral)

Table 2: Quality assessment of included meta-analyses using the "A Measurement Tool to Assess

Systematic Reviews" (AMSTAR) score. Number 0 is used when the item is not fulfilled, number 1

is used when the item is fulfilled.

Table 3: Heterogeneity for the various outcomes in the included meta-analyses. The percentage is

referred to the amount of heterogeneity reported in each study for each outcome after the I² test,

while the p-value is reported when no percentage of heterogeneity is provided. An higher percent-

age identifies an higher heterogeneity, while a p-value < 0.05 identifies the presence of heterogene-

ity and a p-value >0.05 identifies the absence of heterogeneity for a specific outcome of a specific

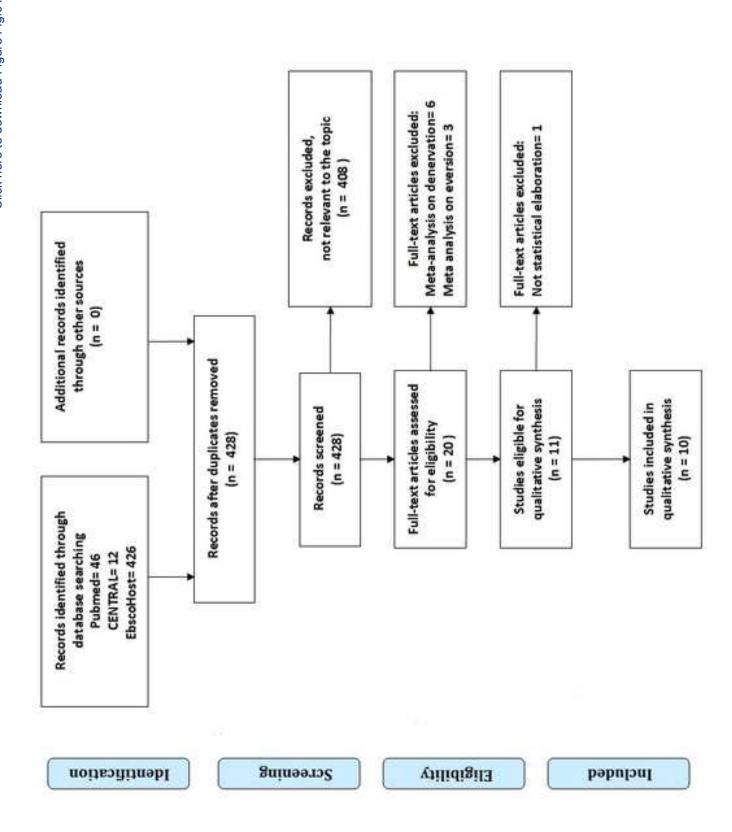
study. (SMD, standardized mean difference; KSS, knee society score; IKS, international knee soci-

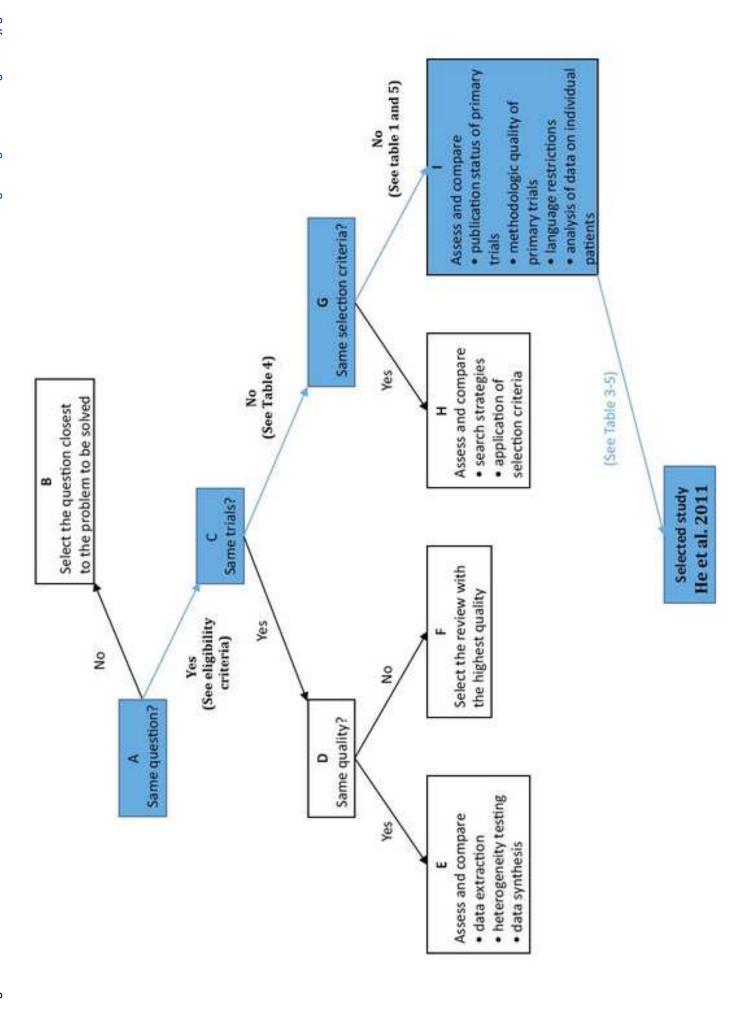
ety score; VAS, visual analogue scale; PF, patello-femoral)

Table 4: Study characteristics of included meta-analyses.

Table 5: List of primary studies included in meta-analyses

Table 6: Search strategies and details of inclusion/exclusion criteria of each meta-analyses





Risk of reoperation Reoperations related to PF joint Reoperations not related to PF joint Complications related to PF joint Anterior knee pain Knee pain score (SMD) VAS for pain Pain during stairs climbing Knee Scores (SMD) IKS score KSS score KSS function score Satisfaction Infections Patellar tilt Patellar shift

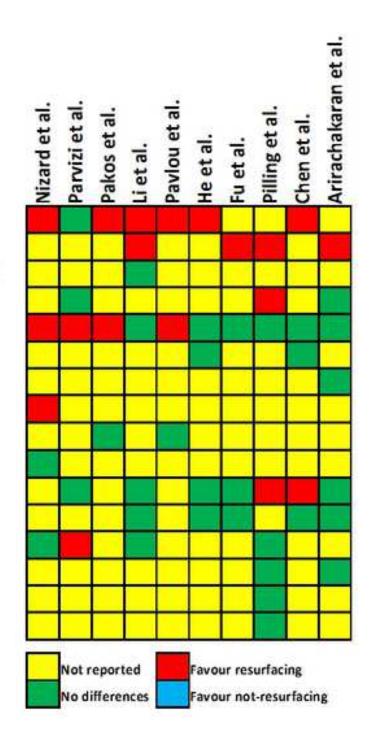


	Table 1. Methodological information of the included meta-analyses.											
Author	Design of included studies	Level of eviden ce	Softwar e	Assessmen t of study quality	GRA DE use	Sensi tivity analy sis	Subgrou p analysis	Meta - regre ssion	Publi catio n bias	PRISMA		
	RCTs or											
Nizard et al.	quasi- randomized	II	RevMen	Ad-hoc checklist	No	Yes	No	No	No	No		
5	RCTs or											
Parvizi et al.	quasi- randomized	II	RevMen	No	No	No	No	No	No	No		
							Yes:					
Pakos et al.	RCTs	II	Stata	No	No	Yes	follow- up	No	Yes	No		
				Cochrane			Yes:					
Li et al.	RCTs	II	RevMen	risk of bias tool	No	Yes	follow- up	No	Yes	No		
Pavlou et al.	RCTs	II	Stata	No	No	No	Yes: PF design	No	No	No		
He et al.	RCTs	II	RevMen	Detsky scale	No	Yes	No	No	No	No		
Tro or an	1015	11	recynten	Scure	110	105	110	110	110	110		
Fu et al.	RCTs	II	RevMen	No	No	No	No	No	No	No		
ru et ai.	KC18	11	Kevivien	Cochrane	NO	INO	INO	NO	NO	NU		
Pilling et	2.00		n 16	risk of bias								
al.	RCTs	II	RevMen	tool	No	No	No	No	No	Yes		
				Cochrane risk of bias								
Chen et al.	RCTs	II	RevMen	tool	No	No	No	No	Yes	No		
Arirachaka	RCTs or quasi-			Cochrane risk of bias								
ran et al.	randomized	II	Stata	tool	No	No	No	Yes	Yes	Yes		

Table 2. Quality assessment of included studies with A Measurement Tool to Assess Systematic Reviews (AMSTAR) score.											
	N i z a r d e t a l	i i i	<u>'</u>	Pakosetal.	L i e t a I	F a v I c c t t a a I))) () () () ()	e (e e : t	. t	C h e e e t	n ream
Was an a priori design provided?	0	0	0)	0	0	0	0	0	0	0
Was there duplicate study selection and data extraction?	1	1	1		1	1	1	0	1	1	0
Was a comprehensive literature search performed?	0	1	1		1	1	1	0	1	1	0
Was the status of publication (i.e., grey literature) used as an inclusion criterion?	0	0	0)	0	0	1	0	0	0	0
Was a list of studies (included and excluded) provided?	1	1	0		0	0	1	0	1	0	0
Were the characteristics of the included studies provided?	1	0	1		1	0	1	1	1	1	0
Was the scientific quality of the included studies assessed and documented?	1	0	0		1	0	1	0	1	1	1
Was the scientific quality of the included studies used appropriately in formulating conclusions?	1	0	0)	1	0	1	0	1	1	0
Were the methods used to combine the findings of studies appropriate?	1	1	1		1	1	1	1	1	1	1
Was the likelihood of publication bias assessed?	0	0	1		1	0	0	0	0	1	1
Was the conflict of interest stated?	1	1	1		1	1	1	1	1	1	1
Total	7	5	6		8	4	9	3	8	8	4

Table 3. Heterogeneity for the various outcomes in the included meta-analyses.										
	N oz ar d et al.	Pa rv izi et al.	Pa ko s et al.	L i e t a I	P a v l o u e t a l	H e e t a l .	Fueta.	Pilingetal.	Chenetal.	Arirachakaranetal.
Risk of reoperation	P=0.310		32%	21%	4.5%	0%			0%	
Reoperations related to PF joint				0%			0%	7%		0%
Reoperations not related to PF joint				0%						
Complications related to PF joint		NA						70%		0%
Anterior knee pain	P=0.088	P=0.009	P<0.050	81%	80.2%	85%	52%	74%	78%	37.6%
Knee pain score (SMD)						0%			0%	
VAS for pain										0%
Pain during stairs climbing	P>0.050									
Knee Scores (SMD)			76%							
IKS score	P=0.005									
KSS score		NA		12%		54%	61%	33%	0%	60%
KSS function score				0%		63%	57%		25%	71.4%
Satisfaction	P>0.050	NA		43%				NA		
Infections								6%		0%
Patellar tilt								NA		
Patellar shift								NA		

Table 4. Study characteristics of included meta-analyses.										
Author	Journal name	Date of last literature search	Date of publication	N° of included trials	N° of include					
Nizard et al.	CORR	August 2003	March 2005	12						
Parvizi et al.	CORR	September 2003	September 2005	14						
Pakos et al.	JBJS Am	November 2004	July 2005	12						
Li et al.	SICOT	January 2009	March 2011	16						
Pavlou et al.	JBJS Am	December 2009	July 2011	18						
He et al.	Knee	December 2009	December 2011	16						
Fu et al.	KSSTA	NA	September 2011	10						
Pilling et al.	JBJS Am	NA	December 2012	16						
Chen et al.	SICOT	NA	June 2013	14						
Arirachakaran et al.	KSSTA	October 2012	June 2015	15						

Table 5: Primary studies included in meta-analyses											
	N i z a r d e t a l .	Parvizietal.	Pakosetal.	L i e t a I	Pavlouetal.	H e e t a I	Fueta.	Pillingetal.	Chenetal.	Arirachakaranetal.	
Levai et al. 1983	+										
Abraham et al. 1988		+									
Enis et al. 1990		+									
Keblish et al. 1994	+	+									
Nicolay et al. 1995	+										
Partio and Wirta 1995	+	+	+	+	+	+		+			
Bourne et al. 1995	+		+	+	+					+	
Barrack et al 1997			+	+	+			+		+	
Feller et al. 1997	+	+	+	+	+	+	+	+	+	+	
Kajino et al. 1997	+	+		+		+					
Schroeder-Boersch et al. 1998		+	+	+		+	+	+	+		
Schroeder-Boersch et al. 1998	+				+						
Newman et al. 2000	+	+	+	+	+	+	+	+	+		
Noble 2000										+	
Pollo et al. 2000		+									
Waikakul et al. 2000		+	+		+	+		+		+	
Barrack et al. 2001	+	+	+	+	+		+		+		
Wood et al. 2002	+	+	+	+	+	+	+	+	+	+	
Waters and Bentley 2003	+	+	+	+	+	+		+	+	+	
Mayman et al. 2003		+	+		+	+	+		+	+	
Kordelle et al. 2003			+	+	+	+		+			
Burnett et al. 2004				+	+	+	+	+	+	+	
Tabutin et al. 2005					+						
Gildone et al. 2005				+				+			
Myles et al. 2006						+		+		+	
Campbell et al. 2006				+	+	+	+	+	+	+	
Burnett et al. 2007					+		+		+		

Huang et al. 2007		+						
Liu et al. 2007						+		
Epinette and Manley 2008			+					
Smith et al. 2008		+	+	+	+	+	+	+
Burnett et al. 2009				+		+	+	
Johnston et al. 2009				+				
Beaupre et al. 2012							+	+
Liu et al. 2012							+	+

Table 6. Search strategies and details of inclusion/exclusion criteria										
Author	Restriction of publication language	Restriction of publication status	PubMed	Embase	Cochrane Library	CINAHL	Others			
Nizard et al.	No	Yes	+		+		+			
Parvizi et al.	Yes	Yes	+		+	+	+			
Pakos et al.	No	Yes	+	+	+					
Li et al.	No	Yes	+	+	+					
Pavlou et al.	No	Yes	+	+	+		+			
He et al.	No	No	+	+	+	+	+			
Fu et al.	Yes	Yes	+		+					
Pilling et al.	No	Yes	+	+	+					
Chen et al.	Yes	Yes	+	+	+					
Arirachakaran et al.	Yes	Yes	+				+			



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Given Name: Stefano Surname: Effective Date: |20 Oct 2017 Zaffagnini (or first) (or last) Format example: 07-August-2008 Testo Are you the corresponding author? X Yes Is patellar resurfacing superior to patellar retention in primary TKA? Manuscript Title: A systematic review of overlapping meta-analyses Manuscript Identifying Number (if you know it): Section 2. Information about the support of the work inder consideration for publication. Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)? Yes, specify nature of compensation Section 3. Information about relevant financial relationships outside the submitted work. Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended). If you have more than one relationship, click "Add +" to add a row. Click "Del ×" to delete an extra row. Money Money to Type of Relationship



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		1				
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Patents (planned, pending or issued)	X					
Royalties	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
					1	
Travel/accommodations expenses covered or reimbursed	X					
Other (err on the side of full disclosure)	X					



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Employment

Expert testimony

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X

X

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Honoraria	X					
		1				
Payment for manuscript preparation	X					
Patents (planned, pending or issued)	X					
Royalties	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
					1	
Travel/accommodations expenses covered or reimbursed	X					
Other (err on the side of full disclosure)	X					



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5. Nonfinancial associations.



Section 1. Identifying Information.

Board membership

Consultancy

Employment

Expert testimony

Given Name: Surname: Effective Date: |20 Oct 2017 Eleonor Svantesson (or first) (or last) Format example: 07-August-2008 Testo Are you the corresponding author? X Yes Is patellar resurfacing superior to patellar retention in primary TKA? Manuscript Title: A systematic review of overlapping meta-analyses Manuscript Identifying Number (if you know it): Section 2. Information about the support of the work inder consideration for publication. Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)? Yes, specify nature of compensation Section 3. Information about relevant financial relationships outside the submitted work. Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended). If you have more than one relationship, click "Add +" to add a row. Click "Del ×" to delete an extra row. Money Money to Type of Relationship No Paid to Your **Entity Comments** (in alphabetical order)

You

X

X

X

X

institution



Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	X					
Grants/grants pending	X					
		Γ				
Honoraria	X					
Payment for manuscript preparation	X					
Patents (planned, pending or issued)	X					
Royalties	T				Γ	
Royaldes	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
Travel/accommodations expenses covered or reimbursed	X					
						
Other (err on the side of full disclosure)	X					



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Berruto

Effective Date: |20 Oct 2017

Surname:

(or last)

Section 1. Identifying Information.

Massimo

Given Name:

(or first)

Employment

Expert testimony

X

X

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Grants/grants pending	X					
		Γ				
Honoraria	X					
Payment for manuscript preparation	X					
Patents (planned, pending or issued)	X					
Royalties	T				Γ	
Royaldes	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
Travel/accommodations expenses covered or reimbursed	X					
						
Other (err on the side of full disclosure)	X					



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Do your chi	ildren (or your	spouse	or partn	ier have	e financia	ıl relations	ships witl	h entitie:	s that l	nave an	interest in	n the	content	of the
submitted w	ork?														
- NT	.1	1	1 . /	11.1	, .		.1 .			a	٠				

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Testo

Ferrua

Effective Date: |20 Oct 2017

Format example: 07-August-2008

Surname:

(or last)

Section 1. Identifying Information.

Paolo

Given Name:

Expert testimony

X

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Royalties	T				Γ	
Royaldes	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
Travel/accommodations expenses covered or reimbursed	X					
						
Other (err on the side of full disclosure)	X					



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Section 1. Identifying Information.

Board membership

Consultancy

Employment

Expert testimony

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You

X

X

X

X

institution



Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	X					
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Honoraria	X					
Payment for manuscript preparation	X					
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Royalties	T				Γ	
Royaldes	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
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3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.



Surname:

Section 1. Identifying Information.

Given Name:

Consultancy

Employment

Expert testimony

X

X

X

Effective Date: |20 Oct 2017 riccardo compagnoni (or first) (or last) Format example: 07-August-2008 Testo Are you the corresponding author? X Yes Is patellar resurfacing superior to patellar retention in primary TKA? Manuscript Title: A systematic review of overlapping meta-analyses Manuscript Identifying Number (if you know it): Section 2. Information about the support of the work inder consideration for publication. Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)? Yes, specify nature of compensation Section 3. Information about relevant financial relationships outside the submitted work. Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended). If you have more than one relationship, click "Add +" to add a row. Click "Del ×" to delete an extra row. Money Money to Type of Relationship No Paid to Your **Entity Comments** (in alphabetical order) You institution Board membership X



Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	X					
Grants/grants pending	X					
		Γ				
Honoraria	X					
Payment for manuscript preparation	X					
Patents (planned, pending or issued)	X					
Royalties	T				Γ	
Royaldes	X					
Payment for development of educational presentations including service on speakers' bureaus	X					
Stock/stock options	X					
Travel/accommodations expenses covered or reimbursed	X					
						
Other (err on the side of full disclosure)	X					



Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the
submitted work?
🗵 No other relationships/conditions/circumstances that present potential conflict of interest

Section 5. Information about relevant nonfinancial associations.

Yes, the following relationships/conditions/circumstances are present (explain below):

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

Ŀ	X	No	releva	nt non	tınancıal	relationsl	nips/o	conditic	ons/cii	cumstances	to report.					
		Ye	s, the fo	ollowin	ıg releva	nt nonfina	ancial	relation	nships/	conditions,	/circumsta	nces are	present	(explai	n below	7):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Signature, date