The effect of bearing surface on risk of prosthetic joint infection in total hip arthroplasty: a systematic review and meta-analysis

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ABSTRACT

Aims: Prosthetic joint infection (PJI) is a serious complication of total hip arthroplasty (THA). Different bearing surface materials have different surface properties and it has been suggested that the choice of bearing surface may influence the risk of PJI after THA. The objective of this meta-analysis was to compare the rate of PJI between metal-on-polyethylene (MoP), ceramic-on-polyethylene (CoP) and ceramic-on-ceramic (CoC) bearings.

Patients and Methods: Electronic databases (Medline, Embase, Cochrane library, Web of Science and CINAHL) were searched for comparative randomised and observational studies that reported the incidence of PJI for different bearing surfaces. Two investigators independently reviewed studies for eligibility, evaluated risk of bias and performed data extraction. Meta-analysis was performed using the Mantel–Haenzel method and random-effects model in accordance with methods of the Cochrane group.

Results: Our search strategy revealed 2272 studies of which 17 met the inclusion criteria and were analysed. These comprised 11 randomised controlled trials and six observational studies. The overall quality of included studies was high but the observational studies were at high risk of bias due to inadequate adjustment for confounding factors. The overall cumulative incidence of PJI across all studies was 0.78% (1514/193378). For each bearing combination the overall incidence was as follows: MoP 0.85% (1353/158430); CoP 0.38% (67/17489); and CoC 0.53% (94/17459). The meta-analysis showed no significant difference between the three bearing combinations in terms of risk of PJI.

Conclusion: On the basis of the clinical studies available, there is no evidence that bearing choice influences the risk of PJI. Future research, including basic science studies and large, adequately controlled registry studies, may be helpful in determining whether implant materials play a role in determining the risk of PJI following arthroplasty surgery.

INTRODUCTION

Total hip arthroplasty (THA) is a successful intervention for patients with end-stage osteoarthritis[1]. Traditionally THA has been performed using a metal (cobalt chrome or stainless steel) femoral head and an ultra-high molecular weight polyethylene (UHMWPE) acetabular component (metal on polyethylene, MoP). MoP THA is associated with failure secondary to wear and aseptic loosening in the medium to long term, particularly in younger, more active patients[2], and so called 'hard on hard' bearing surfaces, such as ceramic on ceramic (CoC) and metal-on-metal (MoM) were developed to address this problem[3]. Whilst the use of MoM bearings has declined precipitously since the problems associated with adverse reactions to metal debris have become apparent[4], ceramic bearings (either CoC or Ceramic on UHMWPE, CoP) are increasingly popular due to their excellent wear properties[5].

Prosthetic joint infection (PJI) is an important complication of THA, which is reported to occur in around 1% of cases[6-8]. PJI is a devastating diagnosis for the patient and can result in prolonged hospital stays and multiple operations with considerable economic burden for healthcare systems[9]. Recent reports suggest the prevalence of PJI may be increasing and that a large proportion (up to 40% by some estimates) of cases of aseptic loosening might represent undiagnosed PJI[8,10]. Recent conference papers and industry reports have suggested that ceramic bearings may be associated with a lower risk of PJI compared to conventional bearings, supported by retrieval studies of hips with PJI that show higher bacterial counts on polyethylene liners compared to ceramic surfaces[11-14]. A previous meta-analysis comparing MoP to CoC hips did not find any significant difference between the two groups in terms of deep infection, but this did not include long-term registry data which might be better powered to detect differences in the incidence of this uncommon complication[15].

The aim of this systematic review and meta-analysis was to compare the effect of MoP, CoP or CoC bearing surfaces on risk of PJI after primary THA.

PATIENTS & METHODS

A literature search was performed using Medline, EMBASE, CENTRAL (Cochrane), Web of Science and CINAHL databases The following search terms were used: ("Prosthesis-Related Infection" OR "Periprosthetic joint infection" OR "Prosthetic joint infection" OR "Implant infection" OR "Hip infection") AND ("Cobalt-chrome" OR "Ceramic" OR "Polyethylene" OR "UHMWPE" OR "Bearing surface" OR "Bearing couples" OR "Articulating surface" OR "Metal-on-metal") AND ("Hip arthroplasty" OR "Hip replacement" OR "Hip prosthesis" OR "Hip operation" OR "Hip joint"). The searches were performed on 9th September 2016 with no date restriction applied. Additional studies were added to the analysis by screening bibliographies of studies.

This meta-analysis included original peer-reviewed studies which reported the rate of PJI in patients undergoing THA, comparing at least two out of MoP, CoP and CoC. We included randomised controlled trials (RCTs) and observational studies (registry data and cohort studies). Studies not in English or those involving MoM hip resurfacing systems or revision cases were excluded.

All studies were initially screened to assess suitability for inclusion according to the criteria by two authors (ATH, SMH). Full manuscripts of studies meeting the criteria were reviewed by the two authors to determine whether information on PJI for each bearing surface was adequately reported. Data extraction forms were used to independently extract data. Studies were excluded if insufficient evidence was present in the paper to identify the incidence of infection for each bearing surface. When data from the same cohort were presented in more than one article, the article with the largest number of patients was chosen. At the end of the review process, the two authors' findings were compared and discrepancies resolved as mutually agreed. To measure the methodological quality of the studies both authors used risk of bias tools developed by the Cochrane group[16]. The Cochrane Risk of Bias 2.0 tool (RoB 2.0) gives an overall risk of bias for randomised trials by scoring them across five domains (randomisation process, deviation from intended interventions, missing outcome data, measurement of the outcome and selection of reported result)[17]. For non-randomised trials, the Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) tool was used. This scores observational studies across seven distinct domains (confounding, participant selection, classification of interventions, deviation from intended intervention, attrition bias, detection bias and reporting bias)[18].

Meta-analysis was undertaken using Review Manager 5.3 (The Cochrane Collaboration, Oxford, UK). The

Mantel–Haenzel method was employed using odds ratios. A random-effects model was used because of the expected heterogeneity in populations studied and methodology amongst studies. Separate analyses were undertaken to compare each bearing surface. The comparisons were MoP versus CoC; CoP versus CoC; and MoP versus CoP. We performed separate analyses for RCTs and observational studies. The overall odds ratio for PJI in one group was not directly compared to that of another because this would require a network meta-analysis and conditions required to perform this are not met in observational studies[19]. As fewer than ten studies were included in the analysis Begg's funnel plot was not undertaken to assess for publication bias as advised by the Cochrane handbook[16]. A p value of less than 0.05 was considered statistically significant. Higgins I^2 statistic was used to assess heterogeneity.

RESULTS

Literature Search

A total of 2248 articles were identified through our literature search and a further 24 studies were included after reading of bibliographies (Figure 1). After removal of duplicates and screening according to inclusion criteria 28 studies underwent full review. Of these, three were excluded as they used the same study population involved in another paper in the meta-analysis and five were removed due to inadequate information on PJI for each bearing surface. A total of 17 articles were included in the meta-analysis, consisting of 11 RCTs and six observational studies.

Study characteristics and quality

The characteristics of the 17 included studies are summarised in Table 1. Seven studies compared MoP to CoC[20-26]; 10 studies compared CoP to CoC[20,22,27-34]; and three studies compared MoP to CoP[22,35,36]. The results of the risk of bias assessments of randomised and observational studies are shown in Tables 2 and 3. There was a lack of consistency over the definition of PJI, with fifteen studies using the term “infection”, “deep infection” or “deep joint infection” and only two using the term PJI. No study included details of the criteria used to diagnose PJI although criteria exist[37]

Of the 11 RCTs, three had high methodological quality and were deemed to be at low risk of bias; eight had some concerns over risk for bias either due to lack of clarity over the randomisation process or due to missing outcome data. None of the studies were adequately blinded, reflecting the difficulty of blinding surgical interventions[38,39]. No study included a power calculation for PJI.

All observational studies included had a serious risk of bias due to inherent risk of confounding. Only two of the six non-randomised studies attempted to adjust for confounders. Bozic et al., in their follow up study of Medicare patients between 2005 and 2009, adjusted for patient differences such as age, sex, race, Charlson comorbidity index as well as institutional factors such as size of the hospital, urban/rural location[24]. Pitto et al, in their 15-year analysis of data from the New Zealand Joint Registry, performed a multivariable assessment adjusting for risks factors including age, sex, operating room type, use of body exhaust suits, mode of fixation,

and surgeon volume[20]. All studies were considered at serious risk of confounding, as they did not adjust for all risk factors for PJI such as body mass index, immunosuppression and diabetes[38].

MoP v CoC

174,870 hips were included across seven studies (Figure 2). The overall incidence of PJI was 0.8% (1440/174,870). The incidence of PJI was 0.85% (1351/158266) in the MoP group compared to 0.54% (89/16604) in the CoC group. Analysis of the three RCTs (n=429 hips) showed no significant difference between MoP and CoC in PJI (odds ratio 0.66; 95% confidence interval 0.06 to 6.90; p = 0.73; heterogeneity, P = 0.11, I^2 =61%). Separate analysis of the observational studies showed no significant difference between MoP and CoC (odds ratio 1.54; 95% confidence interval 0.98 to 2.42; p = 0.06; heterogeneity, P = 0.07, I^2 =58%).

CoP v CoC

27491 hips were included across ten studies and the overall incidence of PJI was 0.35% (95/27491). The incidence was 0.38% (66/17322) in the CoP group and compared to 0.29% (29/10169) in the CoC group (Figure 3). In four of the seven RCTs no PJIs were seen and therefore these studies did not contribute to the analysis. Analysis of the three included RCTs (n=734 hips) showed no significant difference between CoP and CoC in PJI (odds ratio 1.21; 95% confidence interval 0.24 to 6.15; p = 0.82; heterogeneity, P = 0.48, I^2=0%). Separate analysis of the three observational studies showed no significant difference between CoP and CoC (odds ratio 0.65; 95% confidence interval 0.41 to 1.04; p = 0.07; heterogeneity, P = 0.95, I^2 =0%).

MoP v CoP

Three studies (n=889 hips) consisting of two observational studies and one RCT were evaluated (Figure 4). The incidence was 1.16% (7/605) in the MoP group and compared to 1.06% (3/284) in the CoC group. Pooled analysis of these studies revealed no significant differences in PJI between MoP and CoP (odds ratio 0.96; 95% confidence interval 0.26 to 3.53; p = 0.95; heterogeneity, P = 0.61, I^2=0%)

DISCUSSION

PJI is a rare complication of THA and due to the large volume of cases performed a small difference in infection rate might justify a change in practice. However this meta-analysis reveals no significant difference between MoP, CoC or CoP THA in terms of PJI. The overall incidence of PJI was 0.78% (1514/193378), which is comparable with previous systematic reviews pertaining to PJI[41]. For each bearing combination the overall incidence was as follows: MoP 0.85% (1353/158430); CoC 0.53% (94/17459); and CoP 0.38% (67/17489). While the absolute numbers appear to indicate a substantial (and potentially clinically relevant) difference between the rates of infection according to the bearing surface used, no comparison reached statistical significance, the RCTs lacked statistical power even when pooled and the observational studies were at risk of significant confounding. The results varied by study type, with the analysis of non-randomised studies suggesting a trend favouring ceramic bearings but the opposite being shown in the RCTs.

Our study agrees with the findings of a previous meta-analysis that compared MoP to CoC THA[15]. The previous study did not find any significant difference between the two groups in terms of deep infection. Our study examines a broader range of articulating surfaces (including CoP) and includes registry data that has greater power to detect differences, albeit with little or no adjustment for confounders. We excluded MoM from this meta-analysis to ensure focus on currently popular implant materials. Furthermore, although MoM hip systems have been shown to be at increased rate of PJI it is not always straightforward to make a clinical distinction between metallosis and infection which can lead to over-diagnosis of PJI[42,43].

Infection of orthopaedic implants is difficult to eradicate because bacteria attach to the implant surface and form a biofilm[44]**.** In this critical first step in the development of PJI, adherent bacteria synthesise a complex glycocaylx, which provides resistance against the immune system and antimicrobial therapy[45,46]**.** Surface properties such as roughness and hydrophobicity are known to influence the formation of biofilms [47,48], and it is for this reason that it has been suggested that ceramic bearing surfaces may confer a degree of protection against biofilm formation. Ceramics used in arthroplasty are harder than metals and can be polished to a much lower surface roughness; they also have excellent wettability (ie, they are very hydrophilic)[49]. In terms of wear, these characteristics are highly favourable, conferring a high resistance to scratching and a reduced rate of

wear; the high wettability ensures that the synovial fluid is uniformly distributed between implant surfaces, facilitating fluid-film lubrication and reducing friction between articulating surfaces[50]. In terms of infection, research suggests that bacterial adhesion is reduced in less rough surfaces[51]; *Staphylococcus aureus* has been demonstrated to adhere more strongly to hydrophobic surfaces than to hydrophilic surfaces, although the evidence is mixed[52]. Aside from materials studied in this meta-analysis, there is some evidence from basic science studies that stainless steel surfaces are more susceptible to bacterial adherence than titanium alloys, cobalt chrome and tantalum[53,54]. Studies have demonstrated reduced adhesion of biofilm-producing strains of *Staphylococcus aureus* and *Escherichia coli* onto vitamin E blended UHMWPE compared with standard UHMWPE, although others have reported no difference in adhesion[55]. However, *in vitro* findings have not been replicated in retrieval studies. Analysis of 87 retrieved components from patients with confirmed PJI found that the choice of biomaterial or implant component did not influence bacterial adherence to the prosthesis[56].

As with any meta-analysis, this study is limited by the included studies. The RCTs that were included did not have PJI as their primary outcome and are underpowered for evaluation of PJI. Pooling the results of multiple RCTs in a meta-analysis is intended to address this issue but even with the pooled sample sizes achieved here only very large effect sizes are likely to be detected; in fact, were there to be a difference between in the rate of PJI between bearing surfaces such differences are likely to be relatively small. The observational studies included in this meta-analysis were highly powered but had variable adjustment for confounders including mode of fixation, surgical approach, patient factors such as BMI and diabetes, and surgical factors such as the approach and use of prophylactic antibiotics. Ceramic bearing surfaces are likely to be used in younger, fitter patients who have fewer co-morbidities such as diabetes or obesity and may be less susceptible to infection. Conversely, young patients undergoing THA (particularly those with a history of dysplasia or previous trauma) may have had previous surgery; such cases may be more complex, with longer operative times and may be of greater risk of infection. This level of detail is not present within the majority of the included studies. Another deficiency of the studies is a lack of standardized definition of PJI despite there now being an agreed consensus on the definition of PJI[37,57].

There is a need for further clinical and basic science studies in this area. Very detailed patient level data is now available by cross-linking joint registry data to other datasets such as the Hospital Episode Statistics (HES) and national Patient Reported Outcome Measures (PROMs) databases in the UK and there have recently been several studies which use these detailed data to compare implants in groups very closely matched on a large number of variables[58]. A study comparing the rate of infection in matched patients with different prosthesis characteristics may be helpful in further answering this question. Likewise, basic science studies to characterise the biofilms formed *in vivo* by the organisms commonly responsible for PJI would allow the development of *in vitro* models to test the "anti-biofilm" properties of existing and novel implant materials[59].

On the basis of the existing clinical data, we have not found any significant difference between commonly used bearing surfaces and the rate of infection following THA, and we can not justify selection of bearing surfaces on that basis. However, the weak trend towards lower rates of infection in the observational studies, although subject to significant confounding, merits further study. Further studies are needed to clarify the place of implant materials in the susceptibility of patients to PJI following hip and knee arthroplasty.

Table 1. Characteristics of included studies

MoP versus CoC

Author and year	Study Design	Setting	Number of hips	Number of PJI/hips		Average follow-up (years)	Male:Female ratio		Mean age (years)	
				MoP	CoC		MoP	CoC	MoP	CoC
Pitto [20] 2016	Observational	New Zealand Registry	63460	277/54409	22/9051	Median: 9 (1-15)	45:55	53:47	76% >65years	22% >65years
Varnum [21] 2015	Observational	Danish Registry	11096	61/9323	6/1773	10.0 – CoC 11.0- MoP	49:51	53:47	72% >60years	47% >60years
Topolovec [22] 2014	Observational	Slovenia	704	5/441	2/263	Mean: 11.5 (4.1-15.0)	24:76	49:51	69.4 (43-84)	58.3 (26-74)
D'Antonio [23] 2012	RCT	USA Multi-centre	289	2/95	2/194	10.3	60:40	69:31	53.5 (26-75)	54.9 (26-75)
Bozic [24] 2012	Observational	USA (Medicare)	99181	1005/93929	52/5252	4 (2.8-5.2)	36:64	41:59	51.9% >75years	36.5% >75years
Bascarevic [25] 2010	RCT	Serbia	157	0/75	0/82	4.2	31:69	21:79	56	54
Vendittoli [26] 2007	RCT	Canada	140	1/69	5/71	6.6 (4-9)	55:45	42:58	56.8	54.9

CoP versus CoC

Author and year	Study Design	Setting	Number of hips	Number of PJI/hips		Average follow-up (years)	Male:Female ratio		Mean age (years)	
				CoP	CoC		CoP	CoC	CoP	CoC
Pitto [19] 2016	Observational	New Zealand	25554	62/16503	22/9051	Median: 9 (1-15)	52:48	53:47	47% >65years	22% >65years
Topolovec [21] 2014	Observational	Slovenia	380	1/117	2/263	13.5 – CoP 10.0 - CoC	34:66	49:51	67.3 (43-79)	58.5 (36-74)
Beaupre [27] 2013	RCT	Canada	92	0/44	0/48	5	54:46	54:46	53.6	51.3
Cai [28] 2012	RCT	China	113	0/62	1/51	Mean 39.7 (36-44)	54:46	58:42	42.0 (20-59)	42.1 (21-60)
Amanatullah [29] 2011	RCT	USA Multi-centre	357	2/161	1/196	5	58:42	64:36	54.7	50.4
Lewis [30] 2010	RCT	Canada	56	0/26	0/30	Median 8 (1-10)	Unknown	Unknown	42.8 (31-56)	41.5 (19-56)
Hamilton [31] 2010	RCT	Multicentre	264	0/87	2/177	2.5 (1.8-4.0)	54:46	51:49	57.3	56.4
Yoon [32] 2008	Observational	South Korea	127	1/43	1/84	17.2	Unknown	Unknown	Unknown	Unknown
Sonny [33] 2005	RCT	USA Multi-centre	444	0/227	0/217	24 months	47:53	55:45	60.9	55.0
Kim [34] 2005	RCT	South Korea	104	0/52	0/52	7.1 (5-8)	Unknown	Unknown	Unknown	Unknown

MoP versus CoP

Author and year	Study Design	Setting	Number of hips	Number of PJI/hips		Mean follow-up (years)	Male:Female ratio		Mean age (years)	
				MoP	CoP		MoP	CoP	MoP	CoP
Topolovec [21] 2014	Observational	Slovenia	558	5/441	2/117	11.0 – MoP 13.5 – CoP	24:76	34:66	69.4 (43-84)	67.3 (43-79)
Parsons [35] 2014	Observational	USA	63	1/27	0/36	7.55 – MoP 9.9 – CoP	26:74	56:44	64.7 (31-83)	57.8 (42-77)
Bjorgul [36] 2013	RCT	Norway	268	1/137	1/131	7	31:49	41:59	62.8 (25-73)	63.9 (31-74)

Table 2. Quality Assessment of randomised studies

Publication	Description of PJI	Cochrane Rob 2.0 Tool domains					Overall risk of Bias
		Randomisation bias	Deviation from intended intervention	Missing data	Outcome measurement bias	Selection bias	
Beaupre 2013 [26]	Infection	Low	Low	Some concerns	Low	Low	Some concerns
Bjorgul 2013 [35]	Infection	Low	Low	Low	Low	Low	Low
Cai 2012 [27]	Deep infection	Low	Low	Some concerns	Low	Low	Some concerns
D'Antonio 2012 [22]	Deep joint infection	Low	Low	Some concerns	Low	Low	Some concerns
Amanatullah 2011 [28]	Deep infection	Some concerns	Low	Some concerns	Low	Low	Some concerns
Lewis 2010 [29]	Infection	Some concerns	Low	Low	Low	Low	Some concerns
Hamilton 2010 [30]	Deep infection	Low	Low	Low	Low	Low	Low
Bascarevic 2010 [24]	Deep joint infection	Low	Low	Some concerns	Low	Low	Some concerns

Vendittoli 2007 [25]	Deep infection	Low	Low	Low	Low	Low	Low
Sonny Bal 2005 [32]	Infection	Some concerns	Low	Low	Low	Low	Some concerns
Kim 2005 [33]	Infection	Some concerns	Low	Low	Low	Low	Some concerns

Table 3. Quality Assessment of observational studies

Publication	Description of PJI	**Type of bias**							**Overall risk of bias**
		Confounding	**Participant selection**	**Classification of interventions**	**Deviation from intended intervention**	**Attrition bias**	**Detection bias**	**Reporting bias**	
Pitto 2016 [19]	PJI	Serious	Low	Low	Low	Low	Low	Low	Serious
Varnum 2005 [20]	Deep infection	Serious	Low	Low	Low	Low	Low	Low	Serious
Topolovec 2014 [21]	Deep infection	Serious	Low	Low	Low	Low	Low	Low	Serious
Parsons 2014 [34]	Infection	Serious	Low	Low	Low	Low	Low	Low	Serious
Bozic 2012 [23]	PJI	Serious	Low	Low	Low	Low	Low	Low	Serious
Yoon 2008 [31]	Infection	Serious	Low	Low	Low	Low	Low	Low	Serious

FIGURES:

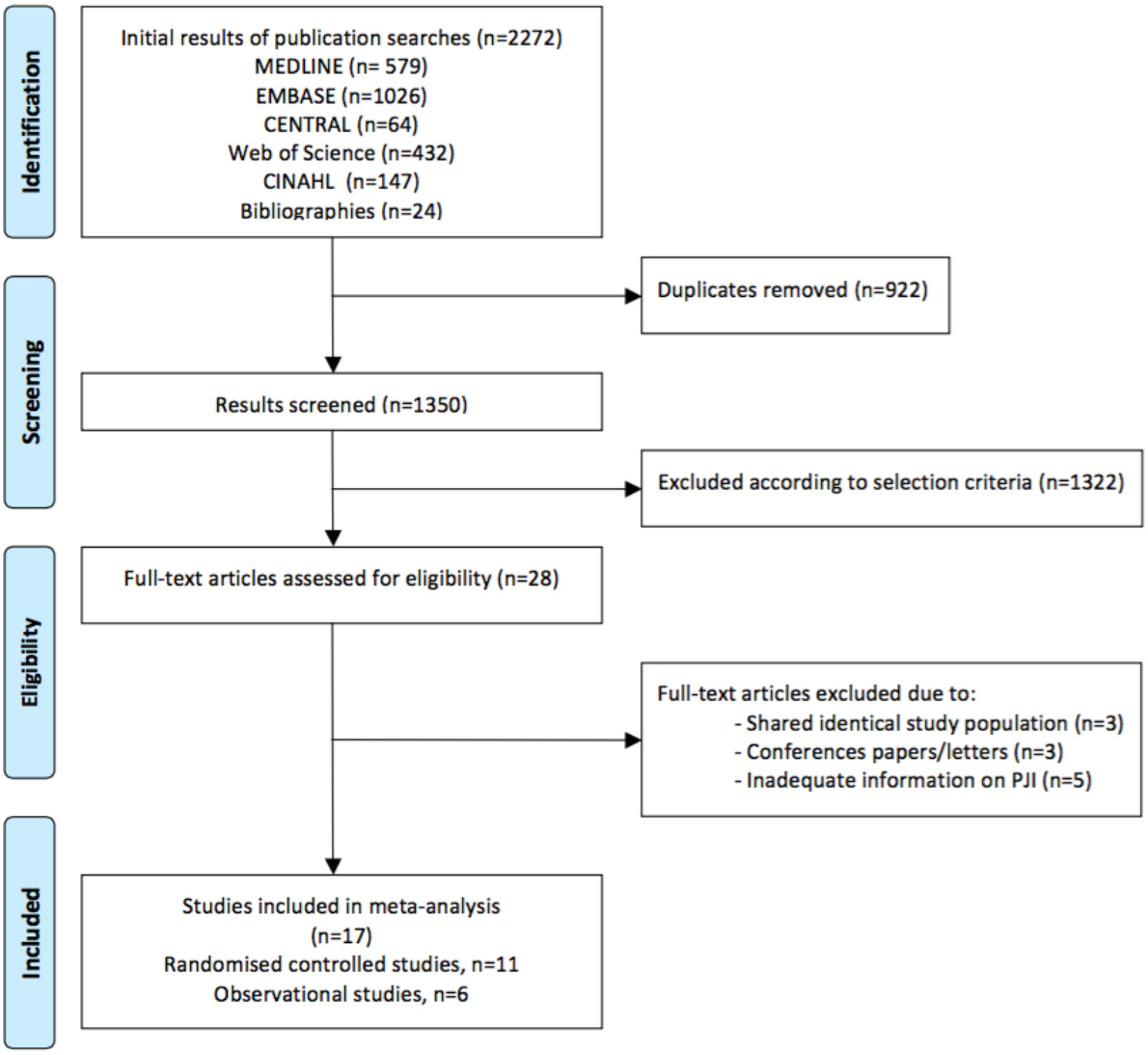

Fig. 1. Flowchart outlining the selection of studies for inclusion in the meta-analysis.

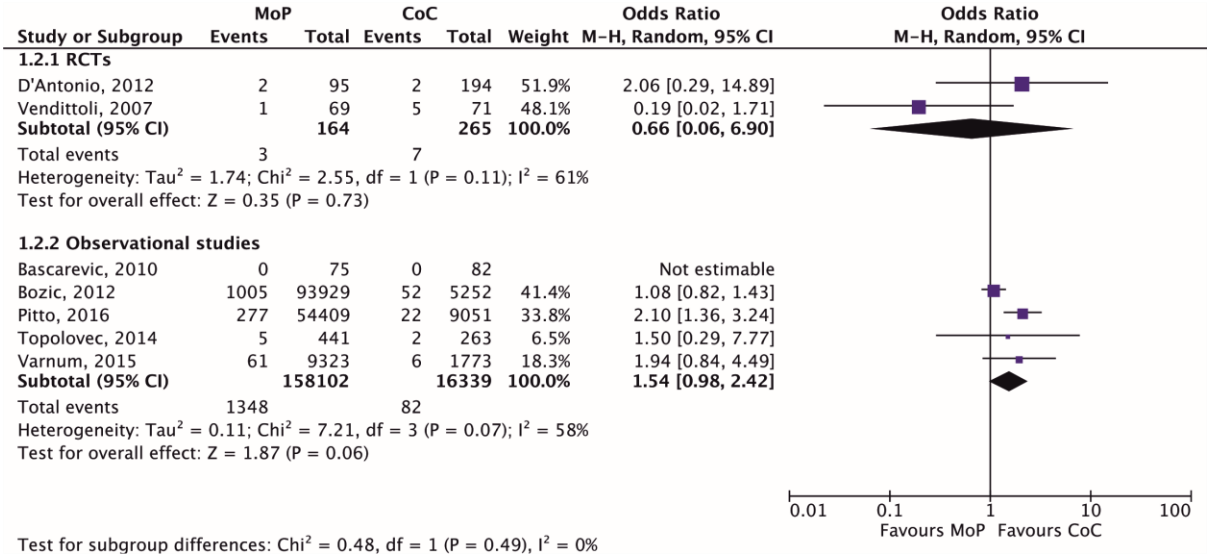

Fig. 2. Forest plot of included studies comparing PJI in MoP versus CoC bearings

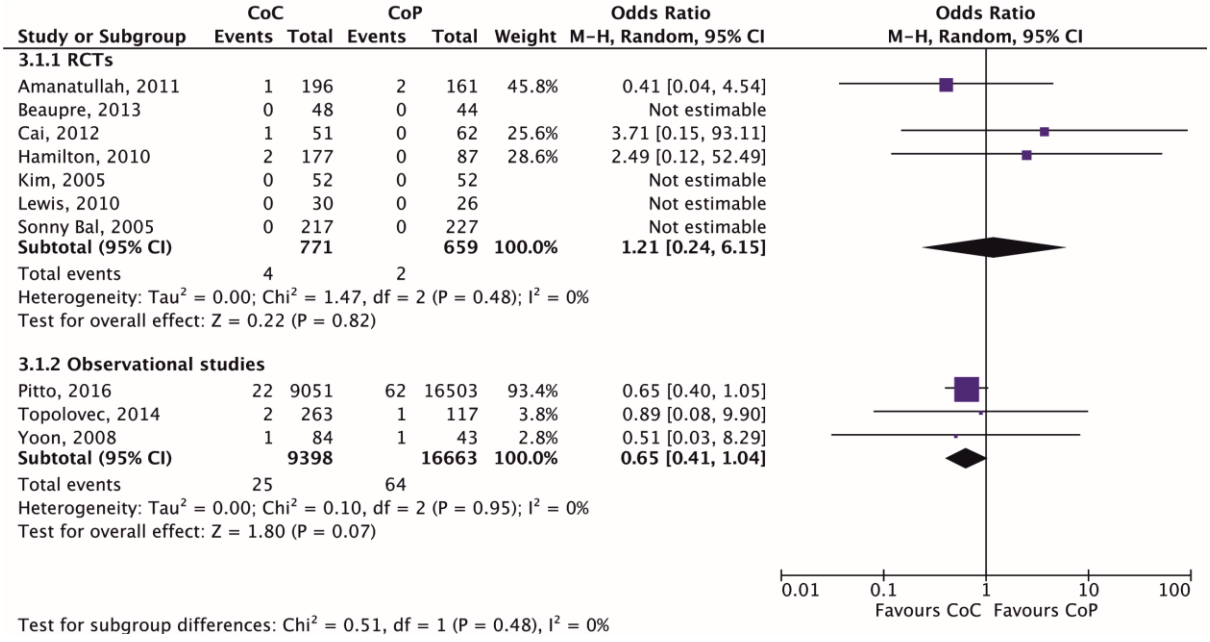

Fig. 3. Forest plot of included studies comparing PJI in CoP versus CoC bearings

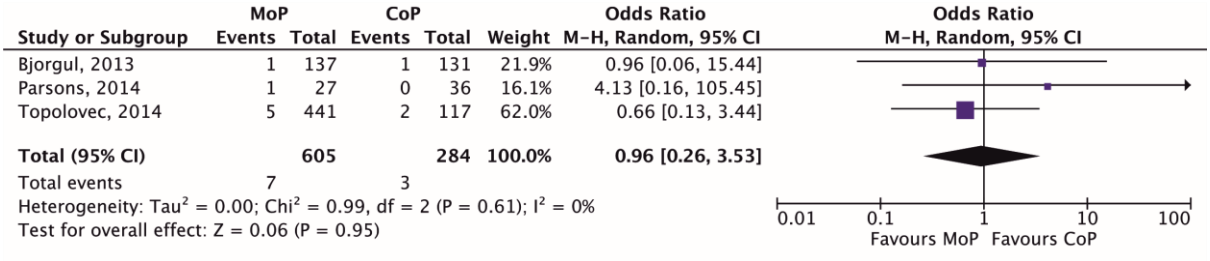

Fig. 4. Forest plot of included studies comparing PJI in MoP versus CoP bearings

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