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.

Materials 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 studies available, there is no clinical 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) but this bearing combination is associated with failure secondary to wear and aseptic loosening in the medium to long term, particularly in younger, more active patients (2). So called 'hard on hard' bearing surfaces, such as ceramic on ceramic (CoC) and metal-on-metal (MoM) were developed to address the problem of failure through wear and loosening(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) are increasingly popular due to their excellent wear properties (5).

Prosthetic joint infection (PJI) is an important yet uncommon complication of THA (6). There is little agreement about the true incidence of PJI (7) but a recent study using multiple data sources reported the "true" 1- and 5-year cumulative incidences of PJI as 0.86% and 1.03% respectively (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 (10) and that a large proportion (up to 40% by some estimates) of aseptic loosening might represent undiagnosed PJI (8). Recent conference papers (11, 12) and industry reports (13) 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 (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 (15), but this did not include long-term registry data which might be better powered to detect differences in the incidence of this uncommon complication.

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.

MATERIALS & METHODS

A literature search was performed using the following databases: Medline, EMBASE, CENTRAL (Cochrane), Web of Science and Cumulative Index to Nursing and Allied Health Literature (CINAHL). 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. References from previous meta-analyses comparing different bearing surfaces in THA were specifically targeted.

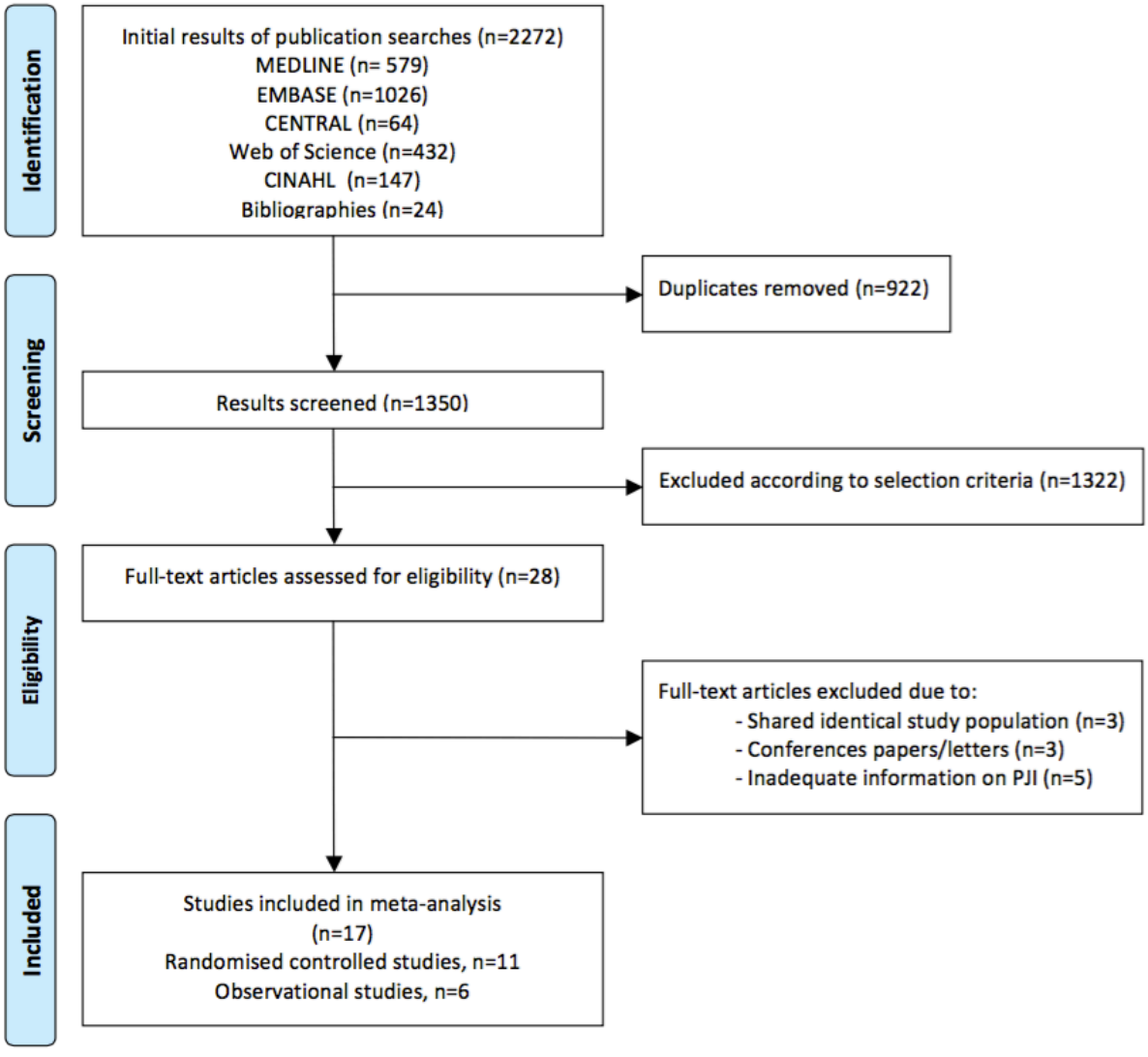
This meta-analysis included original peer-reviewed studies based on the following criteria: (1) comparing at least two different bearing surfaces from MoP, CoP and CoC systems; (2) reporting the rate of PJI in patients undergoing primary hip arthroplasty; (3) published in English language. We included randomised controlled trials (RCTs) and observational studies (registry data and cohort studies). Studies including hip resurfacing systems or revision arthroplasty were excluded.

All studies were initially screened to assess suitability for inclusion according to the criteria by two authors (AH, SH). 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. There are various terms used in the literature for PJI and we accepted terms such periprosthetic joint infection, deep infection and septic loosening. Studies were excluded if

insufficient evidence was present in the paper to identify the incidence of infection for each bearing surface. When data 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 (RoB 2.0) tool (17) 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). The Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) tool (18) scores observational studies across seven distinct domains (confounding, participant selection, classification of interventions, deviation from intended intervention, attrition bias, detection bias and reporting bias).

Meta-analysis was undertaken using Review Manager 5.3 software. The Mantel–Haenzel method was employed using odds-ratios. The random-effects model was chosen instead of the fixed effects model because we included observational studies in our analysis that are at inherent risk of confounding and bias. Comparison of different bearing surfaces was undertaken; 1) MoP versus CoC, (2) CoP versus CoC and (3) MoP versus CoP. Due to the inclusion of different study designs (RCT and observational studies) we performed separate analyses for RCTs and observational studies. The overall overall PJI odds ratio 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 on systematic reviews (16). A p value of less than 0.05 was considered statistically significant. Higgins I^2 statistics was used to assess heterogeneity.

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



RESULTS

Literature Search

A total of 2248 articles were identified through our search literature search and a further 24 studies were including after reading of bibliographies (Figure 1). After removal of duplicates and screening according to inclusion criteria 28 studies underwent full review. Of these three papers were excluded due to using the same study population being 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 Table 2 and Table 3 respectively.

Three of the eleven of the RCTs had high methodological quality and were deemed to be at low risk of bias. Eight of the RCTs were deemed to have “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 (37, 38). No study included a power calculation for PJI.

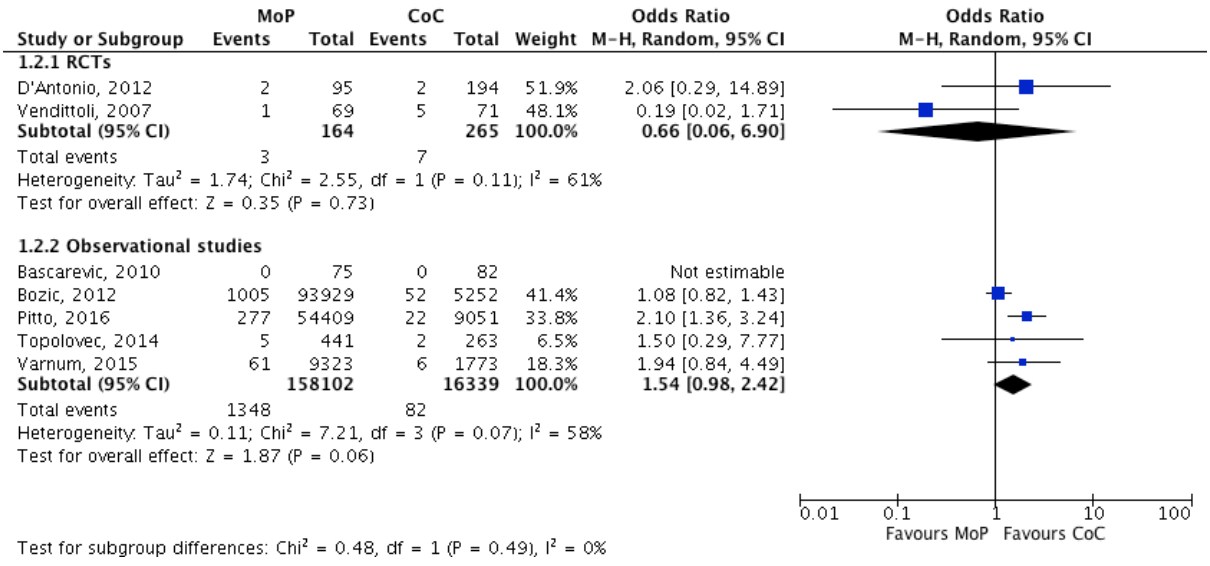
All observational studies included had a serious risk of bias due to inherent risk of confounding. Only two of the six non-randomised studies attempted to adjust for confounding factors. Bozic et al. (24) in their follow up of Medicare patients between 2005-2009 adjusted for patient differences such as age, sex, race, Charlson comorbidity index as well as institutional factors such as size of the hospital, urban/rural location. Pitto et al (20) in their 15-year analysis of the New Zealand registry, performed a multivariable assessment adjusting for risks factors including age, sex, operating room type, use of body exhaust suits, THA fixation mode, and

surgeon volume. All studies were considered as serious risk of confounding, as they did not adjust for all risk factors for PJI such as body mass index, immunosuppression and diabetes (39).

MoP v CoC

174,870 hips were included across seven studies. 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%).

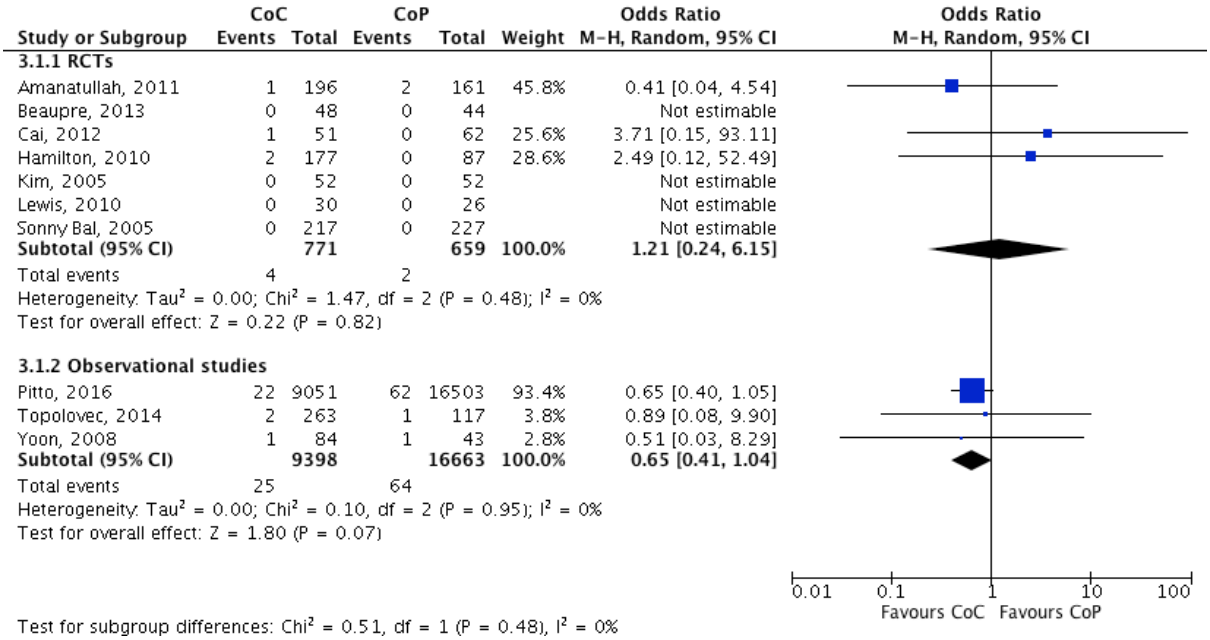
Fig. 2. Forest plot of included studies comparing PJI in MoP versus CoC bearings



CoP v CoC

27491 hips were included across ten studies and the overall incidence of PJI was 0.35% (95/27491). The incidence was 0.37% (64/17322) in the CoP group and compared to 0.29% (29/10169) in the CoC group. 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 1.27; 95% confidence interval 0.30 to 5.44; p = 0.75; heterogeneity, P = 0.48, I^2=0%). Separate analysis of the three observational studies showed no significant difference between CoP and CoC (odds ratio 1.80; 95% confidence interval 0.41 to 1.04; p = 0.07; heterogeneity, P = 0.95, I^2 =0%).

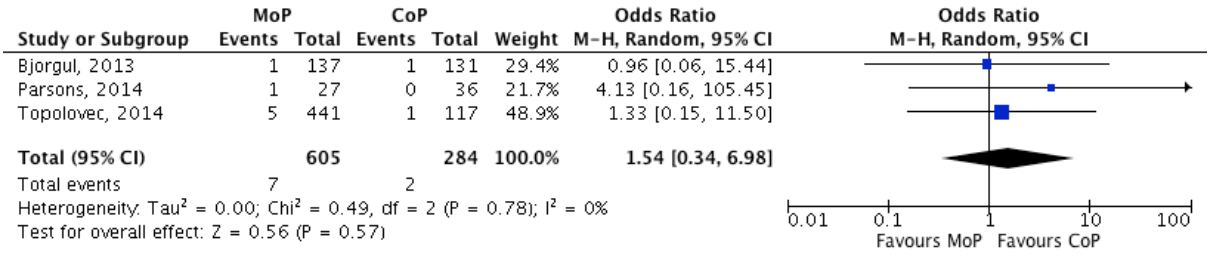
Fig. 3. Forest plot of included studies comparing PJI in CoP versus CoC bearings



MoP v CoP

Three studies (n=889 hips) consisting of two observational studies and one RCT were evaluated. The incidence was 1.16% (7/605) in the MoP group and compared to 0.70% (2/284) in the CoC group. Pooled analysis of these studies revealed no differences in PJI between MoP and CoP (odds ratio 1.54; 95% confidence interval 0.34 to 6.98; p = 0.57; heterogeneity, P = 0.78, I^2=0%)

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



DISCUSSION

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 (40). 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). Whilst none reached statistical significance, the analysis of non-randomised studies suggested a trend favouring CoC bearings but the opposite was 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 (41, 42).

Infection of orthopaedic implants is notoriously difficult to eradicate because bacteria attach to the implant surface and form biofilms (43). In this critical first step in the development of PJI adherent bacteria synthesise a complex glycocaylx (44), which provides resistance against the immune system and antimicrobial therapy (45). Surface properties such as roughness and hydrophobicity are known to influence biofilm formation (46, 47). Current ceramics used for manufacturing bearing surfaces in THA exhibit outstanding tribological properties, the most important of which are hardness and a high degree of wettability. Ceramic has a greater

hardness than metal and can be polished to a much lower surface roughness while excellent wettability (hydrophilicity) ensures that the synovial fluid is uniformly distributed between implant surfaces (48). The former guarantees high resistance to major scratches and reduced wear, while the latter facilitates fluid-film lubrication thus contributing to low friction between articulating surfaces (49). A reduction in the surface roughness has been related to a decrease in bacterial adhesion (50). However the effect of wettability on the adhesion of common pathogens that form biofilms on orthopaedic implants is much less clear and it has been shown that *Staphylococcus aureus* adheres more strongly to hydrophobic surfaces than hydrophilic surfaces (51). Aside from materials studied in this meta-analysis there is some evidence that implant materials can influence susceptibility to PJI. Experimental studies have shown that stainless steel surfaces are more susceptible to bacterial adherence than titanium alloys, cobalt chrome and tantalum (52, 53). Subtle changes in materials can also affect bacterial adherence; quantitative in vitro analysis of the adhesion of biofilm producing strains of *Staphylococcus aureus* and *Escherichia coli* found that vitamin E blended UHMWPE reduces bacterial adhesive ability when compared to standard UHMWPE (54). In vitro studies investigating antibacterial behavior are limited by the fact they do not reflect the dynamic, mechanically variable human in vivo environment (55). A retrieval study of 87 components from 32 patients with who had confirmed PJI did not find a difference in bacterial adherence to particular components or a particular biomaterial, with there being high variability in the adherence of microorganisms even from the same species (56). Relatively little is known about biofilms on current orthopaedic implant materials and further retrieval studies are required to characterise biofilms through imaging of implants and microbiological analysis of the biofilms themselves. Such studies will provide insight into the structure, composition or distribution of biofilms on orthopaedic implant surfaces and thus will facilitate the development of novel implant designs to reduce the susceptibility of PJI. In order to develop “anti-biofilm” implant materials (57), a realistic biofilm model is required that takes into account the morphology of biofilms on orthopaedic implants. Recent scientific forums have recommended research focus on the development of antibacterial implants that minimise bacterial adherence and colonisation (6), and this work must investigate numerous bacteria strains of the same species to evaluate intra-species variability (56). In addition, given the association between MoM articulations and PJI, research is needed to evaluate the association between trunnionosis and PJI (58). Finally little is known about genetic susceptibility (59) and why certain patients develop PJI when others do not despite having the same perioperative experience.

This meta-analysis has limitations. First, the RCTs that were included did not have PJI are their primary outcome and therefore are likely to be underpowered for evaluation of PJI; however, pooling the results of multiple RCTs in a meta-analysis is likely to generate enough power to detect such a difference. Secondly, when determining the relationship between bearing surface and PJI a major challenge is adequately adjusting for confounding hospital, surgical, and patient-related factors. In our study we included registry data of which only two of the six non-randomised studies attempted to adjust for confounding factors. Pitto et al. (20) performed the only study to specifically address the effect of bearing surface on PJI which analysed 97,889 primary THAs from the New Zealand registry over a 15 year period. Considerable efforts were made to adjust for factors that affect PJI, including age, sex, operating room type, use of body exhaust suits, THA fixation mode and surgeon volume. Nevertheless they were unable to adjust for PJI risk factors such as diabetes mellitus, body mass index, immunosuppression, hypoalbuminaemia and coagulopathy (39). The authors concluded that CoC bearings seemed to be associated with a lower risk of revision for late PJI than other bearing couples but taken with the other studies in this meta-analysis we can not confirm this association beyond reporting the trend observed in other studies. Registry studies might be misleading because older patients have more comorbidities associated with PJI such as diabetes and obesity but are more likely to receive MoP than receive CoC. We believe in order to truly determine the impact of bearing surface on PJI an adequately powered registry study that controls for surgeon, implant and patient risk factors of PJI is required. This will be made easier through collaboration with national infection registries and surveillance systems (60), such as the Nosocomial Infection National Surveillance System (NINSS) in the UK (61). The authors agree with recent calls for patient-specific data to be included in national joint registries (7). All infected procedures should be included in registries and the minimum dataset should contain patient factors, operative factors including implant materials, pathogen factors, perioperative microbiological results and details of antibiotic therapy. Only with robust high-quality data such as this and international collaboration will the effect of variables on PJI, such as bearing surface implant materials, be able to be accurately and confidently evaluated.

In conclusion, this study is the first systematic review and meta-analysis to specifically evaluate the association between bearing surface and PJI in THA. No significant difference was seen in PJI between MoP, CoP and CoC

bearings. This study has used best available evidence, which does not support recent reports that ceramic bearings have reduced risk of PJI.

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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	Cochrane Rob 2.0 Tool					Overall Bias
	1	2	3	4	5	
Beaupre [26] 2013	Low	Low	Some concerns	Low	Low	Some concerns
Bjorgul [35] 2013	Low	Low	Low	Low	Low	Low
Cai [27] 2012	Low	Low	Some concerns	Low	Low	Some concerns
D'Antonio [22] 2012	Low	Low	Some concerns	Low	Low	Some concerns
Amanatullah [28] 2011	Some concerns	Low	Some concerns	Low	Low	Some concerns
Lewis [29] 2010	Some concerns	Low	Low	Low	Low	Some concerns
Hamilton [30] 2010	Low	Low	Low	Low	Low	Low
Bascarevic [24] 2010	Low	Low	Some concerns	Low	Low	Some concerns
Vendittoli [25] 2007	Low	Low	Low	Low	Low	Low
Sonny Bal [32] 2005	Some concerns	Low	Low	Low	Low	Some concerns
Kim [33] 2005	Some concerns	Low	Low	Low	Low	Some concerns

Table 3. Quality Assessment of observational studies

Publication	Type of bias							Overall risk of bias
	Confounding	Participant selection	Classification of interventions	Deviation from intended intervention	Attrition bias	Detection bias	Reporting bias	
Pitto [19] 2016	Serious	Low	Low	Low	Low	Low	Low	Serious
Varnum [20] 2015	Serious	Low	Low	Low	Low	Low	Low	Serious
Topolovec [21] 2014	Serious	Low	Low	Low	Low	Low	Low	Serious
Parsons [34] 2014	Serious	Low	Low	Low	Low	Low	Low	Serious
Bozic [23] 2012	Serious	Low	Low	Low	Low	Low	Low	Serious
Yoon [31] 2008	Serious	Low	Low	Low	Low	Low	Low	Serious