Supplementary data

Sensitivity meta-analysis

A systematic review of the effect of antibiotic-loaded bone cement vs. plain bone cement in preventing infection was conducted by Wang et al. (2013). They identified 7 prospective randomized control trials, (Pfarr and Burri 1979, Wannske and Tscherne 1979, McQueen et al. 1987, 1990, Josefsson and Kolmert 1993, Chiu et al. 2002, Hinarejos et al. 2013) yet 1 trial was excluded for having no events in either arm of the trial (Pfarr and Burri 1979). They concluded that antibiotic-loaded cement reduced the incidence of deep infection in comparison with the use of plain bone cement. We updated the systematic review using the following Medline search strategy (December 2015); ("hip"[MeSH Terms] OR "knee"[MeSH Terms] OR "hip"[All Fields] OR "knee"[All Fields] OR "joint"[All Fields]) AND ("arthroplasty"[MeSH Terms] OR "arthroplasty"[All Fields] OR "replacement"[All Fields]) AND ("cement*"[All Fields] OR "methylmethacrylate"[MeSH Terms] OR "methylmethacrylate"[All Fields] OR acrylic[All Fields]) AND ("anti-bacterial agents"[Pharmacological Action] OR "anti-bacterial agents"[MeSH Terms] OR "anti-bacterial"[All Fields] OR R[All Fields] AND "antibiotic"[All Fields] OR "gentamicins"[MeSH Terms] OR "gentamicins"[All Fields] OR "gentamicin"[All Fields]) OR erythomycin[All Fields] OR "colistin"[MeSH Terms] OR "colistin"[All Fields] OR "tobramycin"[MeSH Terms] OR "tobramycin"[All Fields] OR "cefuroxime"[MeSH Terms] OR "cefuroxime"[All Fields]) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]).

No additional trials were identified comparing the effect of antibiotic-loaded bone cement and plain bone cement. However, two longer term updates of a previous trial were examined. Re-analysis of the data including the excluded study (Pfarr and Burri 1979), using a correction for zero cell counts, and the 10-year long-term follow-up of the previous study (Josefsson and Kolmert 1993) demonstrated no statistically significant difference between antibiotic loaded and plain bone cement in patients undergoing total joint replacement (Risk Ratio: 0.602, 95% confidence interval [0.335–1.083], p-value= 0.09) (Supplementary Table 1), with studies regressing towards the null temporally (Supplementary Figure 1).

Chiu F Y, Chen C M, Lin C F, Lo W H. Cefuroxime-impregnated cement in primary total knee arthroplasty: A prospective, randomized study of three hundred and forty knees. J Bone Joint Surg (Am) 2002; 84-A (5): 759-62.

Hinarejos P, Guirro P, Leal J, Montserrat F, Pelfort X, Sorli M L, Horcajada J P, Puig L. The use of erythromycin and colistin-loaded cement in total knee arthroplasty does not reduce the incidence of infection: A prospective randomized study in 3000 knees. J Bone Joint Surg (Am) 2013; 95 (9): 769-74.

Josefsson G, Kolmert L. Prophylaxis with systematic antibiotics versus gentamicin bone cement in total hip arthroplasty: A ten-year survey of 1,688 hips. Clin Orthop Relat Res 1993; (292): 210-14.

McQueen M, Littlejohn A, Hughes S P. A comparison of systemic cefuroxime and cefuroxime loaded bone cement in the prevention of early infection after total joint replacement. Int Orthop 1987; 11 (3): 241-3.

McQueen M M, Hughes S P, May P, Verity L. Cefuroxime in total joint arthroplasty. Intravenous or in bone cement. J Arthroplasty 1990; 5 (2): 169-72.

Pfarr B, Burri C. Prospective study on the effect of gentamycin-Palacos in 200 total hip prostheses. Aktuelle Probl Chir Orthop 1979; (12): 207-10.

Wang J, Zhu C, Cheng T, Peng X, Zhang W, Qin H, Zhang X. A systematic review and meta-analysis of antibiotic-impregnated bone cement use in primary total hip or knee arthroplasty. PLoS One 2013; 8(12): e82745.

Wannske M, Tscherne H. Results of prophylactic use of Refobacin-Palacos in implantation of endoprostheses of the hip joint in Hannover. Aktuelle Probl Chir Orthop 1979; (12): 201-5.

Table 1. Sensitivity meta-analysis of randomized trials identified by Wang et al. (2013) using a continuity correction (+0.5) to cells with zero events, and including the 10-year term follow-up of the trial conducted by Josefsson and Kolmert (1993).

					Antibiotic bone cement		Plain bone cement	
First author	RR	95% CI	p-value	Weight (%)	Total	Events	Total	Events
Pfarr (1979)	1	(0.02–49.9)	1.00	2.2	100	0	100	0
Wannske (1979)	0.18	(0.05–0.64)	0.01	16.3	274	3	202	12
McQueen (1987)	0.51	(0.05–5.57)	0.6	5.5	146	1	149	2
McQueen (1990)	1.00	(0.14–6.99)	1.00	7.9	201	2	200	2
Josefsson (1993)	0.68	(0.29–1.59)	0.4	27.3	821	9	812	13
Chiu (2002)	0.09	(0.01–1.65)	0.1	3.9	178	0	162	5
Hinarejos (2013)	1.00	(0.54–1.85)	1.00	37.1	1,483	20	1,485	20
D+L pooled RR	0.60	(0.33–1.08)	0.09	100				

RR = risk ratio, 95% CI = 95% confidence interval, p = p-value, D+L = DerSimonian & Laird.

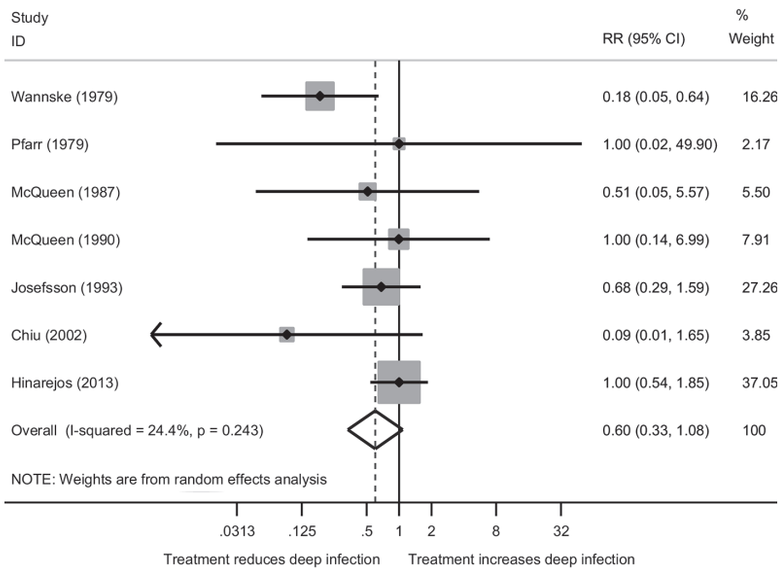

Figure 1. Meta-analysis comparing the relative risk of deep joint infection between antibiotic-loaded and plain bone cement in patients undergoing arthroplasty. Random effects meta-analysis using DerSimonian & Laird estimator of seven randomized studies. RR = relative risk. 95% CI = 95% confidence interval.

Table 4. Summary statistics of bone cement follow-up measured in prosthesis years

Manufacturer Brand	Viscosity	Antibiotic	Prosthesis follow-up, years Mean	(Median)	[IQR]
Heraeus Medical					
Palacos HV		G	3.1	(2.7)	[1.3–4.7]
Palacos HV		–	3.1	(2.8)	[1.2–4.7]
Palacos MV		G	3.6	(3.9)	[1.7–5.6]
Palacos LV		G	4.2	(4.4)	[2.2–6.0]
Stryker					
Simplex MV		T	4.0	(3.7)	[1.5–6.0]
Simplex MV		E/C	4.6	(4.5)	[2.2–6.7]
Simplex MV		–	5.5	(5.6)	[3.4–7.5]
Schering-Plough					
Palacos HV		G	6.8	(7.4)	[5.0–8.7]
Palacos HV		–	6.4	(6.5)	[4.8–8.2]
Palacos LV		G	7.3	(7.9)	[6.3–8.9]
Biomet					
Palacos HV		G	6.3	(6.9)	[3.8–8.7]
Palacos HV		–	4.9	(5.0)	[2.8–6.8]
Biomet HV		G	4.2	(3.7)	[1.8–6.2]
DePuy					
CMW 1 HV		G	4.9	(4.7)	[2.7–7.2]
CMW 1 HV		–	5.7	(5.7)	[3.8–7.8]
CMW 2 HV		G	3.0	(2.2)	[1.0–4.5]
CMW 2 HV		–	4.6	(4.5)	[1.3–7.6]
CMW 3 MV		G	4.5	(4.8)	[2.3–6.6]
SmartSet HV		G	4.7	(5.1)	[2.7–6.6]
SmartSet HV		–	4.6	(4.9)	[3.2–6.3]

Viscosity: HV = high, MV = medium, LV = low.
Antibiotics: G = gentamicin, T = tobramycin, E/C = erythromycin/colistin
IQR = Interquartile range.

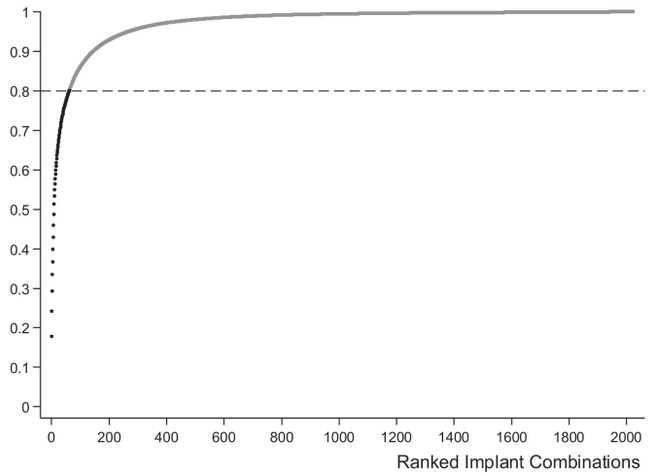

Figure 3. Cumulative proportion of primary procedures ordered by most popular implant combination.

Table 5. Incidence rate ratio of revision of primary total hip replacement by cement type

Manufacturer / Brand	Viscosity	Antibiotic	Adjusted for implant type IRR	SD	95% CI	p	ESS	Fully adjusted model [a] IRR	SD	95% CI	p	ESS
Heraeus Medical												
Palacos HV [b]	G		–	–	–	–	–	–	–	–	–	–
Palacos HV	–		0.72	0.43	(0.22–1.81)	0.3	11,483	0.77	0.47	(0.23–1.94)	0.3	11,093
Palacos MV	G		0.36	0.36	(0.06–1.35)	0.08	10,265	0.37	0.36	(0.06–1.34)	0.08	8,820
Palacos LV	G		1.14	0.31	(0.67–1.87)	0.3	10,401	1.23	0.34	(0.71–2.02)	0.2	9,454
Stryker												
Simplex MV	T		0.96	0.08	(0.81–1.13)	0.3	7,696	0.96	0.08	(0.82–1.14)	0.3	7,586
Simplex MV	E/C		0.87	0.08	(0.73–1.03)	0.05	6,499	0.86	0.08	(0.73–1.02)	0.04	7,615
Simplex MV	–		1.01	0.12	(0.80–1.27)	0.4	9,269	1.01	0.12	(0.80–1.28)	0.5	9,536
Schering-Plough												
Palacos HV	G		0.95	0.06	(0.85–1.06)	0.2	4,777	0.94	0.06	(0.84–1.05)	0.1	4,761
Palacos HV	–		0.75	0.16	(0.48–1.12)	0.08	12,043	0.74	0.16	(0.48–1.11)	0.08	11,470
Palacos LV	G		1.35	0.26	(0.92–1.93)	0.06	8,666	1.36	0.27	(0.92–1.95)	0.06	8,741
Biomet												
Palacos HV	G		0.58	0.42	(0.15–1.66)	0.2	10,272	0.60	0.45	(0.14–1.75)	0.2	10,921
Palacos HV	–		1.08	0.28	(0.65–1.73)	0.4	11,432	1.13	0.29	(0.68–1.79)	0.3	10,364
Biomet HV	G		0.92	0.07	(0.79–1.06)	0.1	6,288	0.94	0.07	(0.81–1.08)	0.2	7,558
DePuy												
CMW1 HV	G		1.01	0.11	(0.81–1.25)	0.5	9,046	1.01	0.11	(0.81–1.24)	0.5	8,989
CMW1 HV	–		0.45	0.19	(0.19–0.91)	0.01	11,345	0.44	0.18	(0.19–0.89)	0.01	10,039
CMW2 HV	G		1.02	0.19	(0.71–1.43)	0.4	10,228	1.01	0.19	(0.70–1.42)	0.5	10,285
CMW2 HV	–		1.20	0.43	(0.58–2.23)	0.3	11,439	1.24	0.45	(0.60–2.31)	0.3	10,189
CMW3 MV	G		1.98	0.29	(1.49–2.61)	< 0.001	10,137	2.03	0.30	(1.51–2.69)	< 0.001	9,864
SmartSet HV	G		0.99	0.16	(0.72–1.33)	0.5	10,437	1.01	0.16	(0.74–1.36)	0.5	10,342
SmartSet HV	–		2.38	1.06	(0.96–5.02)	0.03	10,029	2.65	1.16	(1.12–5.53)	0.02	9,915

IRR = incidence rate ratio (relative to reference). SD = standard deviation of posterior chain. p = directional posterior probability.
95% CI = 95% credible interval, the 2.5th and 97.5th centile for the posterior distribution. ESS = effective sample size.
[a] Adjusted for implant type, age, gender, ASA physical status, surgical approach, and head size.
[b] Heraeus Medical Palacos high-viscosity bone cement with gentamicin is reference.
Antibiotics: G = gentamicin, T = tobramycin, E/C = erythromycin/colistin.

Table 6. Cited reasons for revision for antibiotic-loaded and plain bone cements

	Antibiotic bone cement Revisions n	(%)	PTIR	Plain bone cement Revisions n	(%)	PTIR
All	2,348	(100)	3.08	146	(100)	2.85
No reason recorded	47	(2.0)	0.06	4	(3)	0.08
Dislocation/subluxation	670	(28.5)	0.88	41	(28)	0.80
Aseptic loosening	534	(22.7)	0.70	39	(27)	0.76
Infection	557	(23.7)	0.73	38	(26)	0.74
Pain	329	(14.0)	0.43	23	(16)	0.45
Periprosthetic fracture	321	(13.7)	0.42	11	(8)	0.21
Malalignment	197	(8.4)	0.26	18	(12)	0.35
Lysis	102	(4.3)	0.13	11	(8)	0.21
Implant fracture	42	(1.8)	0.06	0	–	–
Other	236	(10.1)	0.31	9	(6)	0.18

Individuals may have more than one reason for revision cited within the NJR.
PTIR = prosthesis time incidence rate (rate of revision per 1,000 prosthesis-years of follow-up).