TABLE E-1 Study Characteristics of Randomized Trials*

Study (author/year) (arthroplasty/ bisphosphonate)	Sample size (intervention/ control)	**Intervention Group** Age (Mean ± SD) yr Sex (M/F) BMI (Mean ± SD) (kg/m^2) BMD (Mean ± SD) (g/cm^2)	**Control Group** Age (Mean ± SD) yr Sex (M/F) BMI (kg/m^2) BMD (g/cm^2)	Intervention	Duration (weeks)	Outcomes measured	Loss to follow-up	Funding	Quality Score
Wang et al.[13] 2003 (TKA/ alendronate)	96 (48/48)	70.0 ± 7 48 females NA 0.90 ± 0.16	71.0 ± 7 48 females NA 0.85 ± 0.18	o 10 mg alendronate/day x 6 months *vs* no alendronate o Partial weight-bearing immediately + CPM and physiotherapy	52	o Change in periprosthetic BMD, measured with dual energy x-ray absorptiometry, between baseline (preop) and 6 and 12 months o Determined biochemical markers of bone turnover at 12 months	0	o Peer-reviewed: Chang Gung Research Fund	70
Wilkinson et al.[12], 2001 (Hybrid THA/ pamidronate)	47‡ 23/24	58 ± 13 9/14 27 ± 5 1.77 ± 0.15	59 ± 12 12/12 29 ± 5 1.77 ± 0.27	o 90 mg pamidronate in 500 mL NS IV 5th POD *vs* placebo o 6 wk of 50% weight-bearing on 2 crutches starting POD 2 or 3	26	o Change in periprosthetic BMD, measured with dual energy x-ray absorptiometry, between baseline (1 wk postop) and 6, 12 & 26 weeks o Determined biochemical markers of bone turnover preop, day of pamidronate, and at weeks 6, 12 & 26 o Plain radiographs at baseline at week 1 after surgery then at weeks 6,12 & 26 for aseptic loosening & heterotopic ossification o Clinical assessment with Harris hip scores & SF-36 UK preop & at week 12 & 26 postop	4% 2 patients excluded in OR	o Peer-reviewed grants: BOA, RCSE, John Charnley Trust o Industry fund: free drugs, Novartis	85
Venesmaa et al.[10], 2001 (Uncemented THA/ alendronate)	13 8/5	63, range: 50-71 3/5 28.3, range: 23.0-36.2 1.60 ± 0.25	62, range: 57-70 3/2 24.9, range:23.3-29.8 1.58 ± 0.12	o 10 mg alendronate + 500 mg calcium carbonate daily *vs* 500 mg calcium carbonate only o Full weight-bearing immediately	24	o Baseline postop BMD measurement with dual energy x-ray absorptiometry within 2 weeks of THA & then at 3 & 6 months o Clinical & radiographic evaluations during visits	0	None	65
Soininvaara et al.[8], 2002 (Cemented TKA/ alendronate)	19 9/10 §	62 ± 8.6 4/5 28.8 ± 3.6 1.45 ± 0.17	67 ± 8.6 3/7 30.3 ± 3.1 1.39 ± 0.22	o 10 mg alendronate + 500 mg calcium carbonate daily *vs* 500 mg calcium carbonate only o Full weight-bearing immediately	52	o Baseline postop BMD measurement with dual energy x-ray absorptiometry within 1 week of TKA & then 3, 6 & 12 months postop o Clinical & radiographic evaluations during visits	0	None	65
Hennigs et al.[9], 2002 (Uncemented THA/ alendronate)	66 Group 1: 21 Group 2:21 Control: 24	Group 1: 50.5 (33-61) 5/16 N/A 1.25 ± 0.18 Group 2: 52.9 (32-66) 12/9 N/A 1.27 ± 0.14	52.4 (22-65) 12/12 N/A 1.20 ± 0.16	o Group 1: 10 mg alendronate daily for 10 weeks o Group 2: 20 mg alendronate daily for 5 weeks o Control: no treatment	52	o Baseline postop BMD measurement with dual energy x-ray absorptiometry within 1 week of THA & then 2, 4, 6 & 12 months postop	0	Peer-reviewed grants: Association of Orthopaedic Research	70
Lyons[11], 1999 (Cemented THA/ alendronate) (ABSTRACT)	49 Acute: 16 (8/8) Chronic:17 Revision: 16	All 3 subgroups 66.4 ± 7.5 12/13 N/A N/A	All 3 subgroups 65.1 ± 7.9 12/12 N/A N/A	10 mg alendronate + 500 mg calcium supplement daily *vs* 500 mg calcium supplement only	52 original study, 52 extension study¶	o Periprosthetic BMD, Gruen zones 1 to 3 and 5 to 7 o Evaluations of AP and lateral radiographs of prosthetic hip o Bone scintigraphy o QoL measurement with Nottingham Health profile and Brief Pain Inventory	2% 1 in placebo group	Industry fund: Merck & Co., Inc.	Not Applicable

*BMI: Body mass index; BMD: Bone mineral density; THA: Total hip arthroplasty; TKA: Total knee arthroplasty; CPM: continuous passive motion; NS IV: Normal saline solution intravenous; POD: Postoperative day; DEXA: Dual energy x-ray absorptiometry; QoL: Quality of Life; N/A: Not available, BOA: British Orthopaedic Association, RCSE: Royal College of Surgeons of England.

‡Wilkinson et al. recruited 50 patients for their study. 24 received pamidronate. 3 patients were withdrawn from the study after randomization. The results of 47 patients (23 in the intervention group and 24 in the control group) were published. At operation, 2 patients (one from each randomization group) were excluded from analysis. The first author (J.M.W.) was contacted to verify the exact numbers. The exact numbers used in the analysis of the proximal part of the femur were obtained (25 in intervention group, 25 in control group). §Initially, 9 in the intervention group and 10 in the control group. One patient stopped using alendronate because of gastric problems after a few tablets, but she continued in the calcium-only group. After that, the control group consisted of 11 patients and the intervention group consisted of 8. ¶6 from the control group and 7 from the intervention group participated in the extension study.

TABLE E-2 Sensitivity Analysis

N/A = not available. *Weighted mean age of patients with cementless arthroplasty = 55.0 years. Weighted mean age of patients with arthroplasty with cement = 68.0 years.

			3 months		6 months		12 months	
	Number of Trials	Number of Patients	Weighted Mean Difference (95% Confidence Interval)	P Value	Weighted mean difference (95% Confidence Interval)	P Value	Weighted Mean Difference (95% Confidence Interval)	P Value
Cement Use*								
Uncemented	3	78	3.5 (1.4-5.7)	0.96	3.7 (1.2-6.1)	0.34	2.1 (0.61-3.6)	<0.001
Cemented	3	169	3.6 (0.4-6.7)		8.7 (−1.4-18.7)		7.5 (4.3-10.7)	
Region								
Total hip	4	132	3.2 (1.8-4.6)	0.27	2.5 (0.96-4.1)	<0.001	3.2 (0.82-5.6)	0.06
Total knee	2	115	7.3 (0.03-14.6)		14.0 (6.3-21.7)		10.3 (3.4-17.2)	
Type of bisphosphonate								
Alendronate	5	193	3.8 (1.8-5.9)	0.51	5.9 (2.2-9.8)	0.07	N/A	N/A
Pamidronate	1	54	2.9 (1.1-4.7)		1.7 (−0.34-3.8)		N/A	
Study quality score								
Score <70	2	22	6.7 (2.0-11.5)	0.13	8.1 (2.4-13.9)	0.16	15.3 (0.2-30.5)	0.14
Score ≥70	3	210	3.0 (1.6-4.4)		3.5 (0.5-6.5)		3.8 (1.3-6.3)	
Full manuscript vs abstract								
Abstract	1	N/A	N/A	N/A	N/A	N/A	6.8 (3.1-10.4)	0.32
Full manuscript	4	N/A	N/A		N/A		7.9 (0.4-16.6)	
Blinding								
Yes	2	119	3.1 (1.1-5.8)	0.24	2.6 (0.91-4.4)	<0.01	2.1 (0.54-3.2)	0.08
No	4	171	7.2 (0.02-14.9)		13.9 (5.9-23.1)		9.0 (2.8-16.3)	