Sogard, Oliver, and Gregory A. Brown. 2023. "Cost-Effectiveness of Bone Cement With and Without Antibiotics: A Broader Perspective." *Journal of Orthopaedic Experience & Innovation* 4 (2). https://doi.org/10.60118/001c.74412.

Systemic Review

Cost-Effectiveness of Bone Cement With and Without Antibiotics: A Broader Perspective

Oliver Sogard, MD¹^{o^a}, Gregory A. Brown, MD, PhD²^{o^b}

¹ Medical School, University of North Dakota, ² Orthopaedic Surgery, Catholic Health Initiatives Keywords: Antibiotic-laden bone cement, periprosthetic joint infection, periprosthetic femur fracture https://doi.org/10.60118/001c.74412

Journal of Orthopaedic Experience & Innovation

Vol. 4, Issue 2, 2023

Background

Periprosthetic joint infections (PJIs) and periprosthetic femur fractures (PFFs) increase total costs of care. Retrospective registry/institutional studies with selection bias and underpowered meta-analyses have corrupted the evidence base regarding antibiotic-laden bone cement (ALBC) use in total knee arthroplasties (TKAs). Clinical practice guidelines (CPGs) recommend using cement fixation of femoral components in hip fracture patients to prevent PFFs, but have no recommendations regarding ALBC. Hip osteoarthritis CPGs have no bone cement recommendations regarding prevention of PJIs or PFFs. ALBC is potentially cost-effective by reducing PJIs, PFFs, and reducing implant costs.

Methods

A systematic review was conducted to identify randomized controlled trials (RCTs), meta-analyses, and registry reports related to the efficacy of ALBC in reducing PJIs and cemented femoral fixation in reducing PFFs. Numbers needed to treat (NNT) are calculated. Cost-effectiveness margins per case are calculated.

Results

A pooled analysis of four TKA RCTs found ALBC reduces PJI by 0.94% (p=0.027), NNT 106. A total hip arthroplasty (THA) meta-analysis found ALBC reduces PJI by 0.58% (p<0.0001), NNT 172. A hip hemiarthroplasty (HH) RCT found high-dose dual-antibiotic ALBC reduces PJI by 2.35% (p=0.0474), NNT 43. A THA registry report found that cemented fixation compared to ingrowth fixation reduced PFFs by 0.44% (p<0.0001), NNT 229. A pooled analysis of three HH RCTs found that cemented femoral stem fixation reduced PFFs by 5.09% (p-0.0099), NNT 20. Mean PJI treatment costs are \$80,000. Mean PFF treatment costs are \$27,596. Mean HH cemented femoral stem cost reduction: \$685. Using ALBC: TKA margin/case is \$755; THA margin/case is \$586; and HH margin/case is \$3,925. Using plain bone cement: TKA margin/case is \$0; THA margin/case is \$121; and HH margin/case is \$2,065.

a Oliver Sogard, MD, recently graduated from the University of North Dakota. He matched with the Guthrie/Robert Packer Hospital Orthopaedic Surgery Residency Program in Sayre, PA.

Visit Oliver Sogard's Website Connect with Oliver Sogard on LinkedIn Conflicts of Interest Statement for Oliver Sogard

b Gregory A. Brown, MD, PhD, practices general orthopaedics at CHI St. Alexius Health in Williston, ND (a critical access hospital). He was subchair for Clinical Practice Guidelines for the AAOS Committee on Evidence-Based Quality and Value from 2015-2018.
 <u>Connect with Dr. Brown on LinkedIn</u>

Visit the Open Payments Data Page for Dr. Brown Conflicts of Interest Statement for Dr. Brown

Conclusions

A broader perspective demonstrates that ALBC provides significant financial margins in TKAs, THAs, and hip hemiarthroplasties. ALBC is cost-effective when including the additional costs of using ALBC in TKAs, THAs, and hip hemiarthroplasties. Hand-mixed ALBC is more cost-effective than pre-mixed ALBC in all scenarios.

INTRODUCTION

The American Academy of Orthopaedic Surgeons (AAOS) released the *Surgical Management of Osteoarthritis of the Knee* Evidence-Based Clinical Practice Guideline (CPG) in 2015 (McGrory et al. 2016). Regarding antibiotic-laden bone cement (ALBC), the CPG recommended: "Limited evidence does not support the routine use of antibiotics in the cement for primary total knee arthroplasty (TKA)." The CPG was recently updated (American Academy of Orthopaedic Surgeons 2022) and the ALBC recommendation was withdrawn because there is insufficient high-quality evidence to make a recommendation for or against the use of ALBC in TKAs. The prior recommendation was in essence a type II statistical error (finding no difference when a difference may exist).

The literature has been flooded with articles claiming that ALBC is ineffective in TKA. The majority of articles are non-randomized and have selection bias. The selection bias occurs because some orthopaedic surgeons use ALBC on high-risk patients only and use plain bone cement (PBC) on patients without periprosthetic joint infection (PJI) risk factors. Five categories of articles have corrupted the evidence base: (1) registry studies with selection bias (Bohm et al. 2014; Chan et al. 2019; Gutowski et al. 2014; Jameson et al. 2019; Jämsen et al. 2009; Namba et al. 2009, 2020; Sanz-Ruiz et al. 2017; Tayton et al. 2016), (2) institutional studies that are underpowered with selection bias (Anis et al. 2019; Bendich et al. 2020; Eveillard et al. 2003; T. Hoskins et al. 2020; Srivastav et al. 2009; Turhan 2019; Wu et al. 2016; H. Wang et al. 2015; Yayac et al. 2019), (3) randomized controlled trials (RCTs) that are underpowered (Chiu et al. 2001, 2002; Chiu and Lin 2009; Hinarejos et al. 2013), (4) meta-analyses of RCTs that are underpowered (J. Wang et al. 2013; Zhou et al. 2015; Kleppel et al. 2017), and (5) meta-analyses including registry data with selection bias (Sultan et al. 2019; Farhan-Alanie, Burnand, and Whitehouse 2021; Li et al. 2022).

Critical review of the evidence suggests that ALBC does lower PJI rates for TKA. A power analysis of the three metaanalyses of RCTs cited above (J. Wang et al. 2013; Zhou et al. 2015; Kleppel et al. 2017) shows that the number of patients per subgroup required for 80% statistical power is decreasing, and the absolute difference in PJI rates is increasing with each subsequent meta-analysis (<u>Table 1</u>). This would suggest that as more RCTs comparing ALBC and PBC are completed, the clinically-significant differences will become statistically significant.

Reducing TKA PJIs is not the only potential benefit of using PBC or ALBC in hip and knee arthroplasty. ALBC can reduce PJIs in total hip arthroplasty (THA) and hip hemiarthroplasty (HH). Osteoporosis is common in THA patients (Bernatz et al. 2019). The AAOS *Management of Os*- *teoarthritis of the Hip* clinical practice guideline has no recommendation regarding the use of bone cement for THA (Rees 2020). Hip fracture patients have osteoporosis by definition. The AAOS *Management of Hip Fractures in Older Adults* CPG strongly recommends using cemented femoral stems in patients with femoral neck fractures. However, the CPG does not address the use of ALBC (O'Connor and Switzer 2022). Cement fixation (ALBC or PBC) for femoral stems in THA and HH has been shown to reduce the risk of periprosthetic femur fractures (PFFs) (Abdel et al. 2016; Langslet et al. 2014; Barenius et al. 2018; Santini et al. 2005). For patients with femoral neck fractures, cemented fixation of femoral stems allows the use of low-demand fracture stems, thereby reducing implant costs.

The primary aim of the cost-effectiveness analysis is to calculate the potential cost savings (margins) per case for TKA, THA, and HH procedures. The secondary aim of the cost-effectiveness analysis is to provide a methodology to calculate ALBC case margins for TKA, THA, and HH procedures at individual hospitals. Hospital-specific PJI rates, PFF rates, and costs can be substituted into the analyses to calculate hospital-specific case margins.

METHODS

Systematic reviews for five clinical scenarios were conducted: PJI rates in TKA, THA, and HH using ALBC and PBC; and PFF rates in THA and HH using bone cement. The purpose of each systematic review was to determine the best available evidence for estimating PJI rates or PFF rates for each scenario. The best evidence is an adequately-powered RCT or adequately-powered meta-analysis of RCTs. If an adequately-powered RCT/meta-analysis is not available, a pooled analysis of RCTs is the next best evidence. If adequately-powered RCT, meta-analysis, or pooled analysis is not available, a large observational registry cohort with no exclusions provides the next best available evidence.

Systematic reviews were performed using PubMed and Embase for each scenario using keywords from each scenario. Articles were included from inception to February 1, 2022. Full text articles published in English were included. The PRISMA flowchart of each systematic review is provided in Table 2.

Economic analyses were conducted using the number needed to treat (NNT) and the mean costs of TKA/THA revisions for periprosthetic joint infection or periprosthetic femur fracture. NNT is calculated as the inverse of the absolute difference in rates (r):

$NNT = 1/(r_{\rm PJI, PBC} - r_{\rm PJI, ALBC})$

The number needed to treat is the number of patients that would need to be treated with ALBC to prevent one periprosthetic joint infection or one periprosthetic femur

 Table 1. Meta-analyses comparing ALBC and PBC periprosthetic joint infection (PJI) rates (Brown and Chen 2022)

Author (Year)	Included trials	ALBC PJI Rates	PBC PJI Rates	Patients Needed per Subgroup	Absolute Difference in PJI Rates
Wang (2013)	2	20/1661 (1.20%)	25/1627 (1.54%)	18,327	0.33%
Zhou (2015)	5	46/3461 (1.33%)	60/3176 (1.89%)	7,620	0.56%
Kleppel (2017)	9	23/1979 (1.16%)	35/1924 (1.82%)	5,282	0.66%

ALBC - antibiotic-laden bone cement, PBC - plain bone cement, PJI - periprosthetic joint infection.



*Advertisement

<u>Click here to learn more about Zilretta</u>

fracture. The margin per case is the revision cost divided by the NNT (margin/case = $COST_{revision}/NNT$).

The NNT for the reduced implant costs in hip hemiarthroplasty is unity (NNT = 1) because the costs are reduced for each case.

Statistical power calculations were performed per Rosner (Rosner 1990). Fisher's exact tests (2x2) and chi-squared tests (2x2) were used to determine statistical significance (p<0.05) (GraphPad - <u>https://www.graphpad.com</u>).

This study is exempt from institutional review board review.

RESULTS

PERIPROSTHETIC JOINT INFECTION IN TOTAL KNEE ARTHROPLASTY USING ALBC OR PBC

Three underpowered meta-analyses comparing PJI rates using ALBC and PBC in TKA were identified but excluded because of the lack of statistical power. Four RCTs comparing PJI rates using ALBC and PBC in TKA were identified (Chiu et al. 2001, 2002; Chiu and Lin 2009; Hinarejos et al. 2013). The RCTs were heterogeneous, including primary TKAs (Chiu et al. 2002), primary TKAs in patients with diabetes (Chiu et al. 2001), revision TKAs (Chiu and Lin 2009), and erythromycin/colistin ALBC in primary TKAs (Hinarejos et al. 2013). Because of the heterogeneity, a pooled analysis was performed (<u>Table 3</u>). The periprosthetic joint infection rates are 1.11% and 2.05% for ALBC and PBC, respectively (p=0.0304). The absolute difference in PJI rates is 0.94%. The NNT is 106.

PERIPROSTHETIC JOINT INFECTION IN TOTAL HIP ARTHROPLASTY USING ALBC OR PBC

Three adequately powered meta-analyses comparing PJI rates using ALBC and PBC in THA were identified (Farhan-Alanie, Burnand, and Whitehouse 2021; Parvizi et al. 2008; Kunutsor et al. 2019). Farhan-Alanie *et al.* was excluded because revision rates were reported, not PJI rates (Farhan-Alanie, Burnand, and Whitehouse 2021). Kunutsor *et al.* was excluded because non-randomized observational cohorts were included in the meta-analysis (Kunutsor et al. 2019). Parvisi *et al.* (Parvizi et al. 2008) reported PJI rates of 0.47% and 1.05% for ALBC and PBC, respectively (p=0.001). The absolute difference in PJI rates is 0.58%. The NNT is 172.

PERIPROSTHETIC JOINT INFECTION IN HIP HEMIARTHROPLASTY USING ALBC OR PBC

One RCT comparing PJI rates using low-dose, single-antibiotic bone cement and high-dose, dual-antibiotic bone cement in hip hemiarthroplasty was identified (Sprowson† et al. 2016). The RCT reported PJI rates of 1.11% and 3.46% for high-dose, dual-antibiotic and low-dose, single-antibiotic ALBC, respectively (p=0.0474). The absolute difference in PJI rates is 2.35%. The NNT is 43.

PERIPROSTHETIC FEMUR FRACTURES IN THA USING CEMENTED AND INGROWTH FEMORAL FIXATION

No meta-analyses or RCTs comparing periprosthetic femur fracture (PFF) rates using cemented or ingrowth femoral fixation in THA were identified. One large, prospective registry cohort was identified (32,644 THAs) (Abdel et al. 2016). The PFF rates from surgery to one year after surgery were 0.601% and 0.165% for ingrowth and cemented

Table 2. PRISMA flow diagrams for systematic reviews.

PRISMA Categories	ALBC & PBC PJI Rates in TKA	ALBC & PBC PJI Rates in THA	ALBC & PBC PJI Rates in HH	Cemented & Ingrowth PFF Rates in THA	Cemented & Ingrowth PFF Rates in HH
Identification					
Number of records identified through database searching	32	258	0	139	36
Number of additional records identified through other sources	179	131	1	55	10
Number of duplicates removed	30	85	0	48	8
Screening					
Number of records screened	149	326	0	91	28
Number of records excluded	138	292	0	78	19
Eligibility					
Number of full-text articles assessed for eligibility	11	34	1	13	9
Number of full-text articles excluded	7	33	0	12	6
Included					
Number of studies included in qualitative synthesis	4	3	1	1	3
Number of studies included in quantitative synthesis	4	1	1	1	3
Randomized Controlled Tri- als	4	0	1	0	3
Meta-Analyses	0	1	0	0	0
Observational/Registry Co-	U	Ŧ	U U	U U	U U
horts	0	0	0	1	0

ALBC – antibiotic-laden bone cement, PBC – plain bone cement, PJI – periprosthetic joint infection, TKA – total knee arthroplasty, THA – total hip arthroplasty, PFF – periprosthetic femur fracture, HH – hip hemiarthroplasty.



<u>Click here to learn more about Stryker Motion Sense</u>

femoral fixation, respectively (p<0.0001). The absolute difference in PFF rates is 0.436%. The NNT is 229.

Table 3. Pooled analysis of RCTs com	paring ALBC and PBC p	eriprosthetic joint infection	(PJI) rates in TKAs.

Author (Year)	ALBC PJI Events	ALBC Total Patients	ALBC PJI Rate	PBC PJI Events	PBC Total Patients	PBC PJI Rate	Absolute Difference in PJI Rates	
Chiu (2001)	0	41	0.00%	5	37	13.51%	13.51%	
Chiu (2002)	0	178	0.00%	5	162	3.09%	3.09%	
Chiu (2009)	0	93	0.00%	6	90	6.67%	6.67%	
Hinarejos (2013)	20	1483	1.35%	20	1465	1.37%	0.02%	
Total	20	1795	1.11%	36	1754	2.05%	0.94%	
p=0.0304								

RCTs – randomized controlled trials, ALBC – antibiotic-laden bone cement, PBC – plain bone cement,

PJI – periprosthetic joint infection.

Table 4. Pooled analysis of RCTs comparing hip hemiarthroplasty periprosthetic femur fracture (PFF) rates.

on Fixation Ingrowth Absolute Total Fixation Difference is Patients PFF Rate in PFF Rates
53 3.77% 3.77%
108 7.41% 6.51%
74 6.76% 3.77%
235 6.38% 5.09%

PFF – periprosthetic femur fracture.

PERIPROSTHETIC FEMUR FRACTURES IN HIP HEMIARTHROPLASTY USING CEMENTED AND INGROWTH FEMORAL FIXATION

No meta-analyses comparing PFF rates using cemented or ingrowth femoral fixation in hip hemiarthroplasty were identified. Three RCTs comparing PFF rates using cemented or ingrowth femoral fixation in hip hemiarthroplasty were identified (Langslet et al. 2014; Barenius et al. 2018; Santini et al. 2005). A pooled analysis was performed (<u>Table 4</u>). The PFF rates were 1.29% and 6.38% for cemented and ingrowth femoral fixation, respectively (p=0.0065). The absolute difference in PFF rates is 5.09%. The NNT is 20.

CEMENTED FRACTURE FEMORAL STEM AND INGROWTH FEMORAL STEM COST DIFFERENTIAL

Two vendors at the senior author's institution were queried for average contract pricing for their most common cemented fracture femoral stem and their most common ingrowth (porous) femoral stem. Smith and Nephew reported that the average contract price differential between the Synergy porous femoral stem and the Conquest cemented fracture femoral stem was \$770. Stryker reported that the average contract price differential between the Accolade 2 porous femoral stem and the Exeter cemented fracture femoral stem was \$600. The mean price differential was \$685. The NNT is 1 for the use of a cemented fracture femoral stem because costs are reduced for each case.

REVISION THA AND TKA COSTS FOR PJI AND PFF

Cost estimates of revision total joint arthroplasty for periprosthetic joint infection and periprosthetic femur fracture were obtained from the literature. All costs were included in the estimates, not only hospital costs. Preference was given to more recent estimates. The cost of a PJI-related revision joint arthroplasty is estimated to be \$80,000 (Leta et al. 2021). The cost of a PFF-related revision joint arthroplasty is estimated to be \$27,596 (Hevesi et al. 2019).

MARGINS PER CASE

The margins per case were calculated by dividing the cost of the revision surgery by the NNT and summing the potential

	Treatment Costs	TKA NNT	TKA Margin per Case	THA NNT	THA Margin per Case	HH NNT	HH Margin per Case
Periprosthetic Joint Infection	\$ 80,000	106	\$755	172	\$465	43	\$1,860
Periprosthetic Femur Fracture	\$ 27,596			229	\$121	20	\$1,380
Reduced Implant Costs	\$ 685					1	\$685
Total Margin per Case			\$755		\$586		\$3,925

Table 5. Margin per case when using ALBC for hip and knee arthroplasty procedures.

ALBC - antibiotic-laden bone cement, TKA - total knee arthroplasty, NNT - number needed to treat, THA - total hip arthroplasty, HH - hip hemiarthroplasty.

	Table 6. Margin p	er case when using	g PBC for hip an	nd knee arthroplasty procedures.
--	-------------------	--------------------	------------------	----------------------------------

	Treatment Costs	TKA NNT	TKA Margin per Case	THA NNT	THA Margin per Case	HH NNT	HH Margin per Case
Periprosthetic Joint Infection	\$ 80,000		\$O		\$O		\$O
Periprosthetic Femur Fracture	\$ 27,596			229	\$121	20	\$1,380
Reduced Implant Costs	\$ 685					1	\$685
Total Margin per Case			\$0		\$121		\$2,065

PBC – plain bone cement, TKA – total knee arthroplasty, NNT – number needed to treat, THA – total hip arthroplasty, HH – hip hemiarthroplasty.

savings for PJI reduction, PFF reduction, and lower implant costs. Using ALBC: TKA margin per case is \$755; THA margin per case is \$586; and hip hemiarthroplasty margin per case is \$3,925 (<u>Table 5</u>). Using PBC: TKA margin per case is \$0; THA margin per case is \$121; and hip hemiarthroplasty margin per case is \$2,065 (<u>Table 6</u>).

ADDITIONAL COSTS FOR USING PRE-MIXED OR HAND-MIXED ALBC

Representative costs for bone cement and high-viscosity (HV) bone cement are \$50 per batch. A representative cost for bone cement with 1 g of tobramycin is \$250 per batch. A representative cost of HV bone cement with 0.8 g of gentamicin is \$150 per batch. Representative costs of tobramycin 1.2 g and gentamicin 0.8 g are \$30 and \$5, respectively. Since most TKAs are cemented, the differential cost of using two batches of pre-mixed HV ALBC with gentamicin is \$200 (\$150-\$50)x2. The differential cost of using two batches of hand-mixed HV ALBC with gentamicin is \$10 (\$5)x2. Since most THAs and hip hemiarthroplasties are not cemented, the differential cost of using two batches of pre-mixed ALBC with tobramycin is \$500 (\$250)x2. The differential cost of using two batches of hand-mixed ALBC is \$160 (\$50+\$30)x2. The net cost savings per case for premixed ALBC and hand-mixed ALBC are reported in Table 7 and Table 8, respectively.

DISCUSSION

The withdrawal of the recommendation to not use ALBC in primary TKAs in the recently released *Surgical Management of Osteoarthritis of the Knee* CPG (American Academy of Orthopaedic Surgeons 2022) acknowledges the lack of evidence regarding ALBC in primary TKAs. This lack of evidence of ALBC effectiveness is confused with evidence of lack of effectiveness. The level IV non-randomized studies need to be removed from the discussion. The underpowered meta-analyses need to be removed from the discussion (J. Wang et al. 2013; Zhou et al. 2015; Kleppel et al. 2017). The pooled analysis in this study found a statistically significant difference when using ALBC in TKAs, but the pooled analysis constitutes level II evidence due to the heterogeneity of the studies.

Clinical significance and statistical significance must not be confused. The three meta-analyses (J. Wang et al. 2013; Zhou et al. 2015; Kleppel et al. 2017) listed in <u>Table 1</u> all found clinically-significant differences in PJI rates when using ALBC (0.33%-0.66%). Clinically-significant differences in PJI rates provide positive margins per case for TKA, THA, and hip hemiarthroplasty. The ALBA trial is a registrybased RCT being conducted in Norway comparing ALBC and PBC with a minimum of 9,172 patients undergoing primary TKA (Leta et al. 2021). This trial should provide robust evidence on the effectiveness of ALBC in primary TKAs.

The use of ALBC in primary THA has not been controversial in the United States, probably because the use of ce-

Table 7. Net cost savings per case using pre-mixed antibiotic-laden bone cement (ALBC).

	Total	Total	
	Knee	Hip	Hip
	Arthroplasty	Arthroplasty	Hemiarthroplasty
Margin per case	\$ 755	\$ 586	\$ 3,925
Additional costs of ALBC	\$ 200	\$ 500	\$ 500
Net cost savings per case	\$ 555	\$86	\$ 3,425

Table 8. Net cost savings per case using hand-mixed antibiotic-laden bone cement (ALBC).

	Total	Total	
	Knee	Hip	Hip
	Arthroplasty	Arthroplasty	Hemiarthroplasty
Margin per case	\$ 755	\$ 586	\$ 3,925
Additional costs of ALBC	\$ 10	\$ 160	\$ 160
Net cost savings per case	\$ 745	\$ 426	\$ 3,765

iovera°

*Advertisement

Click here to learn more about Iovera

mented femoral fixation in primary THA has been so low. All three meta-analyses comparing ALBC and PBC in THA found ALBC was protective in reducing PJIs (Farhan-Alanie, Burnand, and Whitehouse 2021; Parvizi et al. 2008; Kunutsor et al. 2019). Additionally, a cost-effectiveness modeling study evaluating strategies to reduce the risk of PJI in primary THAs found that the most effective approach was systemic antibiotics, ALBC, and conventional ventilation (Graves et al. 2016).

Most ALBC cost-effectiveness analyses focus on primary TKAs and fail to consider the broader perspective that includes THA or hip hemiarthroplasty. They also fail to include the cost benefit of cemented femoral components reducing periprosthetic femur fractures and the lower cost of cemented fracture femoral stems. Given that primary TKAs, primary THAs, and hip hemiarthroplasties were all included in the Comprehensive Care for Joint Replacement (CJR) bundled payment program, ALBC cost-effectiveness should include all three procedures and all three cost benefits. The results of this study show that ALBC is most effective for hip hemiarthroplasty with a margin per case of \$3,925. This cost benefit is consistent with the AAOS Management of Hip Fractures in Older Adults clinical practice guideline which gives a "Strong" recommendation to use cemented femoral stems in "patients undergoing arthroplasty for femoral neck fractures" (O'Connor and Switzer 2022).

High-dose ALBC spacers are routinely used in TKA and THA two-stage revisions for periprosthetic joint infections. The high-dose ALBC has to be hand-mixed in the operating room because pre-mixed ALBC is not available in high enough antibiotic concentrations to treat periprosthetic joint infections. Consequently, hand-mixing ALBC in the operating room is already a routine practice for using ALBC and does not represent a "new" practice in the operating room.

The evidence for using ALBC in hip hemiarthroplasty is so compelling that the British have instituted the WHiTE 8 COPAL RCT comparing low-dose, single-antibiotic ALBC and high-dose, dual-antibiotic ALBC in patients undergoing hip hemiarthroplasty for femoral neck fracture (Agni et al. 2021). A minimum of 4,920 patients will be recruited to detect an absolute difference of 1.5% in PJI rates with 90% power. The results of the study are intended to inform policy and CPGs for the National Institute for Health and Care Excellence (NICE).

These cost-effectiveness analyses are limited by the lack of adequately powered RCTs evaluating ALBC efficacy preventing PJIs in primary TKA and primary THA and ALBC/ PBC efficacy preventing PFFs in THA. The analyses do find clinically-significant differences in PJI rates for TKA and

BE A PART OF BETTER ORTHOPAEDIC CARE. CLICK HERE TO LEARN HOW.

THE ORTHOPAEDIC IMPLANT COMPANY



*Advertisement

<u>Click here to learn more about The Orthopaedic Implant Company</u>

clinically-significant differences in PJI and PFF rates for THA with the best available evidence. Namba *et al.* found that ALBC did reduce the risk of PJI in patients with diabetes undergoing primary TKA in the Kaiser Permanente Total Joint Replacement Registry (Namba et al. 2020).

The Australian Orthopaedic Association National Joint Replacement Registry asked the question: "What can we learn from surgeons who perform THA and TKA and have the lowest revision rates?" (W. Hoskins et al. 2021) They found: "Low revision rate THA surgeons were more likely to use cement fixation selectively." High-quality RCTs are needed to justify the widespread use of ALBC in primary TKA and primary THA (Sultan et al. 2019). Until more robust evidence is available, the selective use of ALBC for patients undergoing primary TKA and primary THA with PJI and/or PFF risk factors is cost-effective.

The cost-effectiveness analyses included in this study have intentionally used simplified average costs. Average cost-effectiveness ratios (ACERs) and incremental cost-effectiveness ratios (ICERs) have been avoided (Bang and Zhao 2014). The methods used in this article allow individual institutions and health systems to substitute their specific PJI rates, PFF rates, and implant costs to determine if ALBC is cost effective for their institution/health system.

CONCLUSIONS

The use of antibiotic-laden bone cement is cost-effective by reducing periprosthetic joint infections in TKA, THAs, and hip hemiarthroplasties. Antibiotic-laden bone cement and plain bone cement are cost-effective by reducing periprosthetic femur fractures in THAs and hip hemiarthroplasties. Cemented fixation allows the use of lower cost fracture stems in hip hemiarthroplasties. Hand-mixed ALBC is more cost-effective than pre-mixed ALBC in all scenarios.

Submitted: February 20, 2023 EDT, Accepted: April 15, 2023 EDT



This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CCBY-NC-ND-4.0). View this license's legal deed at https://creativecommons.org/licenses/by-nc-nd/4.0 and legal code at https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode for more information.

REFERENCES

- Abdel, M. P., C. D. Watts, M. T. Houdek, D. G. Lewallen, and D. J. Berry. 2016. "Epidemiology of Periprosthetic Fracture of the Femur in 32 644 Primary Total Hip Arthroplasties: A 40-Year Experience." *The Bone & Joint Journal* 98-B (4): 461–67. <u>https://doi.org/</u> 10.1302/0301-620x.98b4.37201.
- Agni, Nickil Ramesh, Matthew L. Costa, Juul Achten, Heather O'Connor, May Ee Png, Nicholas Peckham, Susan J. Dutton, Stephanie Wallis, Svetlana Milca, and Mike Reed. 2021. "A Randomized Clinical Trial of Low Dose Single Antibiotic-Loaded Cement versus High Dose Dual Antibiotic-Loaded Cement in Patients Receiving a Hip Hemiarthroplasty after Fracture: A Protocol for the WHiTE 8 COPAL Study." *Bone & Joint Open* 2 (2): 72–78. https://doi.org/ 10.1302/2633-1462.22.bjo-2020-0174.
- American Academy of Orthopaedic Surgeons. 2022. "Surgical Management of Osteoarthritis of the Knee Evidence-Based Clinical Practice Guideline."
- Anis, Hiba K., Nipun Sodhi, Mhamad Faour, Alison K. Klika, Michael A. Mont, Wael K. Barsoum, Carlos A. Higuera, and Robert M. Molloy. 2019. "Effect of Antibiotic-Impregnated Bone Cement in Primary Total Knee Arthroplasty." *The Journal of Arthroplasty* 34 (9): 2091-2095.e1. <u>https://doi.org/10.1016/j.arth.2019.04.033</u>.
- Bang, Heejung, and Hongwei Zhao. 2014. "Cost-Effectiveness Analysis: A Proposal of New Reporting Standards in Statistical Analysis." *Journal of Biopharmaceutical Statistics* 24 (2): 443–60. https://doi.org/10.1080/10543406.2013.860157.
- Barenius, B., C. Inngul, Z. Alagic, and A. Enocson. 2018. "A Randomized Controlled Trial of Cemented versus Cementless Arthroplasty in Patients with a Displaced Femoral Neck Fracture: A Four-Year Follow-Up." *The Bone & Joint Journal* 100-B (8): 1087–93. <u>https://doi.org/10.1302/</u> 0301-620x.100b8.bjj-2017-1593.r1.
- Bendich, Ilya, Ning Zhang, Jeffrey J. Barry, Derek T. Ward, Mary A. Whooley, and Alfred C. Kuo. 2020.
 "Antibiotic-Laden Bone Cement Use and Revision Risk After Primary Total Knee Arthroplasty in U.S. Veterans." *Journal of Bone and Joint Surgery* 102 (22): 1939–47. https://doi.org/10.2106/jbjs.20.00102.
- Bernatz, James T., Andrew E. Brooks, Matthew W. Squire, Richard I. II Illgen, Neil C. Binkley, and Paul A. Anderson. 2019. "Osteoporosis Is Common and Undertreated Prior to Total Joint Arthroplasty." *The Journal of Arthroplasty* 34 (7): 1347–53. https://doi.org/10.1016/j.arth.2019.03.044.
- Bohm, Eric, Naisu Zhu, Jing Gu, Nicole de Guia, Cassandra Linton, Tammy Anderson, David Paton, and Michael Dunbar. 2014. "Does Adding Antibiotics to Cement Reduce the Need for Early Revision in Total Knee Arthroplasty?" *Clinical Orthopaedics & Related Research* 472 (1): 162–68. <u>https://doi.org/</u> 10.1007/s11999-013-3186-1.

- Brown, Gregory A., and Antonia F. Chen. 2022. "Clinical Practice Guidelines and Appropriate Use Criteria to Guide Care." In *Quality Improvement and Patient Safety in Orthopaedic Surgery*, edited by Samora J. Balch and K. G. Shea, 109–25. Cham, Switzerland: Springer International Publishing. <u>https://doi.org/</u> 10.1007/978-3-031-07105-8_11.
- Chan, Jimmy J., Jonathan Robinson, Jashvant Poeran, Hsin-Hui Huang, Calin S. Moucha, and Darwin D. Chen. 2019. "Antibiotic-Loaded Bone Cement in Primary Total Knee Arthroplasty: Utilization Patterns and Impact on Complications Using a National Database." *The Journal of Arthroplasty* 34 (7): S188-S194.e1. <u>https://doi.org/10.1016/</u> j.arth.2019.03.006.
- Chiu, Fang-Yao, CHUAN-MU Chen, CHIEN-FU JEFF Lin, and WAI-HEE Lo. 2002. "Cefuroxime-Impregnated Cement in Primary Total Knee Arthroplasty: A Prospective, Randomized Study of Three Hundred and Forty Knees." *The Journal of Bone and Joint Surgery-American Volume* 84 (5): 759–62. https://doi.org/10.2106/00004623-200205000-00009.
- Chiu, Fang-Yao, C.-F. J. Lin, C.-M. Chen, W.-H. Lo, and T.-Y. Chaung. 2001. "Cefuroxime-Impregnated Cement at Primary Total Knee Arthroplasty in Diabetes Mellitus." *The Journal of Bone and Joint Surgery. British Volume* 83-B (5): 691–95. https://doi.org/10.1302/0301-620x.83b5.0830691.
- Chiu, Fang-Yao, and Chien-Fu Jeff Lin. 2009. "Antibiotic-Impregnated Cement in Revision Total Knee Arthroplasty." *The Journal of Bone and Joint Surgery-American Volume* 91 (3): 628–33. <u>https://doi.org/10.2106/jbjs.g.01570</u>.
- Eveillard, Matthieu, Patrice Mertl, Blaise Tramier, and François Eb. 2003. "Effectiveness of Gentamicin-Impregnated Cement in the Prevention of Deep Wound Infection after Primary Total Knee Arthroplasty." *Infection Control & Hospital Epidemiology* 24 (10): 778–80. <u>https://doi.org/</u> 10.1086/502134.
- Farhan-Alanie, Muhamed M., Henry G. Burnand, and Michael R. Whitehouse. 2021. "The Effect of Antibiotic-Loaded Bone Cement on Risk of Revision Following Hip and Knee Arthroplasty." *The Bone & Joint Journal* 103-B (1): 7–15. <u>https://doi.org/10.1302/0301-620x.103b1.bjj-2020-0391.r1</u>.
- Graves, Nicholas, Catherine Wloch, Jennie Wilson, Adrian Barnett, Alex Sutton, Nicola Cooper, Katharina Merollini, et al. 2016. "A Cost-Effectiveness Modelling Study of Strategies to Reduce Risk of Infection Following Primary Hip Replacement Based on a Systematic Review." *Health Technology Assessment* 20 (54): 1–144. https://doi.org/10.3310/ hta20540.

- Gutowski, C. J., B. M. Zmistowski, C. T. Clyde, and J. Parvizi. 2014. "The Economics of Using Prophylactic Antibiotic-Loaded Bone Cement in Total Knee Replacement." *The Bone & Joint Journal* 96-B (1): 65–69. <u>https://doi.org/10.1302/</u> 0301-620x.96b1.31428.
- Hevesi, Mario, Cody C. Wyles, Jie J. Yao, Hilal Maradit-Kremers, Elizabeth B. Habermann, Amy E. Glasgow, Katherine A. Bews, et al. 2019. "Revision Total Hip Arthroplasty for the Treatment of Fracture: More Expensive, More Complications, Same Diagnosis-Related Groups: A Local and National Cohort Study." *Journal of Bone and Joint Surgery* 101 (10): 912–19. https://doi.org/10.2106/jbjs.18.00523.
- Hinarejos, Pedro, Pau Guirro, Joan Leal, Ferran Montserrat, Xavier Pelfort, M.L. Sorli, J.P. Horcajada, and Lluis Puig. 2013. "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." *Journal of Bone and Joint Surgery* 95 (9): 769–74. https://doi.org/10.2106/jbjs.1.00901.
- Hoskins, Tyler, Jay K. Shah, Jay Patel, Chris Mazzei, David Goyette, Eileen Poletick, Thomas II Colella, and James Wittig. 2020. "The Cost-Effectiveness of Antibiotic-Loaded Bone Cement versus Plain Bone Cement Following Total and Partial Knee and Hip Arthroplasty." *Journal of Orthopaedics* 20 (July):217–20. <u>https://doi.org/10.1016/</u> j.jor.2020.01.029.
- Hoskins, Wayne, Sophia Rainbird, Michelle Lorimer, Stephen E. Graves, and Roger Bingham. 2021. "What Can We Learn From Surgeons Who Perform THA and TKA and Have the Lowest Revision Rates? A Study from the Australian Orthopaedic Association National Joint Replacement Registry." *Clinical Orthopaedics & Related Research* 480 (3): 464–81. https://doi.org/10.1097/corr.00000000002007.
- Jameson, Simon S., Asaad Asaad, Marina Diament, Adetatyo Kasim, Theophile Bigirumurame, Paul Baker, James Mason, Paul Partington, and Mike Reed. 2019. "Antibiotic-Loaded Bone Cement Is Associated with a Lower Risk of Revision Following Primary Cemented Total Knee Arthroplasty: An Analysis of 731,214 Cases Using National Joint Registry Data." *The Bone & Joint Journal* 101-B (11): 1331–47. https://doi.org/10.1302/ 0301-620x.101b11.bjj-2019-0196.r1.
- Jämsen, Esa, Heini Huhtala, Timo Puolakka, and Teemu Moilanen. 2009. "Risk Factors for Infection After Knee Arthroplasty." *The Journal of Bone and Joint Surgery-American Volume* 91 (1): 38–47. https://doi.org/10.2106/jbjs.g.01686.
- Kleppel, Donald, Jacob Stirton, Jiayong Liu, and Nabil A Ebraheim. 2017. "Antibiotic Bone Cement's Effect on Infection Rates in Primary and Revision Total Knee Arthroplasties." *World Journal of Orthopedics* 8 (12): 946–55. https://doi.org/10.5312/wjo.v8.i12.946.

- Kunutsor, Setor K., Andrew D. Beswick, Michael R. Whitehouse, Ashley W. Blom, and Erik Lenguerrand. 2019. "Implant Fixation and Risk of Prosthetic Joint Infection Following Primary Total Hip Replacement: Meta-Analysis of Observational Cohort and Randomised Intervention Studies." *Journal of Clinical Medicine* 8 (5): 722. <u>https://doi.org/10.3390/</u> jcm8050722.
- Langslet, Ellen, Frede Frihagen, Vidar Opland, Jan Erik Madsen, Lars Nordsletten, and Wender Figved. 2014. "Cemented versus Uncemented Hemiarthroplasty for Displaced Femoral Neck Fractures: 5-Year Followup of a Randomized Trial." *Clinical Orthopaedics & Related Research* 472 (4): 1291–99. <u>https://doi.org/</u> 10.1007/s11999-013-3308-9.
- Leta, Tesfaye H, Jan-Erik Gjertsen, Håvard Dale, Geir Hallan, Stein Håkon Låstad Lygre, Anne Marie Fenstad, Gro Sævik Dyrhovden, et al. 2021. "Antibiotic-Loaded Bone Cement in Prevention of Periprosthetic Joint Infections in Primary Total Knee Arthroplasty: A Register-Based Multicentre Randomised Controlled Non-Inferiority Trial (ALBA Trial)." *BMJ Open* 11 (1): e041096. <u>https://doi.org/</u> 10.1136/bmjopen-2020-041096.
- Li, Hao-Qian, Peng-Cui Li, Xiao-Chun Wei, and Jun-Jun Shi. 2022. "Effectiveness of Antibiotics Loaded Bone Cement in Primary Total Knee Arthroplasty: A Systematic Review and Meta-Analysis." *Orthopaedics* & *Traumatology: Surgery & Research* 108 (5): 103295. https://doi.org/10.1016/j.otsr.2022.103295.
- McGrory, Brian, Kristy Weber, John A. Lynott, John C. Richmond, Charles Moore Davis, Adolph Yates, Atul F. Kamath, et al. 2016. "The American Academy of Orthopaedic Surgeons Evidence-Based Clinical Practice Guideline on Surgical Management of Osteoarthritis of the Knee." *Journal of Bone and Joint Surgery* 98 (8): 688–92. <u>https://doi.org/10.2106/</u> jbjs.15.01311.
- Namba, Robert S., Yuexin Chen, Elizabeth W. Paxton, Tamara Slipchenko, and Donald C. Fithian. 2009. "Outcomes of Routine Use of Antibiotic-Loaded Cement in Primary Total Knee Arthroplasty." *The Journal of Arthroplasty* 24 (6): 44–47. <u>https://doi.org/</u> 10.1016/j.arth.2009.05.007.
- Namba, Robert S., Heather A. Prentice, Elizabeth W. Paxton, Adrian D. Hinman, and Matthew P. Kelly. 2020. "Commercially Prepared Antibiotic-Loaded Bone Cement and Infection Risk Following Cemented Primary Total Knee Arthroplasty." *Journal of Bone and Joint Surgery* 102 (22): 1930–38. <u>https://doi.org/</u> 10.2106/jbjs.19.01440.
- O'Connor, Mary I., and Julie A. Switzer. 2022. "AAOS Clinical Practice Guideline Summary: Management of Hip Fractures in Older Adults." *Journal of the American Academy of Orthopaedic Surgeons* 30 (20): e1291–96. <u>https://doi.org/10.5435/jaaos-d-22-00125</u>.
- Parvizi, Javad, Khaled J Saleh, Phillip S Ragland, Aidin Eslam Pour, and Michael A Mont. 2008. "Efficacy of Antibiotic-Impregnated Cement in Total Hip Replacement." *Acta Orthopaedica* 79 (3): 335–41. https://doi.org/10.1080/17453670710015229.

- Rees, Harold W. 2020. "Management of Osteoarthritis of the Hip." *Journal of the American Academy of Orthopaedic Surgeons* 28 (7): e288–91. <u>https://doi.org/</u> <u>10.5435/jaaos-d-19-00416</u>.
- Rosner, B. 1990. *Fundamentals of Biostatistics*. Boston, Massachusetts: PWS-Kent Publishing Company.
- Santini, S., A. Rebeccato, I. Bolgan, and G. Turi. 2005. "Hip Fractures in Elderly Patients Treated with Bipolar Hemiarthroplasty: Comparison between Cemented and Cementless Implants." *Journal of Orthopaedics and Traumatology* 6 (2): 80–87. https://doi.org/10.1007/s10195-005-0086-5.
- Sanz-Ruiz, Pablo, Jose Antonio Matas-Diez, Mar Sanchez-Somolinos, Manuel Villanueva-Martinez, and Javier Vaquero-Martín. 2017. "Is the Commercial Antibiotic-Loaded Bone Cement Useful in Prophylaxis and Cost Saving After Knee and Hip Joint Arthroplasty? The Transatlantic Paradox." *The Journal of Arthroplasty* 32 (4): 1095–99. https://doi.org/10.1016/j.arth.2016.11.012.
- Sprowson[†], A. P., C. Jensen, S. Chambers, N. R. Parsons, N. M. Aradhyula, I. Carluke, D. Inman, and M. R. Reed. 2016. "The Use of High-Dose Dual-Impregnated Antibiotic-Laden Cement with Hemiarthroplasty for the Treatment of a Fracture of the Hip: The Fractured Hip Infection Trial." *The Bone* & Joint Journal 98-B (11): 1534–41. <u>https://doi.org/</u> 10.1302/0301-620x.98b11.34693.
- Srivastav, AmitK, Biren Nadkarni, Shekhar Srivastav, Vivek Mittal, and Shekhar Agarwal. 2009.
 "Prophylactic Use of Antibiotic-Loaded Bone Cement in Primary Total Knee Arthroplasty: Justified or Not?" *Indian Journal of Orthopaedics* 43 (3): 259–63. https://doi.org/10.4103/0019-5413.53456.
- Sultan, Assem A., Linsen T. Samuel, Erica Umpierrez, Andrew Swiergosz, Jacob Rabin, Bilal Mahmood, and Michael A. Mont. 2019. "Routine Use of Commercial Antibiotic-Loaded Bone Cement in Primary Total Joint Arthroplasty: A Critical Analysis of the Current Evidence." Annals of Translational Medicine 7 (4): 73–73. https://doi.org/10.21037/atm.2018.11.50.

- Tayton, E. R., C. Frampton, G. J. Hooper, and S. W. Young. 2016. "The Impact of Patient and Surgical Factors on the Rate of Infection after Primary Total Knee Arthroplasty: An Analysis of 64,566 Joints from the New Zealand Joint Registry." *The Bone & Joint Journal* 98-B (3): 334–40. <u>https://doi.org/10.1302/</u> 0301-620x.98b3.36775.
- Turhan, Sadullah. 2019. "Does the Use of Antibiotic-Loaded Bone Cement Have an Effect on Deep Infection in Primary Total Knee Arthroplasty Practice?" *Surgical Infections* 20 (3): 244–46. https://doi.org/10.1089/sur.2018.123.
- Wang, Hai, Gui-Xing Qiu, Jin Lin, Jin Jin, Wen-Wei Qian, and Xi-Sheng Weng. 2015. "Antibiotic Bone Cement Cannot Reduce Deep Infection After Primary Total Knee Arthroplasty." Orthopedics 38 (6): e462-466. https://doi.org/10.3928/01477447-20150603-52.
- Wang, Jiaxing, Chen Zhu, Tao Cheng, Xiaochun Peng, Wen Zhang, Hui Qin, and Xianlong Zhang. 2013. "A Systematic Review and Meta-Analysis of Antibiotic-Impregnated Bone Cement Use in Primary Total Hip or Knee Arthroplasty." *PLoS One* 8 (12): e82745. https://doi.org/10.1371/journal.pone.0082745.
- Wu, Cheng-Ta, I-Ling Chen, Jun-Wen Wang, Jih-Yang Ko, Ching-Jen Wang, and Chen-Hsiang Lee. 2016.
 "Surgical Site Infection After Total Knee Arthroplasty: Risk Factors in Patients With Timely Administration of Systemic Prophylactic Antibiotics." *The Journal of Arthroplasty* 31 (7): 1568–73. https://doi.org/10.1016/j.arth.2016.01.017.
- Yayac, Michael, Alexander J. Rondon, Timothy L. Tan, Hannah Levy, Javad Parvizi, and P. Maxwell Courtney. 2019. "The Economics of Antibiotic Cement in Total Knee Arthroplasty: Added Cost with No Reduction in Infection Rates." *The Journal of Arthroplasty* 34 (9): 2096–2101. <u>https://doi.org/10.1016/j.arth.2019.04.043</u>.
- Zhou, Yiqin, Lintao Li, Qi Zhou, Shuai Yuan, Yuli Wu, Hui Zhao, and Haishan Wu. 2015. "Lack of Efficacy of Prophylactic Application of Antibiotic-Loaded Bone Cement for Prevention of Infection in Primary Total Knee Arthroplasty: Results of a Meta-Analysis." Surgical Infections 16 (2): 183–87. <u>https://doi.org/ 10.1089/sur.2014.044</u>.