dictory results were reported in the remaining four prospective and randomized clinical trial studies that showed no statistical difference between the two groups in terms of the incidence of deep or superficial SSIs [21]. In another meta-analysis, Kleppel et al. reported on 4,092 patients following TKA (3,903 primary TKA and 189 revision TKA). At the average follow-up time of 47.2 months for primary TKA, the use of antibiotic-loaded cement did not have a significant reduction in PJI/SSI [22]. Additionally, an analysis of 64,566 joints from the New Zealand Joint Registry demonstrated that the use of antibiotic-laden cement was actually associated with an increase in revision for PJI after a multivariate analysis (odds ratio (OR) 1.93, 95% confidence intervals (CI) 1.19 to 3.13) [23].

We must also consider the cost associated with the use of the antibiotic-loaded cement. Industrially manufactured antibiotic-loaded bone cement may be preferred, due to the ease of access [24]. However, biomechanical and elution testing has demonstrated 1-gram of vancomycin in handmade antibiotic-loaded cement can reduce the cost without compromising the mechanical strength or elution of the drug [25]. Additionally, vancomycin potentially has a higher antimicrobial activity when compared with gentamicin for methicillin-resistant *Staphylococcus aureus* (MRSA) while remaining heat-stable with adequate elution [26–28].

Overall, the literature still lacks an appropriately sized randomized clinical trial to better support the use of antibiotic-loaded cement.

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QUESTION 3: What is the optimal antibiotic(s) dosage to be used in cement during reimplantation that does not significantly interfere with the mechanical strength of cement used for fixation?

RECOMMENDATION: The mechanical strength of most cement is maintained if ≤5% (w/w) of antibiotics is added (equating to 2 grams in a 40 gram packet).

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 92%, Disagree: 3%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

Several publications have investigated the mechanical characteristics of bone cement in vitro [1-12]. When reviewing in vitro studies on the mechanical strength of bone cement, one must assume that mechanical fixation strength in bone after a one- or two-stage revision for infection would equate to fixation of bone for a primary joint arthroplasty. The mechanical strength of antibiotic-loaded bone cement (ALBC) depends on the following: antibiotic dose, type of antibiotic, number of antibiotics, time of elution, method of mixing and incorporation of impurities/fat/blood [1-15]. Different types of cement also show a variable response to different doses of antibiotics [1, 4, 6, 9, 14].

Unfortunately, most investigations of one and two-stage exchange for prosthetic joint infections (PJIs) did not include details of antibiotic loading into reimplantation cement or used multiple different antibiotic loading regimens. Ultimately, 24 investigations with a consistent antibiotic loading of bone cement before prosthetic reimplantation during one- or two-stage revision for PJI were identified (Table 1). The collective information regarding the details of antibiotic loading in the reimplantation cement was compiled (Table 2).

Investigations examining the mechanical properties of ALBC are all in vitro investigations. Therefore, the loading conditions at the revision total hip and knee arthroplasty (THA, TKA) in vivo bone-implant interface are 1) poorly understood and 2) not adequately modeled to translate the mechanical behavior of ALBC from in vitro studies to these complex in vivo environments. In general, the addition of up to 2 gm of a single powdered antibiotic per 40 gm pack of polymethyl methacrylate (PMMA) has not been shown to have significant deleterious effects on ALBC mechanical properties [16]. More contemporary investigations quantifying the mechanical properties of dual-antibiotic loaded PMMA demonstrate that up to 3 gm total of powdered antibiotics can be included into a 40gm pack of PMMA before compressive strength is decreased below the International Organization for Standardization (ISO) standard [17].

Investigations in this literature review (Table 1) rarely addressed prosthetic aseptic failure following revision for PJI. Furthermore,

TABLE 1. Summary of literature pertaining to antibiotic-loaded cement

PubMed ID	One-stage vs. Two-stage	# Investigated Prostheses	Follow-up Interval (months)	ALBC Details	% Failure
24923669 [18]	One	28	78	1 gm Gent, 1 gm Vanc per pack	0
7497685 [19]	Two	26	31	1.2 gm Tobra per pack PMMA	0
10535593 [20]	Two	40	40	1.2 gm Tobra per pack	25
10990301 [21]	Two	45	48	1.2 gm Tobra per pack	9
11097443 [22]	Two	69	63	1 gm Tobra per pack	9
11216723 [23]	Two	53	56	1.2 gm Tobra per pack	17
12051001 [24]	Two	10	18	0.5 gm Gent per pack	0
15343539 [25]	Two	24	33	2.4 gm Tobra, 1 gm Vanc per pack	8
15991126 [26]	Two	44	65	1.2 gm Tobra per pack	3
15662313 [27]	Two	50	73	1.2 gm Tobra per pack	4
17162176 [28]	Two	21	52	1 gm Tobra per pack	5
17966006 [29]	Two	24	48	1 gm Gent, 1 gm Clinda per pack	4
19553076 [30]	Two	53	49	750mg cefuroxime	17
19299221 [31]	Two	13	48	2 gm Vanc per pack	0
20087702 [32]	Two	27	58	1 gm Gent, 1 gm Clinda per pack	4
20202852 [33]	Two	10	31	0.5 gm Gent, 1 gm Vanc per pack	0
22863338 [34]	Two	21	32	0.5 gm Gent, 1 gm Vanc per pack	4
26272061 [35]	Two	82	36	0.5 gm Gent per pack	15
21866421 [36]	Two	117	46	1.2 gm tobra,1 gm Vanc per pack	28
14563794 [37]	Two	58	41	0.6 gm Tobra per pack	4
15190550 [38]	One	22	120	1.2 gm Tobra per pack	9
10611868 [39]	One	24	108	2 gm 1st Generation Cephalosporin per pack	8.3
721853 [40]	One & Two	67	24	0.5 gm Gent per pack	12
3769248 [41]	One	100	38	0.5 gm Gent per pack	9

TABLE 2. Summary of pooled data pertaining to antibiotic-loaded cement at reimplantation

Variable	Tobra (T)	Gent (G)	Vanco (V)	Cefuroxime	1st Gen cephalosporin	V+T	V+G	G+Clinda (C)
Number of studies	10	4	1	1	1	2	3	2
Two-stage	9	3*	1	1	-	2	2	2
One-stage	1	2*	-	-	1	-	1	-
Dose per 40 gm PMMA pack	0.6-1.2 gm	0.5 gm	2.0 gm	750mg	2.0 gm	1.0 gm V 1.2-2.4 gm T	1.0 gm V 0.5-1.0 gm G	1.0 gm G 1.0 gm C
Number of prostheses	428	259	13	53	24	141	59	51
Average follow-up (mo)	59	29	48	49	108	40	47	53
PJI recurrence incidence (%): range and average	0-25 8.5	0-15 9	0 0	17 17	8 8	8-28 18**	0-4 1.3	4 4

* Numbers do not add up due to one study containing both one-stage and two-stage procedures
** Average significantly skewed to lower value as one study with 28% PJI recurrence incidence included 117 of the total 141 patients

reports of aseptic prosthetic loosening in the setting of prior revision THA or TKA for PJI must be cautiously interpreted as it may represent PJI recurrence. Therefore, conclusions cannot be drawn regarding the clinical effectiveness of any specific ALBC formulation in the prevention of aseptic THA or TKA loosening following revision for PJI.

At this time, there is no definitive conclusion on what prosthetic reimplantation ALBC formulation provides the best eradication of PJI and/or is most protective against subsequent prosthetic aseptic loosening. Any inferences made as a result of this review must be cautiously adopted into clinical practice due to the multiple confounding variables present in different PJI treatment investigations (e.g., patient characteristics, organism resistance profiles, antibiotic spacer differences, length of antibiotic treatment before and after prosthetic re-implantation, etc.). This review demonstrates that prosthetic reimplantation bone cement can be loaded with a wide range of single or dual antibiotics and provide successful PJI control following one- or two-stage PJI revision surgery in a high percentage of prostheses. However, when only ALBC regimens supported by more than one study and 50 patients are considered, prosthetic re-implantation using ALBC containing either 1 gm vancomycin and 0.5-1 gm gentamicin per 40 gm pack of PMMA or 1 gm clindamycin and 1 gm gentamicin per 40 gm pack of PMMA appear to have the optimal ability to control PJI while not resulting in mechanical compromise of the PMMA.

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1.5. PREVENTION: OPERATING ROOM ENVIRONMENT

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QUESTION 1: Does performing a primary total joint arthroplasty (TJA) after a dirty case (infection or open abdomen) in the same operating room increase the risk of surgical site infections/periprosthetic joint infections (SSIs/PJIs)?

RECOMMENDATION: The little data on this subject suggests that the risk of PJIs may be higher when an elective arthroplasty follows a contaminated case. The risk may be reduced if terminal cleaning of the operating room can be done after the dirty case. Further studies are necessary to elucidate this connection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 4%, Abstain: 3% (Super Majority, Strong Consensus)

RATIONALE

A comprehensive literature review was performed in order to identify all studies on the effect of infection risks in primary TJA following a contaminated case. Searches for the terms "total joint arthroplasty," "infection risk," and "infected case" with different Boolean operators were performed using the search engines Medline, Embase and Cochrane that were searched through February 2018. Inclusion criteria for our systematic review were all English studies (Level I-IV evidence) that reported on infection risk for primary TJA following a contaminated case. Exclusion criteria were non-English language articles, studies > 10 years old, nonhuman studies, retracted papers, case reports, review papers, studies with less than <10 patients in the sample size, studies without clinical follow-up/infection rates and technique papers without patient data. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria were followed. The initial search resulted in 921 papers. After removal of duplicates and evaluation of titles, 170 titles were evaluated, 24 full text papers were read and 4 studies met full inclusion and exclusion criteria to allow for analysis.

There is limited data in literature specific to infection risk when performing primary TJA after a contaminated case, as the number of studies is limited and the number of TJAs performed after an infected case is also restricted. A systematic review was performed specifically evaluating whether nosocomial pathogens persist on inanimate surfaces, such as pathogens from infected surgical cases remaining on surfaces in the operating room [1]. Almost all pathogens including respiratory and gastrointestinal viruses persisted for days on inanimate surfaces, with many gram-positive, gram-negative and fungal pathogens remaining for months. However, pathogen persistence was disrupted if preventative surface disinfection was performed and this was corroborated in a study of 31,499 TJAs where terminal cleaning was effective at reducing bioburden after an infected case and did not increase the likelihood of infection when a case was performed the next day [2]. On the other hand, this same study also demonstrated that infection risk increased by 2.4 times if a TJA case followed an infected case in the same room on the same operative day. Another study