Clin Orthop Relat Res (2019) 477:922-937
DOI 10.1097/CORR.0000000000000690

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Meta-analysis

Is the Risk of Infection Lower with Sutures than with Staples for Skin Closure After Orthopaedic Surgery? A Meta-analysis of Randomized Trials

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Received: 13 June 2018 / Accepted: 30 January 2019 / Published online: 17 April 2019

Abstract

Background Two previous meta-analyses comparing staples versus sutures have led to conflicting relative risks for surgical site infection between skin closure methods after orthopaedic surgery. Consequently, the choice of sutures or staples for skin closure continues to be a subject of conversation. Recently, additional randomized trials have been published, and an updated meta-analysis is needed to inform this debate.

Questions/purposes To determine using a meta-analysis of randomized trials (1) whether there is a difference in surgical site infection (SSI) between staples and sutures for skin closure after orthopaedic surgery, and (2) whether that finding remains the same when the analysis is limited to randomized trials with a low risk of bias.

Methods A systematic review and meta-analysis of randomized controlled trials (RCTs) comparing staples with sutures for skin closure after orthopaedic surgery was conducted. We excluded barbed sutures, surgical zippers, and skin adhesives from this meta-analysis. Medline,

One of the authors (YRR) received personal fees from Medtronic (Minneapolis, MN, USA) outside the submitted work.
Each author certifies that his or her institution waived approval for the reporting of this investigation and that all investigations were conducted in conformity with ethical principles of research.
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All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research®* editors and board members are on file with the publication and can be viewed on request.

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Embase, CINAHL, Cochrane Library, and Global Index Medicus were searched from date of inception to October 18, 2017. The sole outcome of interest was SSI as defined by the original study authors, with preference given to Center for Disease Control and Prevention (CDC) definitions whenever possible, recognizing that this may result in the pooling of more common minor events with rarer, more severe events, and in so doing, overestimate between-group differences. Because of this, subgroup analysis was planned based on severity of infection. Relative risk was calculated using a random-effects model (relative risk [RR], 95% confidence interval [CI]). Heterogeneity was estimated using I^2. Publication bias was explored using visual inspection of the funnel plot and Egger's test. Subgroup analysis was planned for type of orthopaedic surgery, suture material, SSI category, and country development index. Subgroup interaction p values were calculated. The Cochrane risk of bias tool was used to assess study quality. Sensitivity analysis was planned to assess whether the results changed when the analysis was limited to studies with low risk of bias. In total, 17 RCTs (2446 patients) were eligible, of which five RCTs (501 patients) were at low risk of bias.

Results In the primary analysis, patients randomized to staples had a higher risk of SSI versus those who received sutures for skin closure (RR, 2.05; 95% CI,1.38–3.06; I^2 = 0%). However, most of the events were driven by superficial SSI, and only two deep infections were explicitly reported in total (one in each group). After a post-hoc sensitivity analysis excluded a highly influential trial with high risk of bias, the results were highly fragile, relying on a difference of only four additional events in the staples group. When we limited the analysis to RCTs with low risk of bias, no difference was found between sutures and staples in terms of SSI (RR, 1.45; 95% CI, 0.31–6.79; I^2 = 46%). Effect sizes were consistent across subgroups (p value for subgroup interaction was not significant for elective versus trauma; hip versus knee arthroplasty; suture material; high versus middle- versus low-income settings).

Conclusions Even in this relatively large meta-analysis, existing RCTs do not provide definitive evidence of a difference in SSI risk when staples are used instead of sutures for skin closure after orthopaedic surgery. Currently, the total body of evidence remains weak and, even when limiting to only low risk of bias studies, it is not possible to rule in or rule out clinically important differences between staples and sutures. Until randomized studies of adequate power and followup duration are performed to definitively inform this issue, the choice between staples versus sutures should be based on other factors such as local availability, surgeon preference, and cost.

Level of Evidence Level I, therapeutic study

Introduction

Surgical site infections (SSI) remain an important concern after orthopaedic surgery. While the most common SSIs are superficial wound infections, even these seemingly minor events may lead to serious complications, including deep infections, prosthetic joint infections, sepsis, and revision surgery. SSIs place an increased burden on the healthcare system, increasing length of stay, rehospitalization rates, and healthcare costs, and adversely affect patient quality of life and function [1, 35, 37]. SSIs also contribute to antibiotic resistance through increasing exposure to broad-spectrum antibiotics, often requiring prolonged antibiotic treatment for deep and prosthetic joint infections. Given the severity of SSIs, in recent years, an increased focus on SSI prevention has emerged [9], culminating with the release of evidence-based recommendations to minimize the risk of postoperative infections by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) [2, 38]. However, the guidelines did not address the issue of staples versus sutures for wound closure.

Whether the relative risk of SSI is different for sutures versus staples in orthopaedic surgery remains uncertain. Two previous meta-analyses on this topic have been published, one in 2010 [30] and another in 2016 [20], with conflicting results. Both meta-analyses combined non-randomized trials [20, 30] and observational studies [20] with randomized trials, which may have biased estimates of relative treatment effects. In addition, prior meta-analyses reported on clinically heterogeneous groups of orthopaedic patients without separating by trauma and elective populations. This may be problematic because local and systemic inflammatory responses associated with trauma may elevate the risk of SSI compared with patients undergoing elective procedures. In addition, all suture types (absorbable and nonabsorbable) were reported together despite their different biologic and physical properties. These potential risk factors for SSI would suggest the need for adjusted or subgroup analysis; however, they were not performed, thus limiting confidence in the two currently available systematic review and meta-analyses. Furthermore, since the most recent meta-analysis [20], several additional randomized controlled trials (RCTs) have been identified [3, 11, 15, 16, 23, 26, 29]. Consequently, an updated meta-analysis is warranted to assess whether current RCT evidence supports the superiority of staples or sutures for wound closure after orthopaedic surgery, or whether more research is needed before definitive clinical recommendations can be made regarding SSI reduction. If this meta-analysis suggests that the existing evidence is sufficient, the information will be useful to direct clinical decision-making regarding choice of closure. On the other hand, if the existing evidence is insufficient for definitive

conclusions, then this updated analysis will facilitate estimation of sample size requirements for future clinical trials to definitively answer the question. Because of the global importance of SSI on patient risk of morbidity and mortality, recent priority-setting initiatives are in the process of redefining priorities for research and knowledge translation to reduce surgical site infections in high- and low-income settings. [2, 38]. Therefore, an updated meta-analysis is needed to clarify the state of the evidence to inform ongoing global priority-initiatives for SSI reduction.

Thus, we sought to determine in the context of a meta-analysis of randomized trials (1) whether there is a difference in SSI between staples and sutures for skin closure after orthopaedic surgery, and (2) whether that finding remains the same when the analysis is limited to randomized trials with a low risk of bias.

Materials and Methods

This systematic review and meta-analysis was conducted according to Cochrane guidelines and is reported in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [13, 21]. Ethics approval was not required for this study.

Search Strategy

We searched Medline-Ovid, Embase-Ovid, CINAHL, Cochrane Library, and Global Index Medicus using database specific search strings (see Table 1 in Appendix, Supplemental Digital Content 1, http://links.lww.com/CORR/A156). Gray literature was also explored, including Web of Science, ProQuest dissertations, Theses Global, and dissertations and theses at the University of Western Ontario. In addition, the first five pages of Google and Google Scholar were searched to capture potential additional sources of RCTs from nonindexed journals and conferences. No restrictions by language or year of publication were imposed on the searches.

Study Selection

Two study authors (RJK, IS) independently conducted title, abstract, and full-text screening to determine article eligibility. While a third author was available for arbitration of disagreements, arbitration was not necessary since no major disagreements were noted for both screening levels. The inclusion criteria were adapted from prior meta-analyses on this topic [20, 30]. We considered any RCTs that compared sutures with staples for skin closure after orthopaedic surgery. No distinctions were made between clips and staples. We excluded barbed sutures, surgical zippers, and skin adhesives from this meta-analysis.

The decision to pool varying suture material into one treatment category was made under the presumption that sutures, regardless of material or technique, reflect a distinct class of wound closure compared with staples. If data allowed, we planned to perform subgroup analyses based on suture material as outlined in the analysis section below. No restrictions were applied for language, study location, and date or type of publication (abstract or full report). To allow for a full synthesis of the existing evidence base, we included all studies that met the inclusion criteria regardless of followup time.

The primary endpoint for this meta-analysis was SSI (superficial or deep). Definitions of SSI include a range of categories from superficial to deep wound infections, and the most-feared is the prosthetic joint infection. As recommended by the WHO for meta-analysis of interventions for preventing SSI, we used CDC definitions for data synthesis across trials when the source studies provided outcomes according to those definitions recognizing that this may result in the pooling of more-common minor events with rarer, more-severe events, and in so doing, might overestimate between-group differences, particularly with respect to clinically relevant differences [2]. However, when definitions different from those of the CDC for SSI were provided by authors, we used the authors' own definitions in our meta-analysis, with further exploration through subgroup and sensitivity analysis [2, 38]. This methodology is similar to other meta-analyses where SSI is the focus [2, 6, 38], since a strict requirement that each included study adhered exactly to CDC definitions would ignore important randomized studies on this topic; furthermore, this approach allows for potentially informative sensitivity analyses to determine whether definition influenced effect size. Since SSI may range from the mild and relatively trivial (superficial wound infection) to the devastating (prosthetic joint infection), we also planned to perform subgroup analysis (post-hoc subanalysis) to determine the impact of assessing different categories of severity of wound infection on the effect size. This inclusive approach allows us to present the totality of evidence for superficial, deep, and prosthetic joint infections, as far as the evidence is provided to inform these categories.

Study Identification

The systematic search initially retrieved 1912 unique articles. During title and abstract screening, 1864 studies were excluded, leaving 48 studies available for full-text screening. Thirty articles were excluded during full-text screening (see Table 2 in Appendix, Supplemental Digital

Content 1, http://links.lww.com/CORR/A156). In total, 18 studies met the inclusion criteria (see Table 3 in Appendix, Supplemental Digital Content 1, http://links.lww.com/CORR/A156) [3-5, 8, 11, 12, 15-17, 22-24, 26-29, 34, 39]. One RCT was not appropriate for meta-analysis as a result of irresolvable inconsistencies in data reporting [4], leaving 17 RCTs (involving 2446 patients) available for the meta-analysis (Fig. 1) [3, 5, 8, 11, 12, 15-17, 22-24, 26-29, 34, 39]. Of these, five RCTs (involving 501 patients) were at low risk of bias [8, 17, 27, 28, 39].

Data Extraction

Relevant baseline characteristics were collected. Country income classifications were defined according to the World Bank. Two authors (RJK, IS) extracted data from the included studies; a third author (PK) verified the final data extraction sheet. Conflicts were discussed by three of the authors (RJK, IS, PK) and resolved through negotiated consensus. If needed, another author (EJC) adjudicated equivocal cases. For the nonEnglish trial [15], relevant data were provided by the study author on request (Rudolf Hlubek, personal communication).

Study Characteristics

Eighteen studies met the inclusion criteria [3-5, 8, 11, 12, 15-17, 22-24, 26-29, 34, 39]. One RCT was not appropriate for meta-analysis as a result of irresolvable inconsistencies in data reporting [4], leaving 17 RCTs (involving 2446 patients) available for the meta-analysis (Fig. 1) [3, 5, 8, 11, 12, 15-17, 22-24, 26-29, 34, 39]. Six trials included only patients undergoing elective THA or TKA [3, 8, 12, 15, 23, 39]. Three trials included only trauma patients [16, 24, 28]. Eight trials involved heterogeneous populations, including elective, trauma, and otherwise non-specified patients [5, 11, 17, 22, 26, 27, 29, 34]. One trial stratified results by THA and TKA [17] (Table 1).

Nonabsorbable sutures were used in eight studies [3, 5, 11, 15, 22, 24, 29, 34] and absorbable sutures were used in five studies [8, 12, 17, 26, 28]. Two studies used both

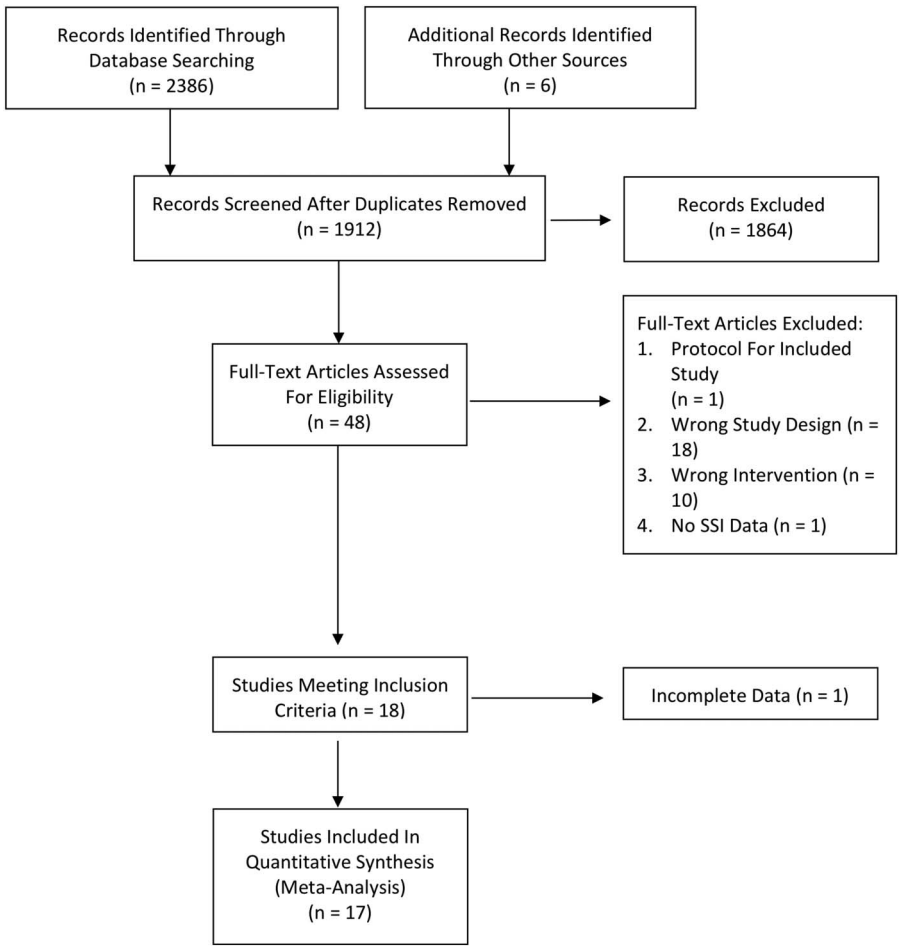

Fig. 1 Prisma Flow Diagram.

Table 1. Baseline characteristics of included studies

Study	Country	World Bank income classification	Surgical population	Surgery type	Suture type		SSI Definition
Buttaro et al., 2015 [3]	Argentina	Upper middle income	Elective	THA	NAB	Continuous 3-0 intradermal polypropylene suture	Not specified
Clayer and Southwood, 1991 [5]	Australia	High income	Elective/ trauma/NOS	THA, Austin-Moore hemiarthroplasty, compression hip screw and plate, gamma nail	NAB	2-0 subcuticular polypropylene suture	Not specified
Eggers et al., 2011 [8]	USA	High income	Elective	TKA	AB	Monocryl 4-0 sutures	Not specified
Gohiya et al., 2015 [11]	India	Lower middle income	Elective/ trauma/NOS	Closed fractures and all elective orthopaedic surgery	NAB	Nylon sutures	Positive culture with associated wound discharge
Graham et al., 2000 [12]	UK	High income	Elective	TKA	AB	Subcuticular 4-0 Vicryl Suture	Not specified
Hlubek et al., 2014 [15]	Czech Republic	High income	Elective	TKA	NAB	Ethilon 2-0	Not Specified*
Kazemian et al., 2014 [16]	Iran	Upper middle income	Trauma	Intertrochanteric fracture correction	-	-	Not specified
Khan et al., 2006 [17]	Australia	High income	Elective and elective/ trauma/NOS	THA and TKA	AB	Continuous 3-0 subarticular absorbable poliglecaprone suture	Positive culture or clinical evidence of cellulitis
Liew and Haw, 1993 [22]	Australia	High income	Elective/ trauma/NOS	No details provided	NAB	Interrupted 3-0 nylon suture	Not specified
Mallee et al., 2017 [abstract] [23]	Netherlands	High income	Elective	THA	-	-	Not specified
Murphy et al., 2004 [24]	Ireland	High income	Trauma	Fracture fixation of ankle, tibia, patella, femur, forearm, olecranon, and humerus	NAB	Interrupted nylon suture	Wound discharge, wound required opening, or needed to be treated with antibiotics
Rui et al., 2017 [26]	China	Upper middle	Elective/ trauma/NOS	THA	AB	Running 4-0 subcuticular Vicryl suture	SSI defined by clinical signs/symptoms (redness and/or pain, local swelling etc), purulent discharge, and/or positive culture within 1 year of surgery. Infections limited to cutaneous and subcutaneous layers were considered superficial. Infections involving muscle or fascia were considered deep.

Table 1. continued

Study	Country	World Bank income classification	Surgical population	Surgery type	Suture type		SSI Definition
Shantz et al., 2013 [27]	Canada	High income	Elective/ trauma/NOS	Arthroplasty, IM nail, ORIF, soft tissue, and other	AB and NAB	-	SSI was suspected if patient needed reoperation or intravenous/oral antibiotics from the surgical procedure. Relevant patient charts were then reviewed; confirmed SSIs were those that met CDC compliant definitions.
Shetty et al., 2004 [28]	UK	High income	Trauma	Cemented hemiarthroplasty, dynamic hip screw, cannulated hip screw	AB	3-0 subcuticular undyed Vicryl suture with Steri-Strips	Wound discharge with positive culture
Singh et al., 2017 [29]	India	Lower middle income	Elective/ trauma/NOS	Open reduction and internal plating, open reduction and internal fixation with tension band wiring, internal fixation with cannulated screws, THA, and TKA	NAB	Nylon OR silk suture	SSI defined by: at least one clinical sign/ symptom (pain or tenderness, localized swelling, redness or high temperature); (2) purulent drainage; (3) positive culture; (4) stitch abscess.
Stockely and Elson, 1987 [34]	UK	High income	Elective/ trauma/NOS	Arthroplasty, hip osteotomy, internal fixation of femoral neck, internal fixation of supracondylar fracture and tibial plateau fracture	NAB	Nylon suture	Not specified
Wyles et al., 2016 [39]	USA	High income	Elective	TKA	AB and NAB	Running subcuticular 3-0 Monocryl suture OR vertical mattress 2-0 nylon suture	Not specified

*Google Translate was used for language translation into English; NOS = not otherwise specified; IM = intramedullary; ORIF = open reduction and internal fixation; NAS = nonabsorable; AB = absorbable.

suture materials [27, 39] (Table 1; Table 4 in Appendix, Supplemental Digital Content 1, http://links.lww.com/CORR/A156). The followup time from surgery to SSI assessment varied from 1 week to 1 year; where multiple time points were reported, the longest available followup was selected (see Table 5 in Appendix, Supplemental Digital Content 1, http://links.lww.com/CORR/A156). Two studies did not report a quantifiable length of followup; in this case, SSI events were extracted after hospital discharge for both studies [3, 17]. Information regarding type of antibiotic prophylaxis was provided in only eight studies (see Table 6 in Appendix, Supplemental Digital Content 1, http://links.lww.com/CORR/A156).

Risk of Bias

We used the Cochrane risk of bias tool to categorize the included studies as high, unclear, and low risk of bias [14]. This method rated bias within six main domains, with an additional option to also report any "other" sources of bias. Two study authors (IS, PK) independently assessed risk of

Table 2. Risk of bias for included trials

Study	Randomization sequence	Allocation concealment	Blinding of participants	Blinding of outcome assessors	Incomplete outcome data	Selective reporting	Other biases
Buttaro et al., 2015 [3]	Low	High	High	High	Low	Low	Low
Clayer and Southwood, 1991 [5]	High	High	High	High	Unclear	Low	Low
Eggers et al., 2011[8]*	Low	Low	High	High	Low	Low	Low
Gohiya et al., 2015 [11]	Low	High	High	Low	Low	Low	High
Graham et al., 2000 [12]	Unclear	High	High	High	Low	Low	Low
Hlubek et al., 2014 [15]	High	High	High	Unclear	Low	Unclear	Unclear
Kazemian et al., 2014 [16]	Low	High	High	High	Low	Low	Low
Khan et al., 2006 [17]*	Low	Low	Low	Low	Low	Low	Low
Liew and Haw, 1993 [22]	Unclear	High	High	Unclear	Low	Low	Low
Mallee et al., 2016 [abstract] [23]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Murphy et al., 2004 [24]	Unclear	High	High	High	Low	Low	Low
Rui et al., 2017 [26]	Unclear	Low	High	High	Low	Low	Low
Shantz et al., 2013 [27]*	Low	Low	Low	High	High	Low	Low
Shetty et al., 2004 [28]*	Low	Low	High	High	Low	Low	Low
Singh et al., 2017 [29]	Unclear	High	High	High	Unclear	Low	Low
Stockely and Elson, 1987 [34]	High	High	High	High	Low	Low	Low
Wyles et al., 2016 [39]*	Low	Low	High	High	Low	Low	Low

*Trials were rated low risk of bias if they met at least five of the seven criteria (minimum of five green).

bias for the included trials. Discrepancies were resolved through negotiated consensus. Included articles were rated low risk of bias if they met a minimum of five of the seven criteria. Of the 17 included trials, five RCTs (involving 501 patients) were considered low risk of bias [8, 17, 27, 28, 39], and the remainder were considered unclear or high risk of bias (Table 2). Three trials were pseudorandomized [5, 15, 34]. Adequate methods for allocation concealment were explicitly reported in six articles [8, 17, 26-28, 39]. Blinding was largely absent as a result of the nature of the interventions being studied. Only three articles made some effort to blind the participants, outcome assessors, or the data analyst [11, 17, 27]. High risk for attrition bias was noted in one study [27].

Overall, the most common reason for being rated as unclear or high risk of bias was due to lack of evidence of double- or triple-blinding and allocation concealment, which represents a common level of risk of bias in most surgical trials when blinding is not feasible (Table 2; Tables 7-11 in Appendix, Supplemental Digital Content 1, http://links.lww.com/CORR/A156).

To address our second research objective, whether the results change when the meta-analysis is limited to randomized studies at low risk of bias, we performed a sensitivity analysis by recalculating the results for SSI using only the five RCTs (501 patients) deemed at low risk of bias [8, 17, 27, 28, 39].

Statistical Analysis

For discrete data, relative risk (RR) and 95% confidence intervals (CIs) were calculated using a random-effects model in Stata 15 (StataCorp LP, College Station, TX, USA) [32]. A correction factor of 0.5 was imputed for "zero event trials" [10]. Statistical significance was defined

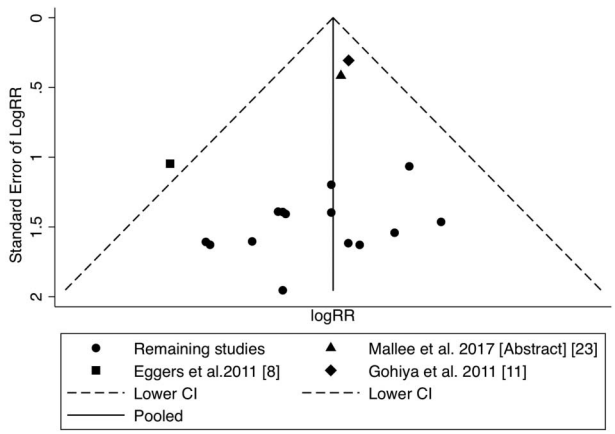

Fig. 2 Funnel plot demonstrating each trial's precision (standard error of the logRR) against its treatment effect (LogRR) for the primary outcome of SSI. Larger trials are on top, whereas smaller studies are scattered along the bottom. The Eggers test for publication bias was not significant (p = 0.149).

as 95% CI excluding the null value. When relevant, the number needed to benefit (NNTB) or harm (NNTH) was calculated for significant results. As a result of the paucity of data derived from within patient randomization (ie, staples versus sutures randomized to right versus left surgical wound in the same patient) [34], bivariate binomial distribution meta-analysis was unnecessary to manage correlated data (that is, in total, only one SSI event occurred in the two studies reporting split-body randomization) [25]. Heterogeneity was estimated using the I^2 statistic; no heterogeneity was noted for the primary analysis including all studies ($I^2 = 0\%$). However, when limiting to studies of low risk of bias, there was moderate heterogeneity of effect-size between studies ($I^2 = 46\%$).

Preplanned subgroup analysis for SSI included stratification of the results based on surgical population (trauma, elective, or combined/not otherwise specified), anatomic site (hip and knee), country income classification (high income, upper middle income, and lower middle income), and suture material (absorbable or nonabsorbable). Furthermore, a post-hoc subgroup analysis was planned for elective THA and elective TKA to compare staples and sutures within potentially more clinically homogenous patient populations. Meta-regression was used to test for significant differences in effect size across subgroups (subgroup interaction

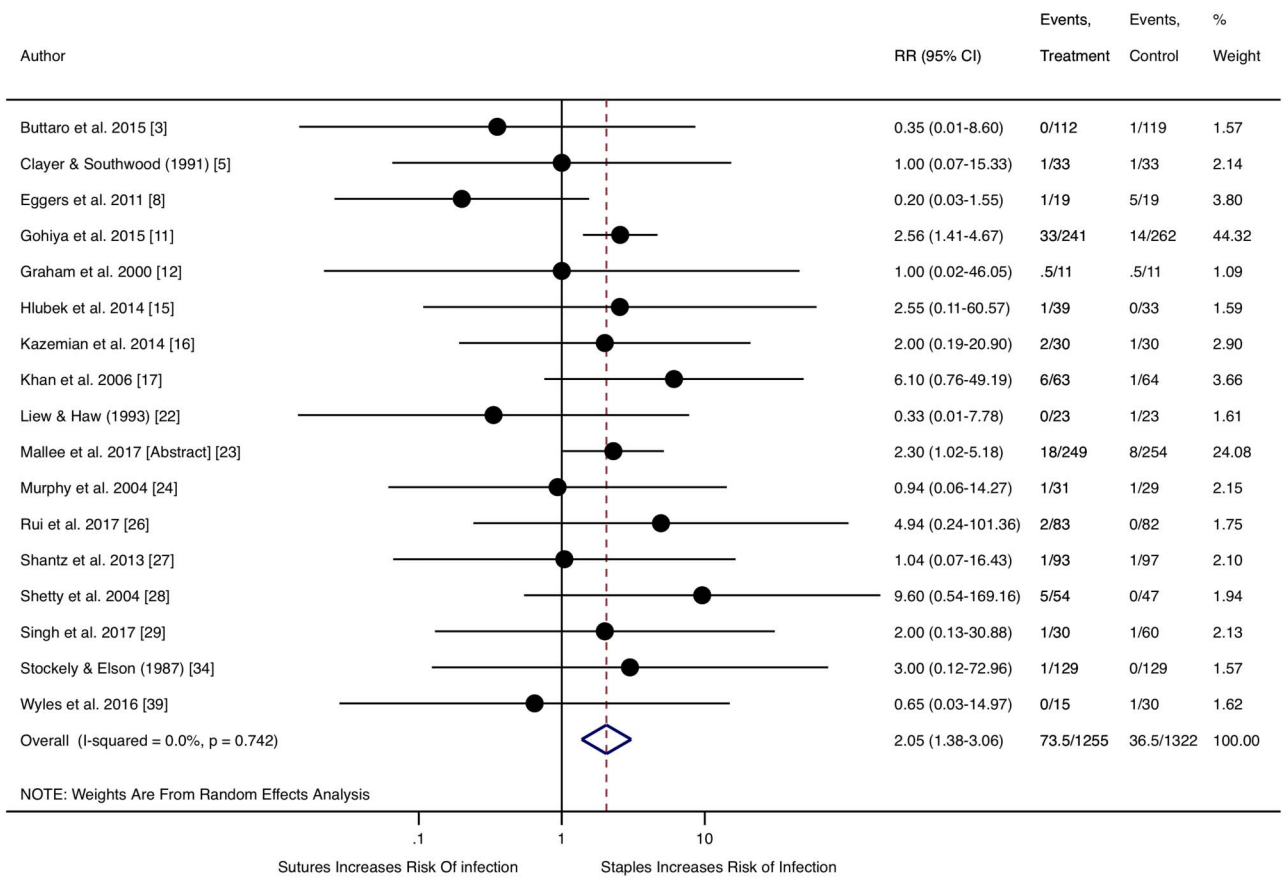

Fig. 3 Forest plot showing the relative risk (RR, 95% CI) of SSI for patients receiving staples versus sutures for skin closure after orthopaedic surgery. The risk of SSI was higher in the staple group (RR, 2.05, 95% CI, 1.38–3.06).

Table 3. Summary of results

Primary analysis	All studies, sensitivity analysis, or subgroup analysis	Number of studies (n = 17)	Staples	Sutures	RR (95% CI)	Number needed to harm (NNTH)	Number of excess events per 1000 patients treated with staples (95% CI)	FI	I^2 (%)	Test for subgroup differences (p value)
SSI	All studies	17	73 of 1254	36 of 1321	2.05 (1.38-3.06)	34.4	29.1 (10.4-56.9)	19	0	NA
SSI (excluding Gohiya et al., 2015)	Sensitivity analysis	16	40 of 1013	22 of 1059	1.72 (1.01-2.94)	65.3	15.3 (0.2-41.2)	4	0	NA
SSI (low risk of bias)	Sensitivity analysis	5	13 of 244	8 of 257	1.45 (0.31-6.79)	-	-	-	46	NA
SSI: subgroup analysis by surgical population	Elective	7	23 of 471	16 of 496	1.43 (0.66-3.09)	-	-	-	8	0.389
	Trauma only	3	8 of 115	2 of 106	2.45 (0.54-11.09)	-	-	-	0	
	Elective/trauma/ not otherwise specified	8	42 of 668	18 of 719	2.37 (1.40-4.01)	29.3	34.2 (9.9-75.3)	11	0	
SSI: subgroup analysis by anatomic site	Hip	9	44 of 790	16 of 795	2.42 (1.40-4.17)	34.1	29.4 (8.3-65.8)	12	0	0.426
	Knee	7	14 of 188	10 of 203	1.59 (0.69-3.67)	-	-	-	0	
SSI: subgroup analysis by elective surgery	THA	2	18 of 361	9 of 373	1.74 (0.48-6.39)	-	-	-	19	0.584
	TKA	5	5 of 110	7 of 123	0.90 (0.27-2.93)	-	-	-	0	
SSI: subgroup analysis by suture type	Absorbable	5	14 of 229	6 of 222	2.10 (0.41-10.73)	-	-	-	47	0.915
	Nonabsorbable	8	38 of 638	19 of 688	2.12 (1.25-3.60)	32.4	30.9 (6.9-71.7)	6	0	
	Both	2	1 of 108	2 of 127	0.85 (0.11-6.73)	-	-	-	0	
SSI: subgroup analysis by country income classification	High income	12	35 of 758	19 of 768	1.72 (0.96-3.07)	-	-	-	0	0.570
	Upper middle income	3	4 of 225	2 of 231	1.67 (0.34-8.27)	-	-	-	0	
	Lower middle income	2	34 of 271	15 of 322	2.53 (1.41-4.55)	14.0	71.4 (19.1-165.5)	9	0	

RR = risk ratio; CI = confidence interval; FI = Fragility Index; SSI = surgical site infection; NA = not applicable; NNTH = number needed to harm.

term). Statistical significance was set at $p < 0.05$ [33]. A sensitivity analysis was also planned for study quality to include only studies with low risk of bias.

The fragility index was used to assess the robustness of outcomes reaching statistical significance using the analytic calculator available at https://clincalc.com/Stats/FragilityIndex.aspx. The fragility index estimates the number of additional SSIs needed to occur within one group to change a significant treatment difference to a nonsignificant result [36].

Publication Bias

A funnel plot and Egger's asymmetry test was used to assess for potential evidence of publication bias (Fig. 2). Visual inspection of the funnel plot revealed some potential asymmetry in the funnel. However, the Egger's test for publication bias did not reach statistical significance ($p = 0.15$). Taken together, this information implies that the potential impact of publication bias on effect size estimates is likely small but cannot be ruled out due to the low power of the Egger's test.

Results

Risk of SSI: Primary Analysis (Including Studies with High Risk of Bias)

When all studies were combined (high and low risk of bias RCTs), patients who received staples (n = 1254; SSI proportion$_{pooled}$ = 5.8%) had a higher risk of SSI compared with those who received sutures (n = 1321; SSI proportion $_{pooled}$ = 2.7%) for skin closure (RR, 2.05; 95% CI, 1.38-3.06; $I^2 = 0\%$; Fragility Index = 19, NNTH = 34.4;

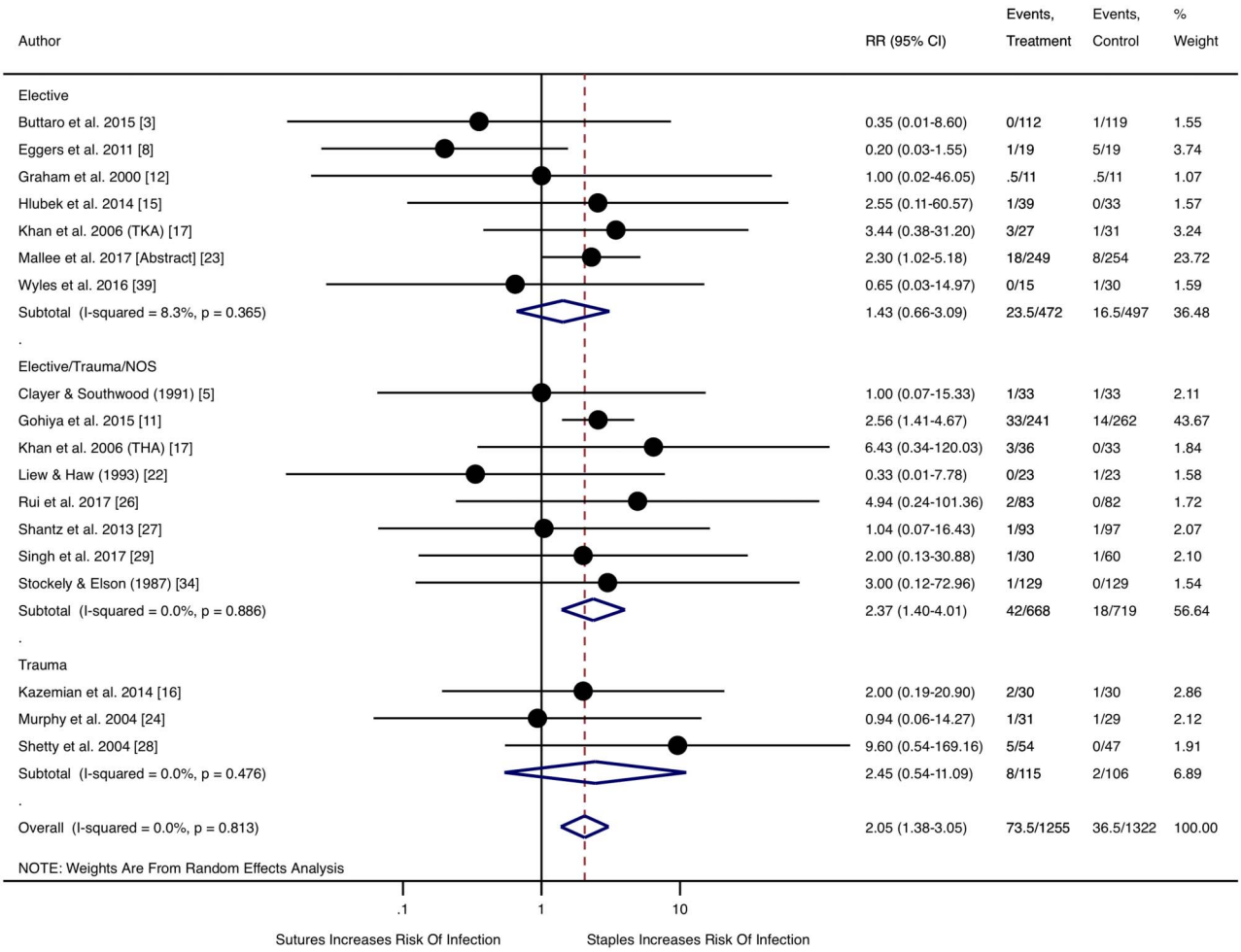

Fig. 4 Forest plot showing the relative risk (RR, 95% CI) of SSI for patients receiving staples versus sutures for skin closure after orthopaedic surgery subgrouped by surgical population. For combined/NOS surgical populations, staples increased the risk of SSI compared with sutures (RR, 2.37; 95% CI, 1.40–4.01). The test for subgroup differences across the subgroups for elective, trauma, and combined/NOS was nonsignificant (p = 0.389).

Fig. 3). This suggests that for every 34 patients receiving staples instead of sutures for skin closure, there will be one additional SSI within 1 year of surgery (Table 3). One trial contributed heavily toward the overall effect due to its high incidence of SSIs [11]. Because this trial had a high risk of bias and a very high event rate (in both study arms) relative to the other studies, we performed a post-hoc sensitivity analysis to exclude this study. After excluding this trial, we still observed a difference in SSI risk (RR, 1.72; 95% CI, 1.01–2.94; $I^2 = 0\%$; NNTH = 65.3; Fragility Index = 4), but the results also became highly fragile with only four additional SSIs in the suture group needed to change the effect to nonsignificance (Fragility Index = 4).

Only two deep SSIs were noted, one occurring in each treatment arm. There was insufficient data to evaluate whether duration of followup affected the distribution and severity of SSIs across treatment groups. For this reason, only superficial SSIs were most likely to be detected. Subgroup analysis by severity of SSI was not informative, as only two events were specified as deep SSIs, and the remainder were either superficial wound SSIs, or were not clearly specified by the study authors. In addition, the I^2 for SSI heterogeneity was 0% in the primary analysis, suggesting that the differences among suture materials did not translate to systematic impact on effect size.

No differences in SSI between staples and sutures were noted for the subgroup for trauma (RR, 2.45; 95% CI, 0.54–11.09) or elective surgery (RR, 1.43; 95% CI, 0.66–3.09; test for subgroup differences, p = 0.389; Fig. 4). With respect to studies that included a mixture of trauma, elective, or other/not specified orthopaedic patients, staples were associated with an increased risk of SSI compared with sutures (RR, 2.37; 95% CI, 1.40–4.01). For the hip surgery subgroup, staples were associated with an increased risk of SSI compared with sutures (RR, 2.42; 95% CI, 1.40–4.17), but not for the knee surgery subgroup (RR, 1.59, 95% CI, 0.69–3.67; test for subgroup differences, p =

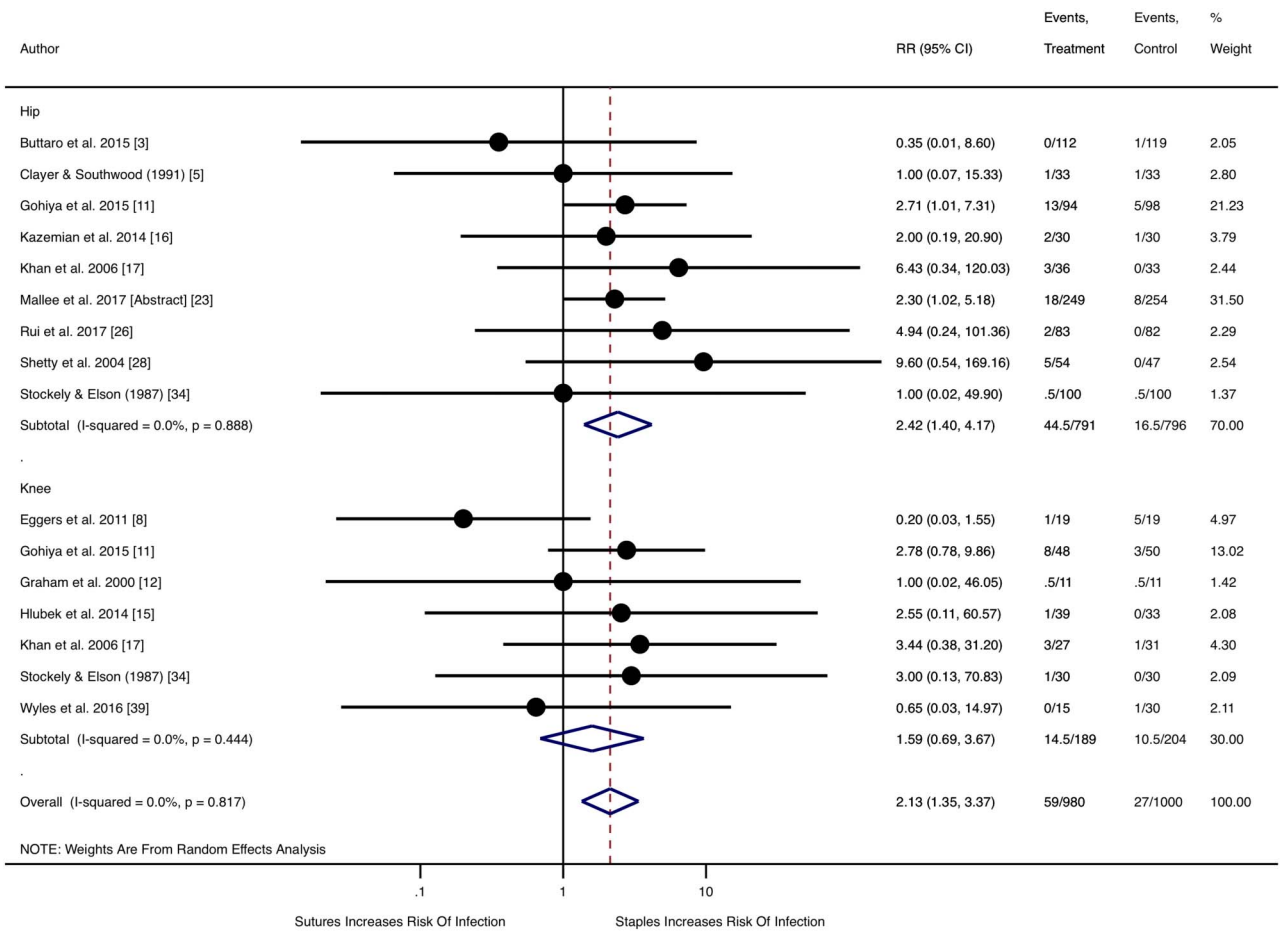

Fig. 5 Forest plot showing the relative risk (RR, 95% CI) of SSI for patients receiving staples versus sutures for skin closure subgrouped by hip and knee surgery. For hip surgery, staples increased the risk of SSI compared with sutures (RR, 2.42; 95% CI, 1.40–4.17). The test for subgroup differences between hip and knee surgery was not significant (p = 0.426).

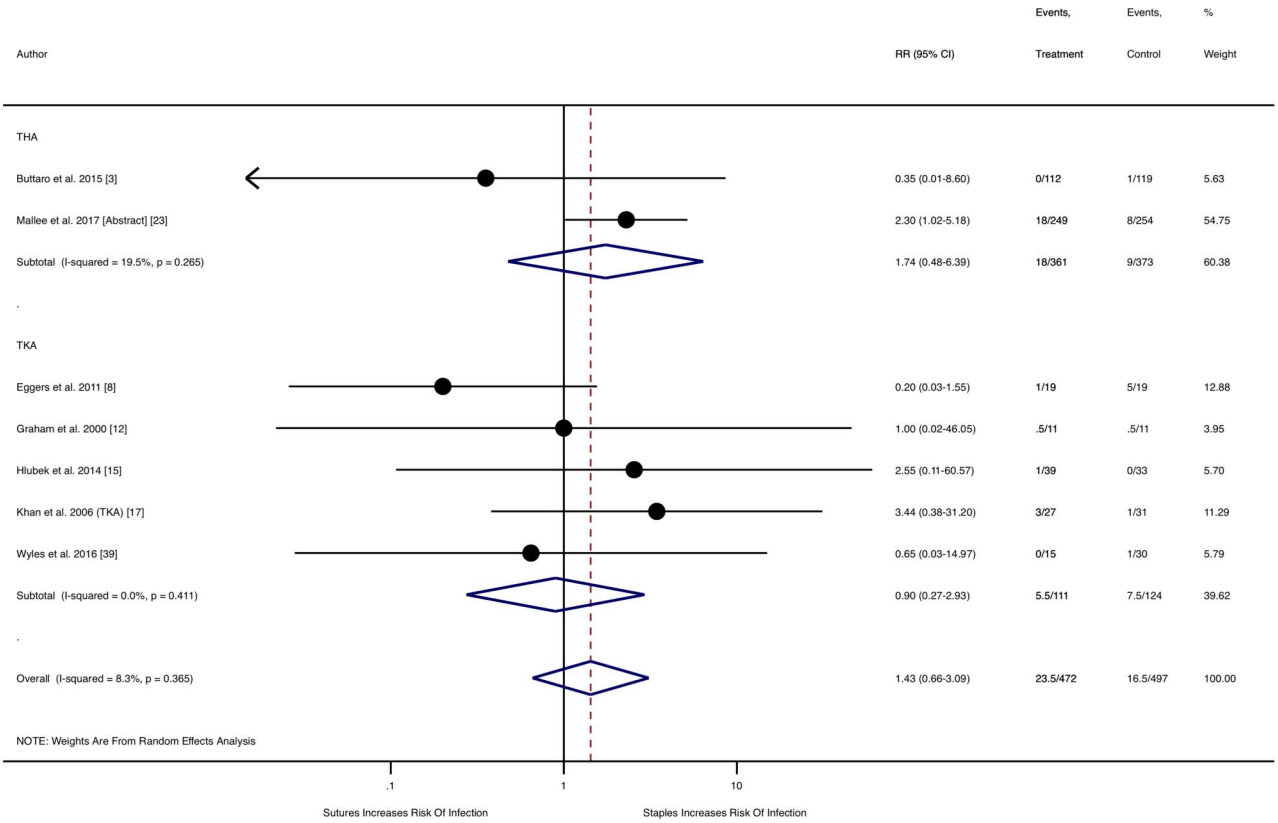

Fig. 6 Forest plot showing the relative risk (RR, 95% CI) of SSI for patients receiving staples versus sutures for skin closure subgrouped by elective THA and TKA. No difference in SSI risk between staples and sutures was noted for patients undergoing elective THA (RR, 1.74; 95% CI, 0.48–6.39) and patients undergoing elective TKA (RR, 0.90; 95% CI, 0.27–2.93; test for subgroup differences, p = 0.584).

0.426; Fig. 5). When limited to elective surgery only, no difference in SSI risk between staples and sutures was noted for patients undergoing elective THA (RR, 1.74; 95% CI, 0.48–6.39) and patients undergoing elective TKA (RR, 0.90; 95% CI, 0.27–2.93; test for subgroup differences, p = 0.584; Fig. 6). Additionally, no subgroup differences in SSI risk were found when stratifying by suture material and country income classification (Fig. 7 and Fig. 8).

Risk of SSI: Sensitivity Analysis (Only Low Risk of Bias Studies)

When we limited the analysis to RCTs with low risk of bias, we found no difference between sutures and staples in terms of SSI (RR, 1.45; 95% CI, 0.31–6.79; I^2 = 46%) [8, 17, 27, 28, 39].

Discussion

SSI remains a risk for patients undergoing orthopaedic surgery. Although research has identified several approaches to prevent SSI in orthopaedic surgery, the degree to which the choice of skin closure modality contributes to differential SSI risk remains contested. Previous meta-analyses on this topic have shown conflicting results [20, 30] . Further, since publication of the most recent meta-analysis [20], several additional randomized controlled trials (RCTs) have been identified [3, 11, 15, 16, 23, 26, 29], warranting an updated meta-analysis to clarify the existing evidence base. Based on the findings of this meta-analysis, no definite differences in SSI risk was found between staples and sutures, regardless of whether the totality of the evidence base is combined or limited to low risk of bias RCTs only. It is clear that the evidence base remains inadequately powered to definitively provide answers regarding differential risk of SSI between staples and sutures. Therefore, until RCTs of adequate power and duration are completed, the choice between staples and sutures can be based on factors such as local availability, surgeon preference, and cost.

The results of this meta-analysis should be interpreted in light of its limitations. Only five of the included

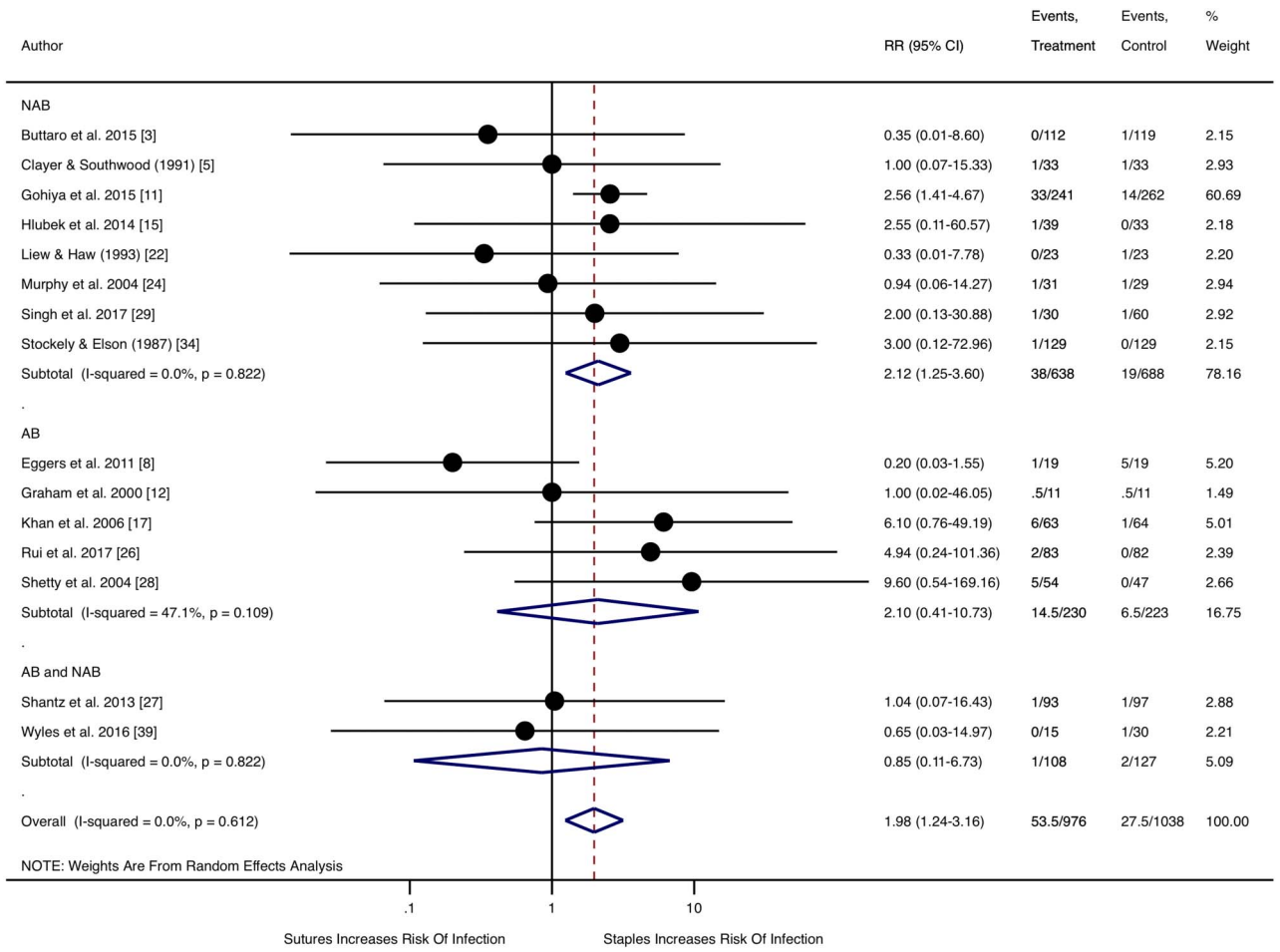

Fig. 7 Forest plot showing the relative risk (RR, 95% CI) of SSI for patients receiving staples versus sutures for skin closure after orthopaedic surgery subgrouped by suture material. Among trials using nonabsorbable sutures (NAB), staples increased the risk of SSI compared with sutures (RR, 2.12; 95% CI, 1.25–3.60). The test for subgroup differences across the subgroups for absorbable (AB) and NAB sutures was not significant (p = 0.92).

randomized studies were rated as low risk of bias [8, 17, 27, 28, 39]. The remainder of the randomized studies were either rated as high or unclear risk of bias. The most common reason for being rated as uncertain risk of bias was due to lack of sufficiently reported details on randomization, allocation concealment, or attrition. The most common reason for being rated as high risk of bias was related to lack of blinding and allocation concealment. However, whether this translated to actual bias in the results, perhaps due to systematic over-reporting of borderline wound infections for staples rather than sutures, seems somewhat unlikely given that there is no strong preconceived popular opinion regarding whether staples or sutures are superior. It is also hard to imagine other economic or professional incentives that would drive systematic differences in ascertainment or diagnosis of SSI to unduly bias the results one way or the other.

We acknowledge that our decision to combine different suture materials (other than barbed sutures, surgical zippers, and skin adhesives, which we excluded altogether from this meta-analysis) may limit the generalizability of the results. The choice to combine different suture materials into one treatment group was twofold: First, despite potential differences in suture material (excluding barbed sutures), there remains insufficient evidence to suggest that any differences between suture materials contributes to differential risk in SSI. Second, compared with staples, sutures reflect a distinct category of skin closure. For example, both staples and sutures require different handling of soft tissue; sutures are passed within or through the dermis and back out of the skin to be tied and secured, whereas staples are applied from external to internal and are then bent internally to achieve and maintain approximation of the skin. They also have different closure times and their removal, if necessary, need different techniques in clinic. Nonetheless, the impact of including different suture materials in this study is likely minimal given that the I^2 for SSI heterogeneity was 0% in the primary analysis,

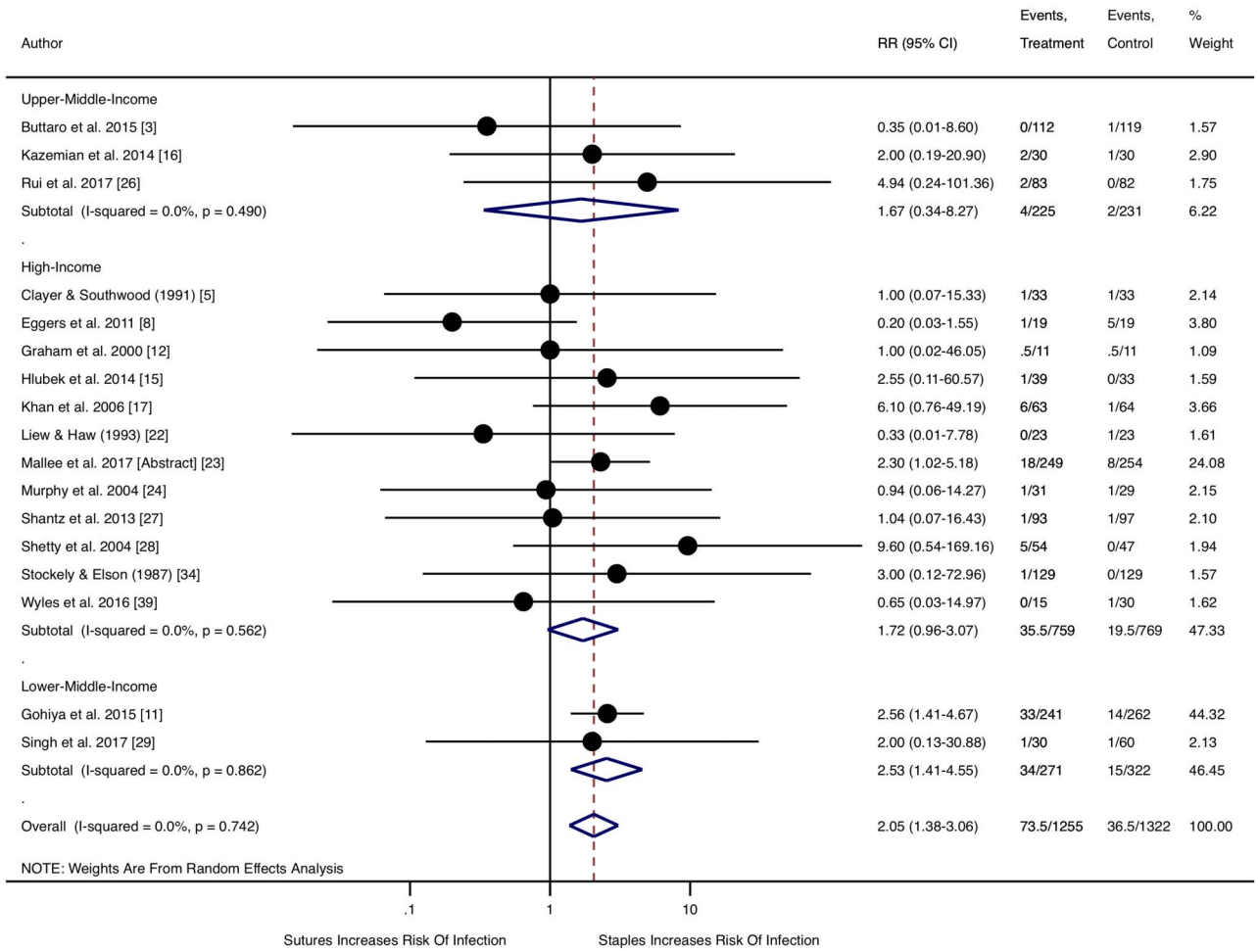

Fig. 8 Forest plot showing the relative risk (RR, 95% CI) of SSI for patients receiving staples versus sutures for skin closure after orthopaedic surgery subgrouped by country income classification. Within lower middle-income countries, staples increased the risk of SSI compared with sutures (RR, 2.53; 95% CI, 1.41–4.55). The test for subgroup differences across the subgroups for lower middle, upper middle, and high-income countries was not significant (p = 0.57).

suggesting that the differences amongst suture materials did not translate to systematic impact on effect size.

In addition, followup time for SSI detection was found to vary between trials, with some studies reporting only short-term followup. This may have underestimated the true rates of SSI, including deep SSIs. Assignment to elective versus trauma subgroups was also challenging because some studies did not state whether elective or trauma patients were enrolled or did not present data separately for elective versus trauma patients. Furthermore, the distribution of potentially important unmeasured prognostic factors remains uncertain. For example, surgical technique, expertise, aseptic technique, antibiotic timing, and patient-specific prognostic factors, such as body mass index, may also influence the quality of skin closure and SSI risk [7, 19, 24, 31] but were rarely reported in the trials. Future studies should ensure high methodologic rigor (randomization, blinding, adequate power, adequate length of followup) and should also report underlying patient populations and important prognostic factors to allow for exploration of the influence on SSI.

Although the primary analysis noted a higher risk of SSI with staples, this finding likely has uncertain clinical importance, given that most were superficial infections. Indeed, this meta-analysis included only two deep SSIs, with one occurring in each treatment arm. To address clinical heterogeneity, we performed several subgroup analyses to further inform clinical relevance across more homogeneous subpopulations of interest. The relative risk of SSI was consistent across all subgroup analyses (as indicated by nonsignificant subgroup interaction p values), suggesting that there were no identifiable subgroups of importance with respect to differential effect of staples versus sutures.

When we limited the analysis to the five RCTs with low risk of bias, we found no difference in SSI risk between staples and sutures. This is not surprising, given that the original finding of a difference in relative risk of SSI for staples versus sutures hinged mostly one trial with high risk of bias [11]. Whether we base our conclusions on the totality of the evidence base (low and high risk of bias) or limit our conclusions to only the low risk of bias studies, it is clear that the conclusions are the same: despite more than 17 randomized trials (involving 2446 patients), no definitive difference in risk of SSI between staples and sutures has been proven. It has been previously proposed that the use of sutures might offer favorable mechanical advantages, such as better skin approximation [18], to reduce SSI risk; however, findings from our study do not conclusively support this hypothesis.

Future studies should be informed by the results of this meta-analysis to calculate the necessary sample size to determine if there are important differences in SSI risk between staples and sutures. Future studies should also incorporate study design and study implementation features that ensure low risk of bias across the domains of patient selection, surveillance for outcomes (in particular by using CDC definitions with followup to 1 year to detect all potentially serious SSI), completeness of patient followup (ensuring low loss to followup, and providing intention-to-treat analysis), and complete reporting (reporting all outcomes as originally planned; and ensuring publication even if results are negative). Since the issue of appropriate skin closure is equally relevant to patient populations in high- and low-income countries alike, global clinical trials are needed to provide answers that apply to all settings.

In conclusion, even after pooling RCTs in a relatively large meta-analysis, we found insufficient evidence to conclude there is a difference in SSI when staples are used instead of sutures for skin closure after orthopaedic surgery. However, the total body of evidence remains weak and, even when limiting to only low risk of bias studies, it is not possible to identify whether there is a clinically important difference between staples and sutures in terms of infection risk. Until randomized studies of adequate power and followup duration are performed to inform this issue, the choice between staples versus sutures should be based on other factors such as local availability, surgeon preference, and cost.

Acknowledgments We thank Dr Rudolf Hlubek for providing additional data from his clinical trial.

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