Secondary Versus Primary Closure Techniques for the Prevention of Postoperative Complications Following Removal of Impacted Mandibular Third Molars: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

*Alonso Carrasco-Labra, DDS,**
Romina Brignardello-Petersen, DDS,†
Nicolás Yanine, DDS, MSc,‡ Ignacio Araya, DDS,§ and
Gordon Guyatt, MD, MSc‖

Purpose: To determine the impact of secondary versus primary closure techniques on the frequency and severity of pain, facial swelling, trismus, infectious complications, and postoperative bleeding after impacted mandibular third molar extraction.

Materials and Methods: Randomized controlled trials were identified through MEDLINE, EMBASE, and CENTRAL, ongoing trial registers, meeting abstracts, doctoral and masters theses, and manual searching of the reference lists of eligible studies. Study selection, data extraction, risk of bias, and Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) rating of confidence in effect estimates were undertaken independently in duplicate.

Results: Of 1,721 identified citations, 14 studies proved eligible. Pain and facial swelling at postoperative days 3 and 7 and infectious complications at day 7 did not differ between techniques. Patients receiving secondary closure had less trismus (in millimeters) at postoperative days 3 (mean difference, 3.72; 95% confidence interval, 1.42 to 6.03, $P = .002$) and 7 (mean difference, 2.35; 95% confidence interval, 0.37 to 4.33; $P = .02$). Four randomized controlled trials reported bleeding: in 2, there was no bleeding in either group; the numbers of bleeding events with primary and secondary closures were 22 and 16 and 5 and 15, respectively, in the other 2. Because of the risk of bias and inconsistency in results, the evidence warranted, at best, low confidence in the estimates of effect across all outcomes.

Conclusions: Although differences between primary and secondary closure techniques after impacted mandibular third molar extraction are likely to be small, available evidence provides only low confidence in the effect estimates. The results do not support a preference for either approach.

J Oral Maxillofac Surg 70:e441-e457, 2012

*Lecturer, Department of Oral and Maxillofacial Surgery and Evidence-Based Dentistry Unit, Faculty of Dentistry, Universidad de Chile, Santiago, Chile; Graduate student, Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada.

†Lecturer, Evidence-Based Dentistry Unit and Pathology Department, Faculty of Dentistry, Universidad de Chile, Santiago, Chile; Graduate student, Department of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada.

‡Lecturer, Department of Oral and Maxillofacial Surgery and Evidence-Based Dentistry Unit, Faculty of Dentistry, Universidad de Chile, Santiago, Chile.

§Lecturer, Department of Oral and Maxillofacial Surgery and Evidence-Based Dentistry Unit, Faculty of Dentistry, Universidad de Chile, Santiago, Chile.

‖Professor, Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada.

Address correspondence and reprint requests to Dr Carrasco-Labra: Sergio Livingstone Pohlhammer 943, Independencia, Santiago, Chile; e-mail: alonsocarrascolabra@gmail.com

0278-2391/12/7008-0$36.00/0
http://dx.doi.org/10.1016/j.joms.2012.03.017

Surgical removal of impacted mandibular third molars (IMTMs) is the most commonly performed procedure in oral and maxillofacial surgery.[1,2] Clinicians make the diagnosis of IMTM when the molar does not erupt properly or there is insufficient space between the mandibular ramus and the second molar.[3] In 1990, North American surgeons removed approximately 10 million IMTMs.[4]

Frequent postoperative sequelae after surgical removal of an IMTM include pain, temporary restricted mouth opening (trismus), and swelling. Less commonly, late or delayed hemorrhage or sepsis may occur.[5] Surgeons have adopted different strategies to decrease these sequelae, including changing the type of surgical closure of the wound.

The classic primary closure technique after IMTM removal is derived from basic surgical principles. When using this technique, the surgeon fully covers and hermitically closes the socket with a flap, allowing primary wound healing. Investigators in favor of this method have suggested that it decreases the risk of postoperative infection.[6,7]

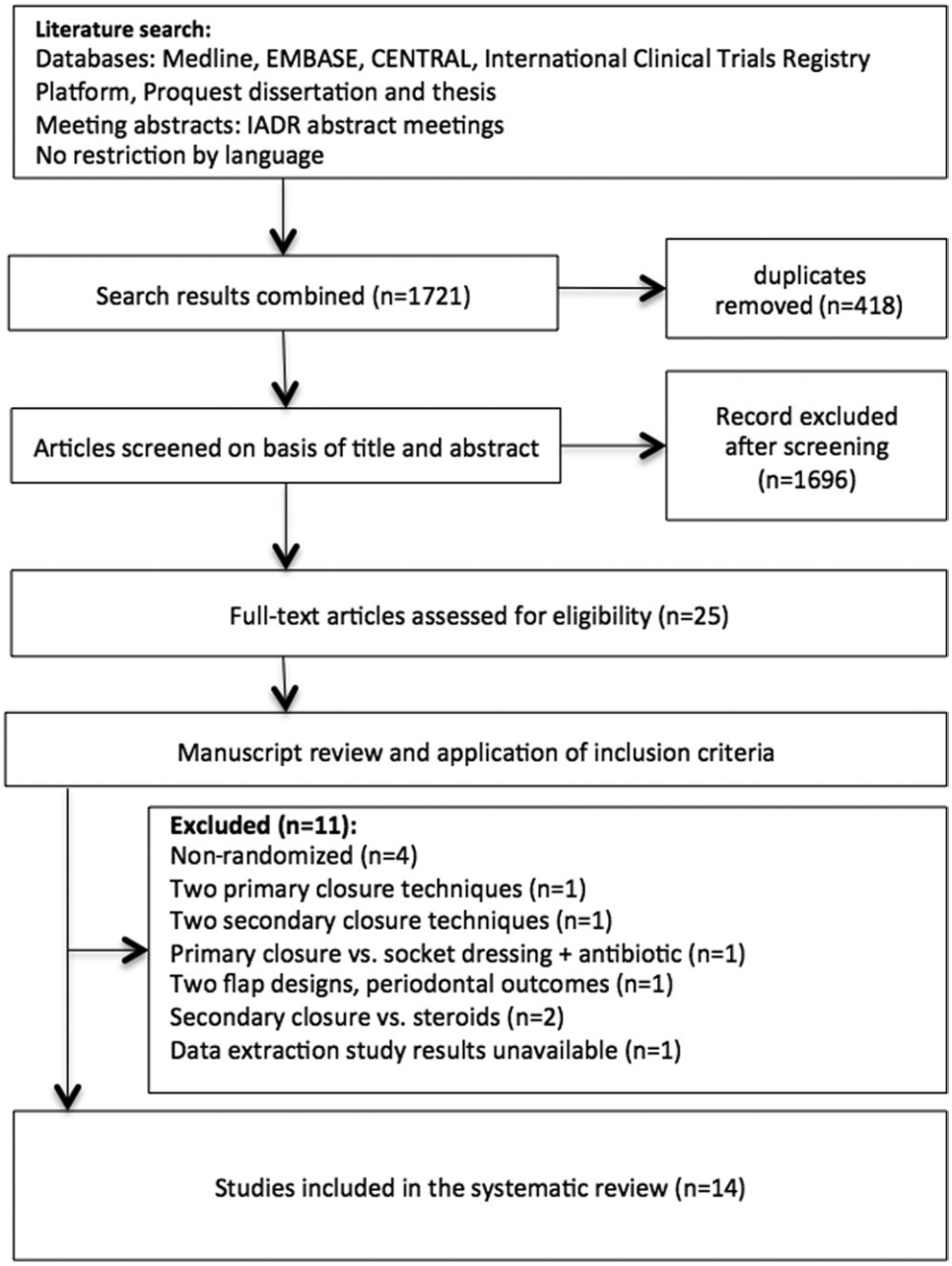

FIGURE 1. Flow chart of article selection process. IADR, International Association for Dental Research.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

Table 1. CHARACTERISTICS OF INCLUDED STUDIES

Study	Year	Location	Design	Participants	Intervention	Comparison	Cointerventions	Secondary (n)	Primary (n)	Age Range (yr)	Mean Age (yr)	Impaction Type
Akota et al[22]	1998	Norway	Split-mouth	Healthy	Gauze drain*	Primary closure	NSAID	30	30	20-37	25	
Bello et al[17]	2011	Nigeria	Parallel	Healthy	Partial closure	Primary closure	ATB-NSAID	40	42	NR	26	Mixed
Cerqueira et al[9]	2004	Brazil	Split-mouth	Healthy	Tube drain (urethral probe #4)	Primary closure	ATB-NSAID	53	53	14-30	21	Mixed
Chukwuneke et al[20]	2008	Nigeria	Parallel	Healthy	Penrose	Primary closure	NSAID	50	50	18-40	NR	Mixed
Danda et al[23]	2010	India	Split-mouth	NR	Wedge of mucosa†	Primary closure	ATB-NSAID	93	93	18-31	24	Mixed
Hashemi et al[18]	2011	Iran	Split-mouth	Healthy	Sutureless	Primary closure	ATB-NSAID	30	30	19-24	22	Bony
Holland and Hindle[16]	1984	England	Split-mouth	NR	Dressing drain‡	Primary closure	Nothing	70	70	20-35	NR	Mixed
Osunde et al[21]	2010	Nigeria	Parallel	NR	Single suture	Multiple sutures	ATB-NSAID	25	25	18-38	26	Mixed
Pasqualini et al[8]	2005	Italy	Parallel	Healthy	Wedge of mucosa†	Primary closure	ATB-NSAID	100	100	19-27	NR	Mixed
Rakprasitkul and Pairuchvej[24]	1997	Thailand	Split-mouth	Healthy	Tube drain	Primary closure	NSAID	23	23	16-35	24	Full bony
Refo'a et al[19]	2011	Iran	Parallel	Healthy	Partial closure§	Primary closure	ATB-NSAID	16	16	20-25	22	Full bony
Sağlam[25]	2003	Turkey	Split-mouth	Healthy	Tube drain	Primary closure	ATB-NSAID	13	13	15-39	24	Full bony
Srinivas[26]	2006	India	Split-mouth	Healthy	Tube drain	Primary closure	NSAID	14	14	15-39	NR	Mixed
Xavier et al[27]	2008	Brazil	Split-mouth	Healthy	Incision drain‖	Primary closure	NSAID	20	20	18-40	NR	Mixed

Abbreviations: ATB, antibiotic prophylaxis; mixed, combination of erupted, partial bony, and full bony teeth extracted; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug.

*A gauze drain impregnated with chlortetracycline ointment was used.

†A wedge of mucosa was removed, creating a drainage path.

‡A ribbon gauze dressing was used.

§A distal extension of 5.0 to 6.0 mm to the second molars was kept open.

‖Vestibular oblique incision was sutured at isolated points.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

Healing by secondary intention or a secondary closure technique refers to the cicatrization process of an intentionally open wound, from the base and borders to the upper face, by deposition of new tissue. Investigators who prefer this approach have suggested that it allows the drainage of inflammatory exudate, because the socket remains in communication with the oral cavity.[8,9]

Investigators have conducted many randomized controlled trials (RCTs) to determine which technique is associated with fewer and less severe postoperative sequelae. The purpose of this study was to summarize the evidence regarding the impact, in patients undergoing surgical removal of an IMTM, of a primary versus a secondary closure technique on the presence and severity of postoperative sequelae, including pain, facial swelling, trismus, infectious complications, and bleeding up to 7 days after surgery.

Methods

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

The present search used the Ovid version of MEDLINE (from 1966 through December 2011) and EMBASE (from 1980 through December 2011), the Cochrane Central Register of Controlled Trials CENTRAL (issue 12, December 2011), and the International Clinical Trials Registry Platform Search Portal (http://apps.who.int/trialsearch) databases. The Appendix presents the medical subject headings and key words used in the search. The literature search was limited to RCTs using the Cochrane Highly Sensitive Search filter.[10] Unpublished studies were sought using the International Association for Dental Research (IADR) abstract meetings database of the previous 20 years and the ProQuest Dissertation and Thesis database. Manual searches of the reference lists of the potentially eligible articles were conducted. There was no restriction by language and translated non-English-language articles.

ELIGIBILITY CRITERIA FOR THE STUDIES

Eligible RCTs enrolled healthy adult participants who underwent surgical removal of an IMTM and compared any type of surgical secondary closure technique determined by the incision or a device (flap design, suture technique, rubber drain, Penrose, gauze drain, modified Foley catheter, etc) with a primary closure technique and followed patients for at least 3 days.

OUTCOMES

Pain, facial swelling, and trismus (in millimeters) were designated as primary outcomes and infectious complications (alveolar osteitis and/or surgical site infection) and postsurgical bleeding as secondary outcomes.

STUDY SELECTION AND DATA EXTRACTION

Two researchers (I.A., N.Y.) independently reviewed the titles and abstracts of all potentially relevant articles. Two reviewers (A.C.-L., R.B.-P.) independently evaluated the eligibility of the full-text of all articles deemed potentially eligible in the title and abstract reviews. A third reviewer (I.A.) arbitrated dis-

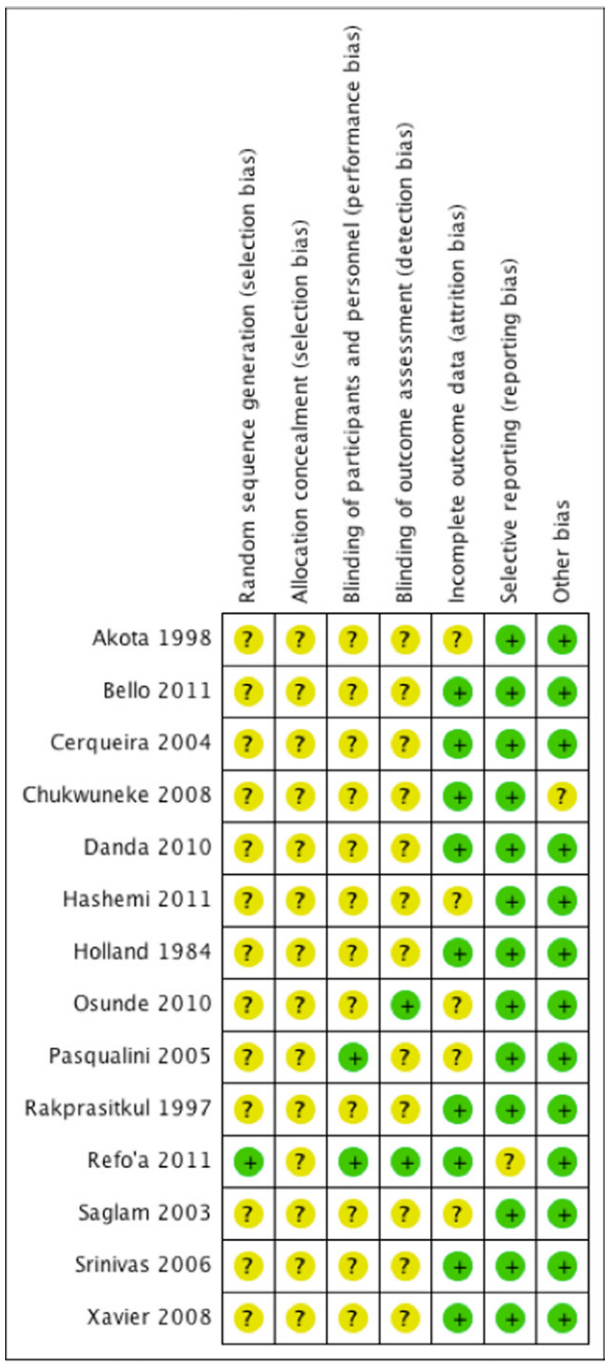

FIGURE 2. Risk of bias summary: reviewers' judgment on each risk-of-bias item for the included studies.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

Table 2. SPECIFIC CHARACTERISTICS OF TRIALS ASSESSING PAIN

Study	Design	Type of Scale	Pain Scale Definition	Outcome Assessment (Postoperative Days)	Imputation of SD
Akota et al[22]	Split-mouth	Continuous	VAS 50 mm	1, 3, 6	Yes
Bello et al[17]	Parallel	Continuous	VAS 6 U	1, 2, 3, 5, 6, 7	No
Cerqueira et al[9]	Split-mouth	Dichotomous	VAS 10 cm‡§	1, 3, 7, 15	No
Chukwuneke et al[20]	Parallel	Continuous	VAS 10 U	1, 3, 5	No
Danda et al[23]	Split-mouth	Continuous	VAS 5 points	7	No
Hashemi et al[18]	Split-mouth	Continuous*	VAS 6 U	1, 3, 7	No
Holland and Hindle[16]	Split-mouth	Dichotomous	Pain/no pain	1-18	No
Osunde et al[21]	Parallel	Continuous	VAS 10 cm	1, 2, 3, 5, 7	No
Pasqualini et al[8]	Parallel	Continuous	VAS 5 cm	6 hr, 1, 2, 3, 4, 5, 6	No
Rakprasitkul and Pairuchvej[24]	Split-mouth	Continuous	VAS 10 U	3, 7§	Yes
Refo'a et al[19]	Parallel	Continuous	VAS 5 U	3	No
Srinivas[26]	Split-mouth	Dichotomous	Pain/no pain	1, 2, 3, 7	No
Xavier et al[27]	Split-mouth	Ordinal†	VAS 100 mm‖	2, 3, 7, 15	No

Abbreviations: SD, standard deviation; VAS, visual analog scale.

*Measured as a continuous variable but reported as a categorical variable (0 to 5).

†Data were transformed to dichotomous to be included in the meta-analysis. Imputation of a paired SD was performed in split-mouth trials that did not analyze and report the results as paired data.

‡VAS cutoff point for pain/no pain not reported.

§Preoperative assessment conducted.

‖Scale: 1 to 25, mild; 26 to 50, moderate; 51 to 75, intense; 76 to 100, unbearable.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

agreements. The investigators were contacted for clarification or to obtain missing information. When data were reported using only graphs, the data were derived from the figures. Using a standardized data extraction form, 2 reviewers independently extracted and tabulated the data from the eligible studies. Two reviewers (A.C.-L., R.B.-P.) independently assessed the risk of bias of the eligible studies using the Cochrane Handbook for Systematic Reviews of Intervention criteria, with disagree-

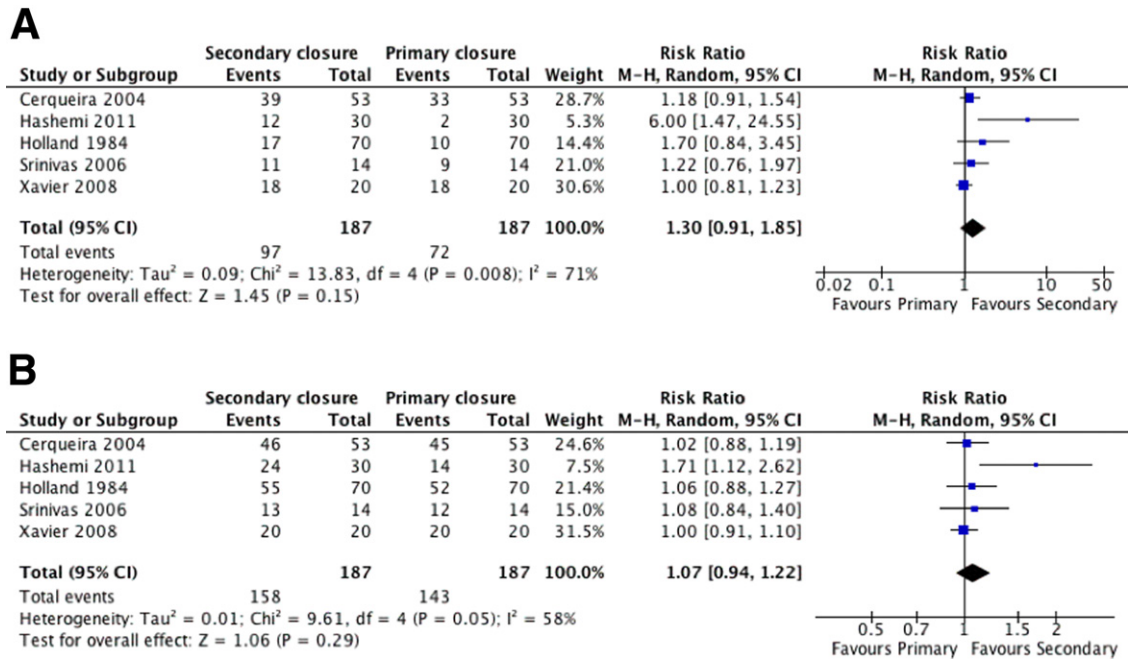

FIGURE 3. Secondary versus primary closure technique for the outcome pain measured as a dichotomous variable at postoperative days *A*, 3 and *B*, 7. CI, confidence interval: M-H, Mantel-Haenszel.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

ments resolved by a third reviewer (N.Y.).[11] The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) rating system was used to evaluate confidence in the effect estimates (quality of evidence) across outcomes.[12] In the GRADE approach, RCTs begin as high-quality evidence, but confidence in estimates decreases if serious risk of bias, inconsistency, imprecision, indirectness, and/or publication bias is present.[13] These evaluations were conducted independently and in duplicate (A.C.-L., R.B.-P.). For the full-text screening and the risk of bias assessment across items, the chance-corrected agreement was calculated using κ statistics.

DATA SYNTHESIS AND STATISTICAL ANALYSIS

For the continuous outcomes (pain, facial swelling, and trismus) using the same measurement instrument, the weighted mean difference (MD) and its 95% confidence interval (CI) were calculated. If the trials used different measurement instruments, the standardized mean differences (SMDs) and their 95% CIs were calculated.

For the dichotomous outcomes (infectious complications and postoperative bleeding), the relative risks (RRs) and 95% CIs were calculated. For the trials assessing the outcome pain using an ordinal scale, the categories were collapsed and the results

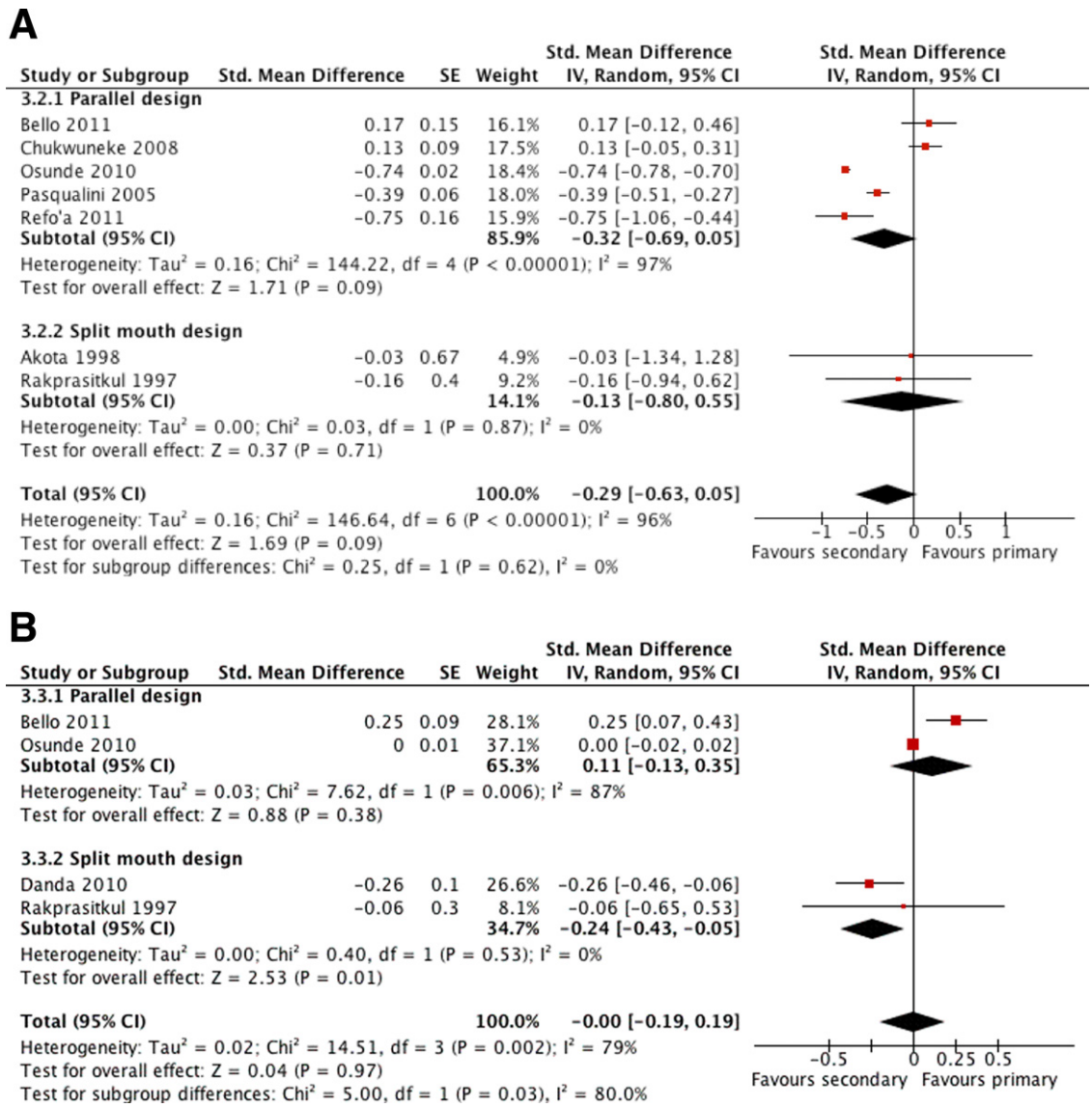

FIGURE 4. Secondary versus primary closure technique for the outcome pain measured as a continuous variable at postoperative days *A*, 3 and *B*, 7. CI, confidence interval; SE, standard error.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

were included in the meta-analysis of dichotomous outcomes.

When CIs crossed the nondifference threshold, the reviewers judged that the results failed to provide convincing evidence of a treatment effect.

Data from parallel-group and split-mouth trials were combined using the procedure described by Lesaffre et al[14] and Elbourne et al.[15] When needed, a paired analysis was approximated by imputing the pooled standard deviation (SD) from the SDs of the 2 groups using a correlation coefficient of 0.75. All analyses used random-effects models.

The analysis was performed using Review Manager 5.1 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark) to obtain the corresponding pooled estimate using the generic inverse variance method. Two sensitivity analyses were undertaken: *1)* the treatment effect for each outcome including or excluding split-mouth trials with imputed SDs and *2)* the treatment effect and its 95% CIs of the outcomes for each imputed correlation coefficient (0.5, 0.75, and 0.9).

HETEROGENEITY AND SUBGROUP ANALYSIS

To estimate the total variation across studies, the Cochran χ^2 test for heterogeneity and the I^2 statistic were used. Three possible explanations of heterogeneity were postulated a priori: *1)* articles having a high risk of bias would show a larger effect of the intervention compared with studies with low risk of bias; *2)* secondary closure would appear superior to primary closure when devices such as rubber tubes,

Table 3. SPECIFIC CHARACTERISTICS OF TRIALS ASSESSING FACIAL SWELLING

Study	Design	Method for Assessing Facial Swelling	Reported Outcome	Outcome Assessment (Postoperative Days)	Imputation of SD
Bello et al[17]	Parallel	Facial references (tape measure)	Mean of facial swelling (mm)	2, 5, 7	No
Cerqueira et al[9]	Split-mouth	Amin and Laskin method[28]	Percent facial swelling	1, 3, 7, 15	Yes
Chukwuneke et al[20]	Parallel	Amin and Laskin method	Percent facial swelling	1, 3, 5	No
Danda et al[23]	Split-mouth	Berge method VAS 1-5 U[29,30]	1 (no swelling) to 5 (extremely severe swelling)¥	7	No
Hashemi et al[18]	Split-mouth	Distance corner of mouth to lower part of the ear lobe (mm) ¥	Mean facial swelling (mm)	1, 3, 7	No
Osunde et al[21]	Parallel	Neupert method modified by Filho[31]	Mean amount of facial swelling	1, 2, 3, 5, 7	No
Pasqualini et al[8]	Parallel	Berge method VAS 0-5 cm[29,30]	0 (no swelling) to 5 (extremely severe swelling)†	6 hr, 1, 2, 3, 4, 5, 6	No
Rakprasitkul and Pairuchvej[24]	Split-mouth	Amin and Laskin method	Percent facial swelling	3, 7	Yes
Refo'a et al[19]	Parallel	Distance from outer canthus of eye to angle of mandible*	Mean vertical swelling size changes*	1, 3, 7	No
Sağlam[25]	Split-mouth	Amin and Laskin method	Mean vertical and horizontal facial swelling	1, 2, 3, 7§	No
Srinivas[26]	Split-mouth	Amin and Laskin method	Mean vertical and horizontal facial swelling	1, 2, 3, 7§	No
Xavier et al[27]	Split-mouth	Amin and Laskin method	Percent facial swelling	3, 7, 15	Yes

Note: The SD of the change from baseline was calculated using the method reported by Markiewicz et al.[32]

Abbreviations: SD, standard deviation; VAS, visual analog scale.

*Not included in the meta-analysis because the investigators considered only a vertical component.

†These were not meta-analyzed because of the different method for assessing the outcome.

§These trials were not included in the meta-analysis because it was not possible to estimate the SD.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

Penrose drainage, or gauze were used rather than when partial closure, incision drain, or a sutureless technique was implemented; and *3)* effect sizes would vary among crossover trials, split-mouth trials, and parallel-group trials. In a posteriori subgroup analyses, the cointerventions (pre- and/or postoperative antibiotic prophylaxis and nonsteroidal anti-inflammatory drugs) reported in the included trials were explored as a source of heterogeneity.

Results

SEARCH

Of 1,721 identified titles and abstracts, 25 proved potentially eligible and 14 of those proved eligible (Fig 1). The κ statistic calculated between the reviewers for the full-text screening was 0.96, indicating excellent agreement.

CHARACTERISTICS OF ELIGIBLE STUDIES

Among the 14 eligible studies, published from 1984[16] through 2011,[17-19] 5 used a parallel-group design[8,17,19-21] and 9 used a split-mouth design.[9,16,18,22-27] Thirteen RCTs were published; 1 was a Master's thesis.[26] Table 1 summarizes the populations, which were described as healthy patients and were similar in age, cointerventions, and impaction type. Five trials used a tube drain as a secondary closure technique,[9,20,24-26] 5 trials implemented modifications in the flap design and/or sutures,[17-19,21,27] 2 used a dressing drain,[16,22] and 2 removed a wedge of mucosa to allow the drainage of the inflammatory

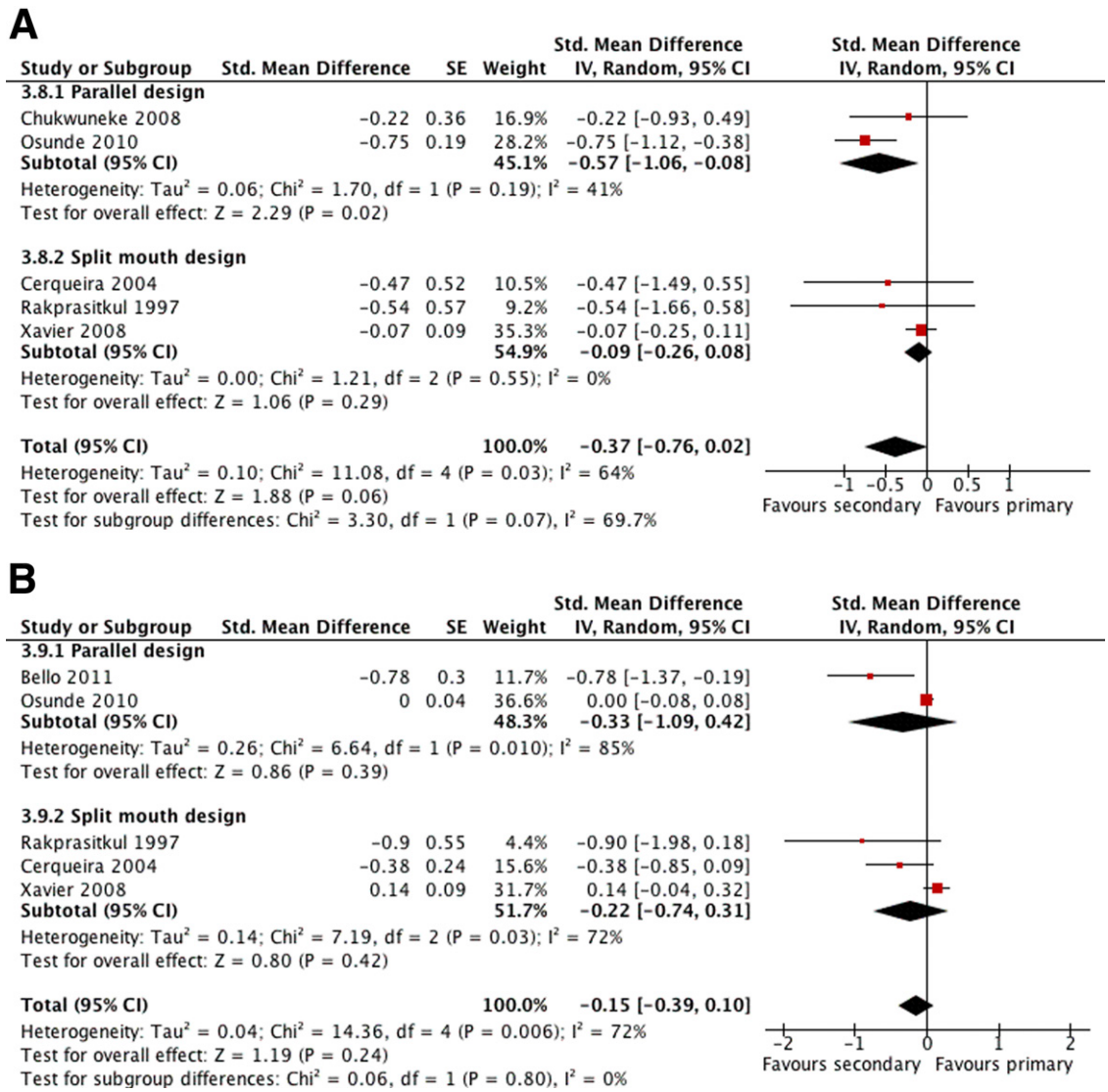

FIGURE 5. Secondary versus primary closure technique for the outcome facial swelling at postoperative days *A,* 3 and *B, 7*. CI, confidence interval; SE, standard error.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

exudate.[8,23] Studies used similar comparison interventions (Table 1).

RISK OF BIAS

All studies ultimately were classified as having an unclear risk of bias, and the agreement between the assessors was high ($\kappa = 0.86$). Because of important missing information in the Methods sections of the reports and unfruitful efforts at contacting the investigators, it was not possible to further specify the risk of bias (Fig 2). Requests for methodologic and result information were sent to 15 investigators; 3 provided informative responses. Sequence generation and allocation concealment constituted the most common unreported methodologic issue. All trials achieved full, or nearly full, follow-up.

One study reported that the investigators did not have conflicts of interest[18]; other studies provided no conflict information.

TREATMENT EFFECT

Primary Outcomes

Pain. All but 1 trial[25] evaluated pain (Table 2). At postoperative days 3 (RR, 1.30; 95% CI, 0.91 to 1.85; heterogeneity, $P = .008$, $I^2 = 71\%$; SMD, −0.29; 95% CI, −0.63 to 0.05; heterogeneity, $P < .00001$, $I^2 = 96\%$; Figs 3A, 4A) and 7 (RR, 1.07; 95% CI, 0.94 to 1.22; heterogeneity, $P = .05$, $I^2 = 58\%$; SMD, 0; 95% CI, −0.19 to 0.19; heterogeneity, $P = .002$, $I^2 = 79\%$; Figs 3B, 4B), there was no difference between closure techniques. None of the a priori hypothesis explained the heterogeneity.

Facial swelling. Twelve studies reported facial swelling.[8,9,17-21,23-27] Two[25,26] used the method of Amin and Laskin,[28] but vertical and horizontal facial references were reported independently and it was not possible to estimate the SD; therefore, these studies were not included in the meta-analysis. In these 2 trials, there was no difference between the closure techniques in the horizontal or vertical components. The trials conducted by Danda et al[23] and Pasqualini et al[8] were not included in the meta-analysis because a visual analog scale was used to measure this outcome (Table 3). Both trials measured the outcome at different time points and reported a statistically significant decrease in facial swelling at postoperative days 3[8] (MD, 0.85; 95% CI, 0.69 to 1.01) and 7[23] (MD, 0.54; 95% CI, 0.30 to 0.77); (both on a 5-U/cm visual analog scale) with secondary closure. Hashemi et al[18] and Refo'a et al[19] measured the outcome using only a vertical component; hence, these studies were excluded from the meta-analysis. In these 2 trials, patients in the secondary closure arm had less mean swelling than those in the primary closure arm at postoperative days 3 (Hashemie et al[18]: MD, −8 mm; $P = .005$; Refo'a et al[19]: MD, −7.9 mm; $P < .001$) and 7 (Hashemie et al[18]: MD, −4.2; $P = .005$; Refo'a et al[19]: MD, −4.6 mm; $P < .001$). For the trial published

Table 4. SPECIFIC CHARACTERISTICS OF TRIALS ASSESSING TRISMUS

Study	Design	Method for Trismus Assessment	Outcome Assessment (Postoperative Days)	Imputation of SD
Bello et al[17]	Parallel	Distance between central incisors (mean of 3 readings)*	2, 5, 7	No
Cerqueira et al[9]	Split-mouth	Maximum mouth opening (cm)	1, 3, 7, 15	Yes
Chukwuneke et al[20]	Parallel	Distance between right central incisors (cm) using dental calipers (cm)	1, 3, 5	No‡
Osunde et al[21]	Parallel	Distance between right central incisors with vernier caliper (cm; mean of 3 readings)	1, 2, 3, 5, 7	No‡
Rakprasitkul and Pairuchvej[24]	Split-mouth	Distance between central incisors (mm)	3, 7	Yes
Refo'a et al[19]	Parallel	Distance between central incisors (mm)†	1, 3, 7	No‡
Sağlam[25]	Split-mouth	Distance between central incisors (mm)	1, 2, 3, 7	Yes
Srinivas[26]	Split-mouth	Distance between central incisors (mm)	1, 2, 3, 7	Yes
Xavier et al[27]	Split-mouth	Distance between central incisors using flexible ruler (mm)	3, 7, 15	Yes

Abbreviation: SD, standard deviation.

*This study was not included in the meta-analysis because the outcome was reported as a percentage of mouth opening.

†Standard error estimated from *P* values.

‡A pooled SD was estimated.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

by Refo'a et al,[19] the results had to be derived from a graph.

At postoperative days 3 (SMD, −0.37; 95% CI, −0.76 to 0.02; heterogeneity, $P = .03$, $I^2 = 64\%$; Fig 5A) and 7 (SMD, −0.15; 95% CI, −0.39 to 0.10; heterogeneity, $P = .006$, $I^2 = 72\%$; Fig 5B), the remaining 5 trials failed to provide convincing evidence of a treatment effect. None of the a priori hypotheses explained the heterogeneity.

Trismus. Nine studies evaluated postoperative trismus,[9,17,19-21,24-27] all of which measured the maximum mouth opening at the specified time points. Five split-mouth trials[9,24-27] reported unpaired SDs; the paired SD was imputed using a correlation coefficient. Of the 4 parallel-group studies, the pooled SD was calculated by assuming equal variances between groups in 3 studies[19-21] (Table 4); in the fourth study,[17] the investigators reported trismus as the per-

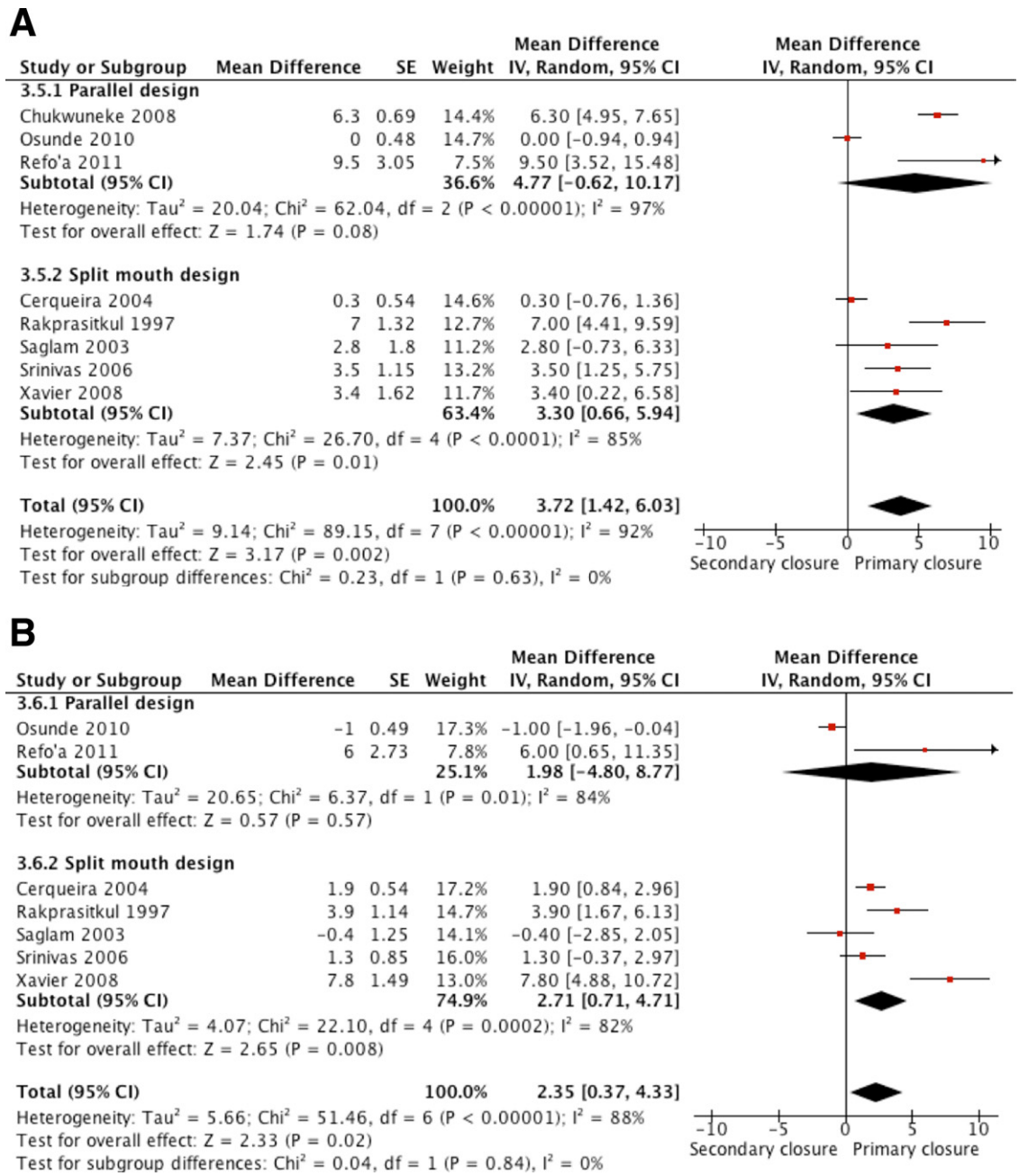

FIGURE 6. Secondary versus primary closure technique for the outcome trismus at postoperative days *A*, 3 and *B*, 7. CI, confidence interval; SE, standard error.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

Table 5. SPECIFIC CHARACTERISTICS OF TRIALS ASSESSING INFECTIOUS COMPLICATIONS: ALVEOLAR OSTEITIS AND/OR SURGICAL WOUND INFECTION

Study	Design	Infectious Complications Definitions*	Outcome Assessment (Postoperative Days)
Akota et al[22]	Split-mouth	Disintegration of blood clot, exposure of alveolar bone, increased pain in alveolus region, and/or irradiating pain after an intermediate period of no or low-intensity pain, foul odor, and exudate and/or pus in socket	6
Bello et al[17]	Parallel	Dry socket, patient with painful and necrotic socket without suppuration; socket infection, patient with history of pus discharge with or without pain, bleeding about ≥1 week, a suppurative socket with or without fever	2, 5, 7, 1 mo
Danda et al[23]	Split-mouth	Alveolar osteitis; outcome definition NR	7
Hashemi et al[18]	Split-mouth	Postoperative infection or alveolar osteitis; outcome definition NR	7
Pasqualini et al[8]	Parallel	Suppurative alveolitis with reinfection of socket; outcome definition NR	6
Refo'a et al[19]	Parallel	Infection or alveolitis; outcome definition NR	NR

Abbreviation: NR, nor reported.

*In this review, infectious complication was considered a composite outcome (alveolar osteitis and/or surgical wound infection).

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

centage of mouth opening and this study was excluded from the meta-analysis. This study failed to show statistically significant differences in the mean percentage of trismus between groups. The pooled analysis showed that at postoperative day 3, the secondary closure decreased trismus by 3.72 mm (MD, 3.72; 95% CI, 1.42 to 6.03; heterogeneity, $P < .00001$, $I^2 = 92\%$; Fig 6A). At postoperative day 7, a 2.35-mm difference in mean trismus was detected in favor of the use of secondary closure techniques (MD, 2.35; 95% CI, 0.37 to 4.33; heterogeneity, $P < .00001$, $I^2 = 88\%$; Fig 6B). None of the a priori hypotheses explained the heterogeneity.

Secondary Outcomes

Infectious complications. Of 6 studies that reported infectious complications,[8,17-19,22,23] 2[17,22] clearly defined alveolar osteitis and surgical-site infection

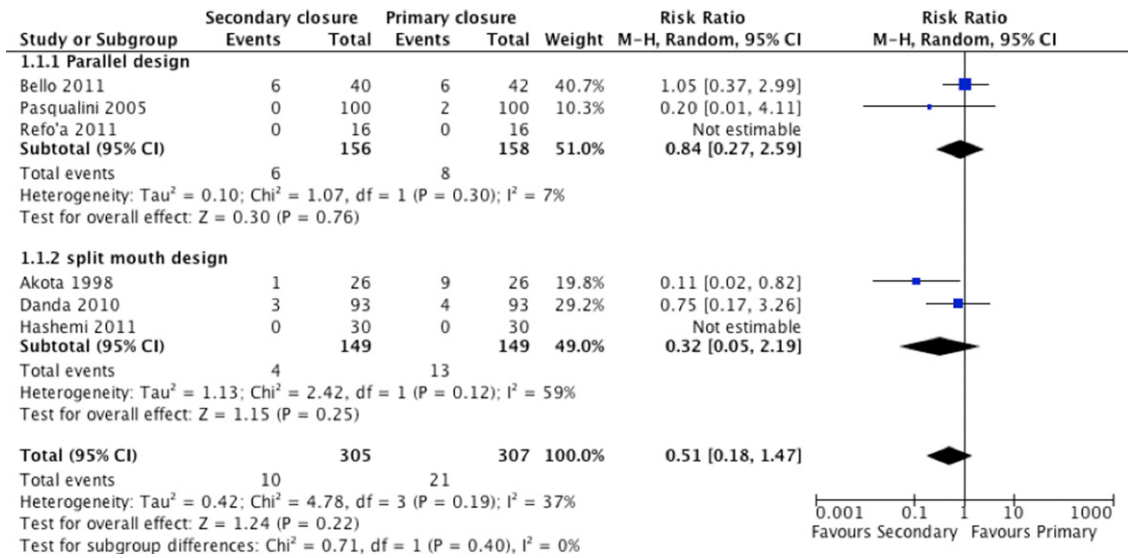

FIGURE 7. Secondary versus primary closure technique for the outcome infectious complications (alveolar osteitis and/or surgical wound infection). CI, confidence interval: M-H, Mantel-Haenszel.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

Table 6. SPECIFIC CHARACTERISTICS OF TRIALS ASSESSING BLEEDING

Study	Design	Type of Outcome	Outcome Definition	Follow-Up (Postoperative Days)
Bello et al[17]	Parallel	Dichotomous	Reactionary bleeding, patient complained of bleeding 48 hr postoperatively	2
Hashemi et al[18]	Split-mouth	Dichotomous	Excessive bleeding or oozing	7
Pasqualini et al[8]	Parallel	Dichotomous	Hemorrhage, formal definition not reported	6
Rakprasitkul and Pairuchvej[24]	Split-mouth	Ordinal	Degree of bleeding*	6

*Grades 0 to 3 according to degree of bleeding measured in gauze bit by the patients.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

and specified the way the outcome was adjudicated (Table 5). The point estimate suggested a large benefit for secondary closure, but the CI included a large benefit for primary closure (RR, 0.51; 95% CI, 0.18 to 1.47; heterogeneity, $P = .19$, $I^2 = 37\%$; Fig 7). Two studies[18,19] reported no events for this outcome. None of the proposed hypotheses explained the heterogeneity.

Postoperative bleeding. Of 4 studies measuring postoperative bleeding,[8,17,18,24] 2[8,18] reported no hemorrhage up to 6 and 7 days after surgery. One study[24] used an ordinal scale with 4 categories, from 0 to 3, using a visual method in which patients were required to bite on a gauze pad that was changed every 2 hours (Table 6). The results suggested a lower incidence of bleeding in surgical wounds treated with secondary closure (secondary closure with at least minimum bleeding, 16/23; primary closure with at least minimum bleeding, 22/23; RR, 0.73; 95% CI, 0.55 to 0.97). The fourth trial[17] reported that 20 patients (62.5%) developed bleeding, 15 (75%) in the secondary closure group and 5 (25%) in the primary closure group (RR, 3.15; 95% CI, 1.26 to 7.86). Because the outcome definition and follow-up for this outcome were not consistent across trials, a pooled estimate was not calculated.

SENSITIVITY ANALYSES

The sensitivity analyses for the outcomes pain and facial swelling suggested no important differences.

For trismus at postoperative days 3 (MD, 4.77; 95% CI, −0.62 to 10.17; heterogeneity, $P < .001$, $I^2 = 97\%$) and 7 (MD, 1.98; 95% CI, −4.80 to 8.77; heterogeneity, $P = .01$, $I^2 = 84\%$), the results were no longer statistically significant when only parallel-group trials were included.[19-21] When the correlation between the 2 sides in the split-mouth designs was changed, no important differences in the effect estimates were found.

PUBLICATION BIAS

Because no more than 7 studies were included in any meta-analysis, funnel plots could not be used to assess publication bias.[33]

CONFIDENCE IN ESTIMATES OF EFFECT

All outcomes at postoperative days 3 and 7 provided low to very low confidence in the estimates (quality of evidence; Tables 7, 8), with serious limitations in the risk of bias, inconsistency, and imprecision.

Discussion

SUMMARY OF RESULTS

The included RCTs suggested that primary and secondary closure techniques differ little in postoperative pain and facial swelling. However, the trials were fraught with problems for risk of bias, inconsistency, and imprecision. Thus, they warranted only low to very low confidence in the estimates, leaving open the possibility that there could be substantial benefits for either technique. The results suggested that patients who undergo a secondary closure may develop less trismus on average at postoperative days 3 (MD, 3.75 mm; 95% CI, 1.42 to 6.03 mm; $P = .002$) and 7 (MD, 2.35 mm; 95% CI, 0.37 to 4.33 mm; $P = .02$), although the effects were small and confidence in the estimates was low.

Six studies that measured the occurrence of alveolar osteitis and/or surgical-site infection failed to detect a difference between the groups. The heterogeneity in this meta-analysis was moderate ($I^2 = 37\%$), and the subgroup analysis hypotheses tested were not able to explain the variation in the results (see evidence profile in Tables 7, 8); overall, the reviewers have low confidence in the effect estimates.

Estimates have suggested the incidence of alveolar osteitis after surgical removal of the IMTM is 9.5% to 14.4%, and the incidence of surgical-site infection is 2% to 4%.[34,35] Of the 14 eligible studies, 8 provided

Table 7. EVIDENCE PROFILE: CONFIDENCE IN EFFECT ESTIMATE ASSESSMENT AND SUMMARY OF FINDINGS FOR EFFECT OF SECONDARY AND PRIMARY CLOSURE TECHNIQUES FOR PREVENTION OF POSTOPERATIVE COMPLICATIONS (FOLLOW-UP, POSTOPERATIVE DAY 3)

Number of Studies	Quality Assessment						Summary of Findings			
							Number of Patients		Effect	
	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Secondary Closure	Primary Closure	Relative (95% CI)	Absolute
Pain (dichotomous)										
5	Serious*	Serious†	No serious indirectness	Serious‡	Unlikely	Very low	97/187 (51.9%)	72/187 (38.5%)	RR 1.30 (0.91-1.85)	116 more per 1,000 (35 fewer to 327 more)
Pain (continuous)										
7	Serious*	Serious†	No serious indirectness	Serious‡	Unlikely	Very low	284	286	—	SMD 0.29 lower (0.63 lower to 0.05 higher)
Facial swelling										
5	Serious*	No serious inconsistency	No serious indirectness	Serious‡	Unlikely	Low	170	170	—	SMD 0.37 lower (0.76 lower to 0.02 higher)
Trismus										
8	Serious*	Serious†	No serious indirectness	No serious imprecision	Unlikely	Low	234	234	—	MD 3.72 higher (1.42 to 6.03 higher)

Abbreviations: CI, confidence interval; MD, mean difference; RR, relative risk; SMD, standardized mean difference.
*All studies were classified as having an unclear risk of bias. Most studies did not provide any information on methodologic issues.
†Substantial heterogeneity not explained by any of the a priori subgroup hypotheses.
‡Large confidence intervals around effect estimates; the included trials had a small number of participants.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

no information on the occurrence of infectious complications. The events are important: they appear to be relatively frequent and can be associated with severe and prolonged pain. Indeed, surgical-site infection and postoperative bleeding are some of the main arguments that surgeons and investigators use to justify one technique over the other.[6-9] Clarifying the impact of the two procedures on these outcomes would require much larger trials.

Four trials reported postoperative bleeding, showing extreme variability: in 2, there was no bleeding in either group; the numbers of bleeding events in the primary and secondary closure techniques were 22 and 16 in the third trial and 5 and 15 in the fourth. Two of these studies[8,18] did not report any approach to the measurement process or the outcome definition (Table 6). The effect of the interventions on bleeding remains uncertain.

None of the prespecified subgroup hypotheses or a post hoc exploration of the possible impact of pre- and/or postoperative antibiotic prophylaxis and nonsteroidal anti-inflammatory drugs provided an explanation for the detected heterogeneity. The paucity of detail regarding the conduct of these trials prevented an effective exploration of the risk of bias as a potential explanation.

CONFIDENCE IN ESTIMATES OF EFFECT

All outcomes were classified as warranting low to very low confidence in the effect estimates (Tables 7, 8). The more serious threats undermining confidence were the risk of bias, imprecision of the results, and the inconsistency that exploration of subgroup hypotheses failed to explain. Trismus showed a possible benefit of the secondary closure over the primary closure technique, but the effect, if true, is likely to be small and not significant to patients, and confidence in the estimates is low owing to limitations in the risk of bias and inconsistency.

STRENGTHS AND LIMITATIONS OF THIS REVIEW

The strengths of this review include a comprehensive search with no language restrictions, a search for unpublished data, a standardized method for title and abstract screening, study eligibility applied independently and in duplicate, the explicit risk of bias assessment using established criteria, and the application of the GRADE system for assessing confidence in the estimates. Although responses from the investigators were limited, the reviewers' efforts to contact them to retrieve more information ensured that the reviewers captured all accessible data. The necessity of imputing paired SDs for some trials that used the split-mouth design, especially for the outcome pain, could weaken inferences from the present results. How-

Table 8. EVIDENCE PROFILE: CONFIDENCE IN EFFECT ESTIMATES ASSESSMENT AND SUMMARY OF FINDINGS FOR SECONDARY AND PRIMARY CLOSURE TECHNIQUE FOR PREVENTION OF POSTOPERATIVE COMPLICATIONS (FOLLOW-UP: 7TH POSTOPERATIVE DAY)

Quality Assessment							Summary of Findings			
							Number of Patients		Effect	
Number of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Secondary Closure	Primary Closure	Relative (95% CI)	Absolute
Pain (dichotomous)										
5	Serious*	No serious inconsistency	No serious indirectness	Serious‡	Unlikely	Low	158/187 (84.5%)	143/187 (76.5%)	RR 1.07 (0.94-1.22)	54 more per 1,000 (46 fewer to 168 more)
Pain (continuous)										
4	Serious*	Serious†	No serious indirectness	Serious‡	Unlikely	Very low	197	199	—	MD 0 higher (0.19 lower to 0.19 higher)
Facial swelling										
5	Serious*	Serious†	No serious indirectness	Serious‡	Unlikely	Very low	161	163	—	SMD 0.15 lower (0.39 lower to 0.1 higher)
Trismus										
7	Serious*	Serious†	No serious indirectness	No serious imprecision	Unlikely	Low	184	184	—	MD 2.35 higher (0.37 to 4.33 higher)
Infectious complications (alveolar osteitis and surgical wound infection)										
6	Serious*	No serious inconsistency	No serious indirectness	Serious‡	Unlikely	Low	10/305 (3.3%)	21/307 (6.8%)	RR 0.51 (0.18-1.47)	4 fewer per 100 (6 fewer to 3 more)
								4.3%§		2 fewer per 100 (5 fewer to 2 more)
Postoperative bleeding										
4	Serious*	Serious‖	No serious indirectness	No serious imprecision	Unlikely	Low	—	—	Not pooled¶	Not pooled¶

Abbreviations: CI, confidence interval; MD, mean difference; RR, relative risk; SMD, standardized mean difference.

*All studies were classified as having an unclear or a high risk of bias. Most studies judged to have an unclear risk of bias did not provide information on methodology.

†Substantial heterogeneity not explained by a priori subgroup hypotheses.

‡Large confidence intervals around effect estimates; the included trials had a small number of participants.

§Control group risk estimates were from the control arms of meta-analyses based on the included studies.

‖Large clinical and outcome definition inconsistencies did not allow the calculation of a pooled estimate.

¶Because outcome definitions, follow-ups, and control event rates were not consistent across trials (0% to 95%), a pooled estimate was not calculated.

Carrasco-Labra et al. Closure Techniques in Third Molar Extraction. J Oral Maxillofac Surg 2012.

ever, the sensitivity analyses proved robust to extreme assumptions.

The reviewers could have chosen 4 possible approaches for including split-mouth trials in this systematic review[14]: *1)* a narrative or qualitative summary using evidence tables only; *2)* analyzing split-mouth studies as if they had a parallel 2-arm design; *3)* meta-analyzing separately only those split-mouth studies reporting the paired SD from the parallel-group trials; and *4)* imputing a measurement representing the similarities among the split-mouth trials using a paired analysis and including all trials in the same meta-analysis. The reviewers chose the last method because it incorporates all possible relevant evidence. The reviewers tested the assumptions used in this approach in a sensitivity analysis.

The risk of bias assessment showed serious deficiencies in the description of the Methods sections of the included trials, reflecting nonadherence to recommendations of the Consolidate Standards of Reporting Trials statement.[36] Most split-mouth trials failed to account for the effect of each treatment, the effect of side, and the effect of each subject on the outcome. Moreover, a carry-across effect could have biased the result of the trials; there is no statistical test to account for these effects.[14] In consequence, the bias that could be introduced to the results of the split-mouth studies owing to a carry-across effect should be justified biologically. Not only did none of the trials address this issue, but also the investigators analyzed and reported the results as if these were from a parallel 2-arm trial. Only 1 study tried to address the paired nature of the data in the analysis; however, the approach used only accounts for the effect of each intervention and each side.

In summary, the small apparent treatment effects suggest that there may not be important differences in outcomes between the secondary and primary closure techniques in patients undergoing surgical removal of an IMTM. However, the risk of bias and the heterogeneity among trials produce a low confidence in the estimates. The results of this review provide little or no reason to choose either procedure.

Acknowledgments

The authors of this review thank Diane Heels-Ansdell for the statistical support, Nancy Santesso and Jan Brozek for providing guidance using the GRADE rating system for evaluating the confidence in the estimates, and Jo-Anne Petropoulos for her support in developing the search strategy.

References

1. Kunkel M, Morbach T, Kleis W, et al: Third molar complications requiring hospitalization. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 102:300, 2006
2. Shepherd JP, Brickley M: Surgical removal of third molars. BMJ 309:620, 1994
3. Adeyemo WL: Do pathologies associated with impacted lower third molars justify prophylactic removal? A critical review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 102:448, 2006
4. American Dental Association: Survey of Dental Services Rendered 1990. Chicago, IL, American Dental Association, 1994
5. Goldberg MH, Nemarich AN, Marco WP II: Complications after mandibular third molar surgery: A statistical analysis of 500 consecutive procedures in private practice. J Am Dent Assoc 111:277, 1985
6. Archer WH: Oral and Maxillofacial Surgery (ed 5). Philadelphia, WB Saunders, 1975
7. Killey HC, Kay LW: The Impacted Wisdom Tooth (ed 2). London, Churchill Livingstone, 1975
8. Pasqualini D, Cocero N, Castella A, et al: Primary and secondary closure of the surgical wound after removal of impacted mandibular third molars: A comparative study. Int J Oral Maxillofac Surg 34:52, 2005
9. Cerqueira PR, Vasconcelos BC, Bessa-Nogueira RV: Comparative study of the effect of a tube drain in impacted lower third molar surgery. J Oral Maxillofac Surg 62:57, 2004
10. Lefebvre C, Manheimer E, Glanville J: Searching for studies, *in* Higgins JP, Green S (eds): Cochrane Handbook for Systematic Reviews of Interventions (version 5.0.1). Cochrane Collaboration, 2008
11. Higgins JP, Altman DG: Assessing risk of bias in included studies, *in* Higgins JP, Green S (eds): Cochrane Handbook for Systematic Reviews of Interventions (version 5.0.1). Cochrane Collaboration, 2008
12. Guyatt GH, Oxman AD, Kunz R, et al: What is "quality of evidence" and why is it important to clinicians? BMJ 336:995, 2008
13. Balshem H, Helfand M, Schünemann HJ, et al: GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 64:401, 2011
14. Lesaffre E, Philstrom B, Needleman I, et al: The design and analysis of split-mouth studies: What statisticians and clinicians should know. Stat Med 28:3470, 2009
15. Elbourne DR, Altman DG, Higgins JP, et al: Meta-analyses involving cross-over trials: Methodological issues. Int J Epidemiol 31:140, 2002
16. Holland CS, Hindle MO: The influence of closure or dressing of third molar sockets on post-operative swelling and pain. Br J Oral Maxillofac Surg 22:65, 1984
17. Bello SA, Olaitan AA, Ladeinde AL: A randomized comparison of the effect of partial and total wound closure techniques on postoperative morbidity after mandibular third molar surgery. J Oral Maxillofac Surg 69:e24, 2011
18. Hashemi HM, Beshkar M, Aghajani R: The effect of sutureless wound closure on postoperative pain and swelling after impacted mandibular third molar surgery. Br J Oral Maxillofac Surg 50:256, 2011
19. Refo'a Y, Quatik N, Golchin F, et al: Comparing primary and secondary wound healing discomfort after mandibular third molar surgery: A randomized, double-blind clinical trial. Gen Dent 59:310, 2011
20. Chukwuneke FN, Oji C, Saheeb DB: A comparative study of the effect of using a rubber drain on postoperative discomfort following lower third molar surgery. Int J Oral Maxillofac Surg 37:341, 2008
21. Osunde OD, Saheeb BD, Adebola RA: Comparative study of effect of single and multiple suture techniques on inflammatory complications after third molar surgery. J Oral Maxillofac Surg 69:971, 2010
22. Akota I, Alvsaker B, Bjørnland T: The effect of locally applied gauze drain impregnated with chlortetracycline ointment in mandibular third-molar surgery. Acta Odontol Scand 56:25, 1998
23. Danda AK, Krishna Tatiparthi M, Narayanan V, et al: Influence of primary and secondary closure of surgical wound after impacted mandibular third molar removal on postoperative pain and swelling—A comparative and split mouth study. J Oral Maxillofac Surg 68:309, 2010

24. Rakprasitkul S, Pairuchvej V: Mandibular third molar surgery with primary closure and tube drain. Int J Oral Maxillofac Surg 26:187, 1997
25. Sağlam AA: Effects of tube drain with primary closure technique on postoperative trismus and swelling after removal of fully impacted mandibular third molars. Quintessence Int 34: 143, 2003
26. Srinivas DR: Effect of Surgical Tube Drain With Primary Closure Technique After the Removal of Impacted Mandibular Third Molars—A Clinical Study. Master's Thesis. Bangalore, Department of Oral and Maxillofacial Surgery, Government Dental College and Hospital Bangalore, Rajiv Gandhi University of Health Science, 2006, p 74
27. Xavier RL, Vasconcelos BC, Caubi AF, et al: Passive drainage through the vestibular oblique incision in impacted inferior third molar surgery: A preliminary study. Acta Odontol Latinoam 21:57, 2008
28. Amin MM, Laskin DM: Prophylactic use of indomethacin for prevention of postsurgical complications after removal of impacted third molars. Oral Surg Oral Med Oral Pathol 55:448, 1983
29. Berge TI: Visual analogue scale assessment of postoperative swelling. A study of clinical inflammatory variables subsequent to third-molar surgery. Acta Odontol Scand 46:233, 1988
30. Berge TI: The use of a visual analogue scale in observer assessment of postoperative swelling subsequent to third-molar surgery. Acta Odontol Scand 47:167, 1989
31. Laureano Filho JR, de Oliveira e Silva ED, Batista CI, et al: The influence of cryotherapy on reduction of swelling, pain and trismus after third-molar extraction: A preliminary study. J Am Dent Assoc 136:774, 2005
32. Markiewicz MR, Brady MF, Ding EL, et al: Corticosteroids reduce postoperative morbidity after third molar surgery: A systematic review and meta-analysis. J Oral Maxillofac Surg 66:1881, 2008
33. Sterne JAC, Egger M, Moher D: Addressing reporting biases, *in* Higgins JP, Green S (eds): Cochrane Handbook for Systematic Reviews of Interventions (version 5.0.1). Cochrane Collaboration, 2008
34. Baqain ZH, Karaky AA, Sawair F, et al: Frequency estimates and risk factors for postoperative morbidity after third molar removal: A prospective cohort study. J Oral Maxillofac Surg 66:2276, 2008
35. Ren YF, Malmstrom HS: Effectiveness of antibiotic prophylaxis in third molar surgery: A meta-analysis of randomized controlled clinical trials. J Oral Maxillofac Surg 65:1909, 2007
36. Moher D, Hopewell S, Schulz KF, et al: CONSORT 2010: Explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol 63:e1, 2010

Appendix

SEARCH STRATEGY

Ovid MEDLINE (1948 Through December 2011)

1. Molar, Third/
2. third molar*.mp.
3. (wisdom adj (tooth or teeth)).mp.
4. 1 or 2 or 3
5. Tooth, Impacted/
6. (impact* adj3 (tooth or teeth or molar)).mp.
7. 5 or 6
8. Tooth Extraction/
9. Tooth Extraction.mp.
10. (remov* adj3 (tooth or teeth or molar)).mp.
11. 8 or 9 or 10
12. (heal* adj3 (primar* or secondar*)).mp.
13. (heal* adj3 (primar* or secondar*)).mp.
14. (clos* adj3 (primar* or second*)).mp.
15. Drainage.mp. or Drainage/
16. Rubber/or rubber drain.mp.
17. Suture Technique.mp. or exp Suture Techniques/
18. 12 or 13 or 14 or 15 or 16 or 17
19. Randomi?ed controlled trial.pt.
20. Controlled clinical trial.pt.
21. Randomi?ed.ab.
22. Placebo.ab.
23. Clinical trials as topic.sh.
24. Randomly.ab.
25. trial.ti.
26. 19 or 20 or 21 or 22 or 23 or 24 or 25
27. exp animals/not humans.sh.
28. 26 not 27
29. Pain/or Pain.mp. or Pain, Postoperative/
30. Trismus.mp. or Trismus/
31. Edema.mp. or Edema/
32. Swelling.mp.
33. 31 or 32
34. infections.mp. or exp Infection/
35. Alveolar osteitis.mp. or exp Dry Socket/
36. Surgical wound infection.mp. or exp Surgical Wound Infection/
37. 34 or 35 or 36
38. 4 or 7 or 11 or 29 or 30 or 33 or 37
39. 18 and 28 and 38

Ovid EMBASE (1980 Through December 2011)

1. Molar, Third/
2. Third molar*.mp.
3. (Wisdom adj (tooth or teeth)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
4. 1 or 2 or 3
5. Tooth, Impacted/
6. (Impact* adj3 (tooth or teeth or molar)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
7. 5 or 6
8. Tooth Extraction/
9. Tooth Extraction.mp.
10. (Remov* adj3 (tooth or teeth or molar)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
11. 8 or 9 or 10
12. (Heal* adj3 (primar* or secondar*)).mp. [mp=title, abstract, subject headings, heading

word, drug trade name, original title, device manufacturer, drug manufacturer]
13. (Heal* adj3 (primar* or secondar*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
14. (Clos* adj3 (primar* or second*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]
15. Drainage.mp. or Drainage/
16. Rubber/or rubber drain.mp.
17. Suture Technique.mp. or exp Suture Techniques/
18. 12 or 13 or 14 or 15 or 16 or 17
19. Pain/or Pain.mp. or Pain, Postoperative/
20. Trismus.mp. or Trismus/
21. Edema.mp. or Edema/
22. Swelling.mp.
23. 21 or 22
24. Infections.mp. or exp Infection/
25. Alveolar osteitis.mp. or exp Dry Socket/
26. Surgical wound infection.mp. or exp Surgical Wound Infection/
27. 24 or 25 or 26
28. 19 or 20 or 23 or 27
29. 18 and 28
30. Randomized controlled trial/
31. 18 and 28 and 30

CENTRAL (Issue 12, December 2011)

#1. MeSH descriptor Molar, Third explode all trees
#2. MeSH descriptor Tooth, Impacted explode all trees
#3. (#1 OR #2)
#4. Drain*
#5. Tube drain
#6. MeSH descriptor Drainage explode all trees
#7. Penrose
#8. Rubber drain*
#9. Secondary closure
#10. Primary closure
#11. (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR 10)
#12. MeSH descriptor Pain explode all trees
#13. MeSH descriptor Trismus explode all trees
#14. Facial edema
#15. MeSH descriptor Edema explode all trees
#16. Swelling
#17. (#14 OR #15 OR #16)
#18. MeSH descriptor Infection explode all trees
#19. MeSH descriptor Dry socket explode all trees
#20. Alveolar osteitis
#21. MeSH descriptor Wound infection explode all trees
#22. (#18 OR #19 OR #20 OR 21)
#22. (#12 OR #13 OR #17 OR #22)
#23. (#3 AND #11 AND #22)