CONCISE REVIEW

M.A. Papadopoulos[1]*, S.N. Papageorgiou[2], and I.P. Zogakis[2]

[1]Department of Orthodontics, School of Dentistry, Aristotle University of Thessaloniki, GR-54124 Thessaloniki, Greece; and [2]School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece; *corresponding author, mikepap@dent.auth.gr

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Clinical Effectiveness of Orthodontic Miniscrew Implants: a Meta-analysis

ABSTRACT

The aim of this meta-analysis was to examine the clinical effectiveness of miniscrew implants (MI) used for anchorage reinforcement compared with that of conventional orthodontic means, as well as to assess the success rates of MIs and the possible risk factors affecting their clinical effectiveness. Literature searches were conducted, and, using specific inclusion and exclusion criteria, two independent investigators performed data extraction and analysis. Overall pooled estimates with 95% confidence intervals (CI) were obtained with the random-effects model. Eight out of 3183 original papers met the inclusion criteria. The mean difference of anchorage loss between the MI and conventional anchorage group was −2.4 mm (95% CI = −2.9 mm to −1.8 mm, p = 0). MIs significantly decreased or negated loss of anchorage. Anchorage loss seemed to be less in the mandible, when the MIs were inserted between the second premolar and the first molar, when 2 MIs were inserted *per* patient jaw, when they were directly connected, as well as when treatment lasted more than 12 months. MIs presented a success rate of 87.7%, with no significant differences between the various subgroups. However, the results of this meta-analysis should be interpreted with some caution because of the number, quality, and heterogeneity of the included studies.

KEY WORDS: miniscrew implant, mini-implant, absolute anchorage, anchorage loss, success rate, micro-implant.

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INTRODUCTION

Control of anchorage during orthodontic treatment is considered of significant importance since it helps avoid undesirable tooth movements that may take place as a consequence of the reaction forces applied to move teeth. Until lately, several conventional orthodontic modalities, such as transpalatal arches, headgears, Nance buttons, or the application of differential forces, were used for this purpose.

Miniscrew implants (MIs) have been recently widely utilized as anchorage reinforcement auxiliaries in orthodontics. MIs are fabricated from stainless steel, commercially pure titanium, or titanium alloy with a diameter of 1 to 2 mm and length of 8 to 20 mm, and they are not osseointegrated (Papadopoulos and Tarawneh, 2007).

Their clinical effectiveness lies in their ability to maintain close contact with the bone (Kim *et al*., 2008), thus remaining stable during orthodontic treatment while resisting reactive forces (Papadopoulos and Tarawneh, 2007), thus minimizing anchorage loss. MI success or survival rates have been the subject of uncontrolled clinical trials (Chen *et al*., 2007; Wiechmann *et al*., 2007) and systematic reviews (Reynders *et al*., 2009; Schätzle *et al*., 2009). The latter indicate MI success rates ranging from 80% to 100%. Jaw, side of placement, insertion site, mobility, and inflammation are some of the risk factors associated with MI failures (Park *et al*., 2006; Antoszewska *et al*., 2009). However, existing evidence relies mainly on studies with minimal evidence, while many investigations examine multiple forms of skeletal anchorage simultaneously.

Therefore, the aim of this investigation was to undertake a meta-analysis to assess the currently existing evidence on the clinical effectiveness of MIs used for orthodontic anchorage reinforcement and to compare it with that of conventional orthodontic anchorage modalities, as well as to evaluate the success rates of MIs and the possible risk factors affecting their clinical effectiveness.

MATERIALS & METHODS

This meta-analysis was based on the PRISMA Statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions (Liberati *et al*., 2009).

Data Sources and Searches

Electronic searches were conducted for studies published up to June 2010. The reference lists of the articles eligible for inclusion in this meta-analysis were also manually reviewed. Citations of articles published in journals, dissertations, and conference proceedings were located from several electronic databases, by a search strategy appropriately adjusted for each individual database (Appendix Table 1).

Table 1. Criteria for Studies Selected to Be Included in the Meta-analysis

Inclusion Criteria	Exclusion Criteria
Randomized Controlled Clinical Trials [RCTs] Prospective Controlled Clinical Trials [CCTs] Retrospective controlled cohort studies	Prospective uncontrolled cohort studies Retrospective uncontrolled cohort studies Case-control observational studies Case series without a control Case reports Unsupported opinion of expert Editor's choices Books' abstracts Conference abstracts Cross-sectional surveys Narrative reviews* Systematic reviews* Meta-analyses* Animal studies Replies (to author/editor) Studies on molecular biology, histology, or genetics *In vitro* studies Studies using mini-plates for orthodontic anchorage Studies using osseointegrated implants for orthodontic anchorage Studies using anchorage systems other than MIs (Orthosystem, Onplant, Orthoimplant)

*prior to exclusion, the corresponding reference lists were checked

No restrictions were applied concerning publication year, language, or status. 'Gray literature' (*i.e.*, materials that cannot be found easily through conventional channels) was not excluded from our search. When additional information was needed, authors were contacted. In total, three authors were contacted with various questions, and all of them responded accordingly.

Study Selection

Two reviewers (SNP and IPZ) independently screened titles, abstracts, and full-text reports. Any disagreement was resolved by consultation with the first author (MAP) until a final consensus was achieved. Inter-reviewer agreement on study eligibility was assessed by Cohen's kappa. Appropriate studies to be included in the meta-analysis fulfilled specific predefined inclusion criteria; only randomized controlled clinical trials (RCTs), *quasi*-randomized controlled clinical trials, and prospective controlled clinical trials (CCTs) were included, while duplicate records were excluded (Table 1).

Data Extraction and Quality Assessment

Two reviewers (SNP and IPZ) independently extracted relevant data in a pre-designed collection form. Any disagreement was resolved by consultation with the first author (MAP) until a final consensus was achieved. Inter-reviewer agreement on data extraction was assessed by Cohen's kappa. For evaluation of the clinical effectiveness of MIs, two variables were taken into consideration: (a) mesiodistal "loss of anchorage" and (b) "anchorage loss ratio".

Mesiodistal "*loss of anchorage*" was measured by assessment of the mesiodistal movement of the first molar, which was connected directly or indirectly to the MIs, by means of superimposition of lateral cephalometric radiographs (n = 7 studies) or of three-dimensional scanning of dental casts (n = 1 study). Low values indicate small anchorage loss, high values indicate large anchorage loss, while negative values indicate molar distal movement (anchorage gain) during treatment.

The ratio "anchorage loss to active movement," hereby named "*anchorage loss ratio*," was defined as the measured anchorage loss of first molars connected to the MIs divided by the active movement of the target tooth or teeth. This was done to correlate the observed amount of anchorage loss with the overall active orthodontic movement. For positive ratios, low or high values indicate small or large gain of anchorage, respectively. In contrast, for negative ratios, low or high values indicate large or small anchorage loss, respectively.

The anchorage loss ratio and the corresponding standard deviation (SD) were calculated, where active movement was provided.

Since some studies evaluated MIs in only one jaw, with others providing data for both jaws, each jaw was considered as a trial arm and was evaluated individually. The jaw of insertion was assessed regarding clinical effectiveness in the subgroup analysis.

For the evaluation of the success rates of MIs, their failures were assessed. A failure was considered when a MI became loose or had to be removed due to inflammation or other issues and was replaced by a new one, as reported by the source articles. MI failure rates (and pooled estimates) were considered only for the experimental group and were not included in the evaluation of the anchorage loss, but only for the success rates.

Strength of evidence was evaluated with respect to pre-established characteristics (Antczak *et al*., 1986; Jadad *et al*., 1996). Studies were categorized as of low (0–5 points), medium (6–8 points), or high (9 or 10 points) quality. Inter-reviewer agreement on quality assessment was evaluated by Cohen's kappa.

Data Synthesis and Analysis

Data were summarized and considered suitable for pooling if, in the corresponding RCTs or CCTs, control groups of conventional orthodontic anchorage were used, similar populations were enrolled, and the same efficacy or safety outcomes were reported. In the absence of adequately reported summary statistics, the required variables were calculated.

Analyses were performed with the statistical software "Comprehensive Meta-Analysis" (Biostat Inc., Englewood, NJ, USA), with the random- and fixed-effects models. Pooled estimates with 95% Confidence Intervals (CI) of the anchorage loss, the anchorage loss ratio, and the incidence of MI failures were obtained. Treatment effect comparisons between experimental groups were considered for anchorage loss and anchorage loss ratio. Subgroup analyses were performed by the approach of Deeks *et al*. (2001). The following subgroups were defined prior to data analysis: *treatment duration* (less than 12 mos, more than 12 mos), *average patient age* (18 yrs or younger, older than 18 yrs), *MI connection method* (direct, indirect), *jaw of MI insertion* (maxilla, mandible), *MI insertion site* (between the roots of the second premolar and the first molar [P2M1], midpalatal area), *number of used MIs* per *jaw* (1, 2), and *existence of anchorage loss* (loss, no loss).

For continuous data, the mean difference (MD) was used as the summary statistic.

Assessment of Publication Bias

Publication bias was evaluated through visual inspection of funnel plot asymmetry (Light and Pillemer, 1984), which however should be seen as a means of examining "small study effects" and not as a tool to diagnose specific types of bias (Sterne *et al*., 2001). Begg and Mazumdar's rank correlation test (1994) was conducted to examine the negative correlation between the standardized effect size and the standard errors of these effects, assessed by means of Kendall's tau and a one-tailed significance test. The linear-regression-based tests proposed by Egger *et al*. (1997) were also conducted to quantify the publication bias captured by the funnel plot.

Heterogeneity Assessment

To assess heterogeneity, we calculated the I^2 statistic. Heterogeneity was defined as low (25%), moderate (50%), or high (75%) (Higgins *et al*., 2003). In addition, the Q-value was also calculated, but only its significance was taken into consideration.

Sensitivity Analyses

Additional meta-analyses were conducted to explore the influence of study design, trial quality, sample adequacy, blinding, method error analysis, publication date, and removal of individual studies on the effect size.

RESULTS

Literature Flow

Initially, the search yielded 5030 records. After subtraction of duplicates, 3180 titles remained, while 3 additional articles were identified through manual searching. In total, 3133 records were excluded for various reasons according to the specific exclusion criteria. Of the remaining 50 articles, 42 studies did not use a proper control group and were excluded. Consequently, 8 studies remained for final evaluation. The selection procedure, the number of excluded studies, and the corresponding reasons for exclusion are provided in Fig. 1. The kappa scores before reconciliation for the selection, data extraction, and quality evaluation procedures were 0.826, 0.968, and 0.823, respectively, which indicated almost perfect agreement.

Description of Studies and Baseline Characteristics

The characteristics of the studies included in the meta-analysis are presented in Appendix Table 2. In total, 297 MIs were placed in 103 patients with a mean age of 19.27 yrs (range: 17.4-22.5 yrs). Conventional anchorage was used in 103 patients with a mean age of 19.3 yrs (range: 16-22.9 yrs). Mean follow-up time ranged from 5.4 to 29.6 mos for all groups. Four trials were defined by the corresponding authors as RCTs and four as CCTs. However, one RCT (Upadhyay *et al*., 2008b) did not report adequate randomization or allocation concealment and was categorized as a CCT, resulting in a total of 3 RCTs and 5 CCTs.

The control groups with conventional anchorage consisted of patients in whom anchorage was reinforced with transpalatal arches, banded molars, headgears, Nance buttons, or application of differential forces. In one study, patient records from a clinic archive were used as a historical control group (Hedayati *et al*., 2007). The activation force producing the necessary tooth movements derived from superelastic springs or elastomeric chains.

The overall quality of the included studies was evaluated as "medium." Three out of 8 studies were of low quality, 4 of medium, and 1 of high quality (Table 2). In half of the studies, the sample was deemed adequate, since 15 or more patients were included in each group; in 5 studies, a method error analysis was used; while no study assessed the possible impact of confounding factors, and only 1 study (Upadhyay *et al*., 2008a) used blinding procedures and adhered to the CONSORT (Consolidated Standards of Reporting Trials) statement (Schulz *et al*., 2010). Treatment changes were measured by cephalometric or study model analysis.

Assessment of Publication Bias

Indications of asymmetry were observed in the funnel plots (Appendix Fig. 1). However, Begg and Mazumbar's test showed no evidence of publication bias concerning overall anchorage loss (1-tailed $p = 0.105$), MD of anchorage loss between groups (1-tailed $p = 0.360$), anchorage loss ratio (1-tailed $p = 0.130$), MD of anchorage loss ratio between groups (1-tailed $p = 0.066$), or MI success rates (1-tailed $p = 0.451$). Egger's linear regression test showed similar results concerning overall anchorage loss (1-tailed $p = 0.373$), MD of anchorage loss between groups (1-tailed $p = 0.104$), anchorage loss ratio (1-tailed $p = 0.221$), MD of anchorage loss ratio between groups (1-tailed $p = 0.059$), or MI success rate (1-tailed $p = 0.452$).

Data Synthesis and Heterogeneity Assessment

Mean Difference of Anchorage Loss between the MI and Conventional Anchorage Groups

Reinforcement of orthodontic anchorage with MIs decreased or negated loss of anchorage. The anchorage loss was lower in the MI group compared with the conventional anchorage group. The MD of anchorage loss between these groups was −2.4 mm (95% CI = −2.9 to −1.8 mm, $p = 0$); however, it presented high heterogeneity ($I^2 = 80\%$).

Stratification by blinding of studies under evaluation yielded safer results. The corresponding MD of anchorage loss was higher in blind studies (−3.9 mm) and lower in non-blind studies (−2.0 mm), with remaining heterogeneity being non-significant ($p = 0.517$ and $p = 0.142$, respectively). The MD of anchorage loss

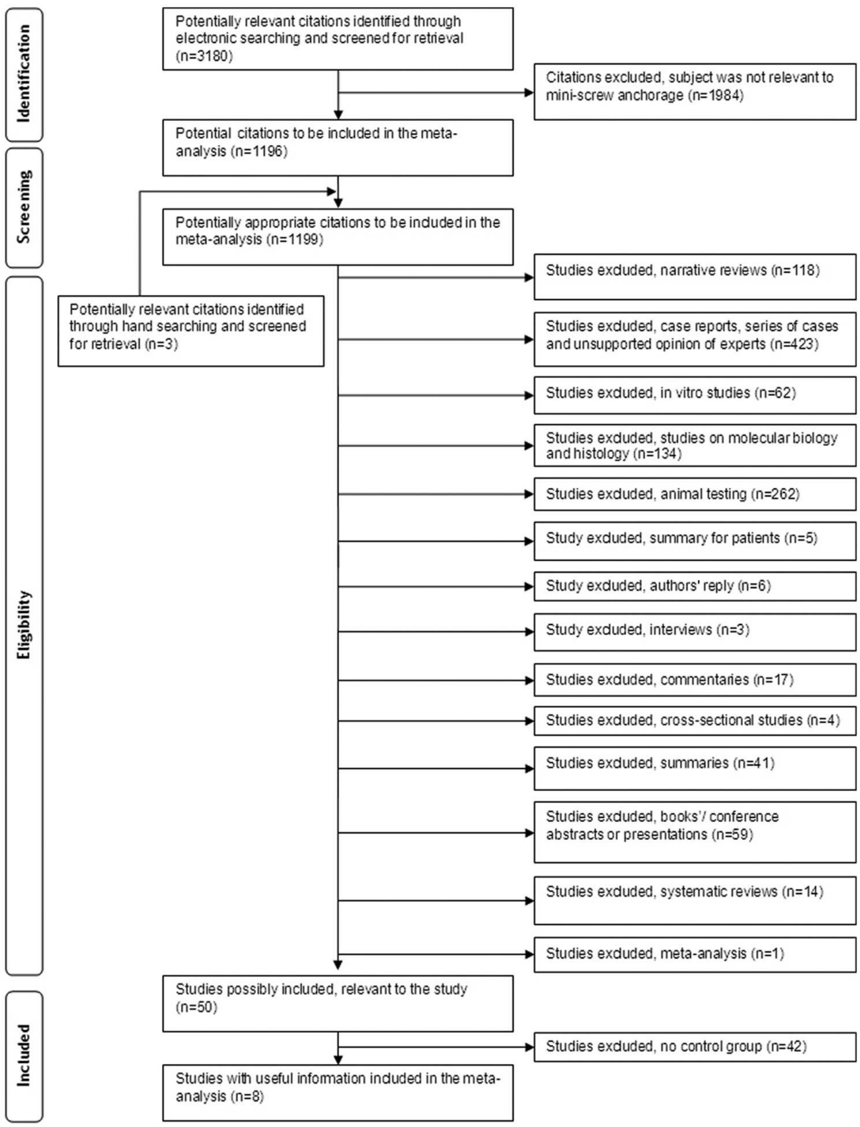


Figure 1. PRISMA flow diagram of the studies retrieved through the selection process.

between the MI and conventional anchorage groups was significantly higher in the mandible than in the maxilla (−3.1 mm *vs.* −2.2 mm), indicating that less anchorage loss was observed in the mandible for the MI group, or that more anchorage loss was observed for the conventional group (Fig. 2, Appendix Tables 3, 4). However, caution is needed for the interpretation of this outcome, due to existing residual heterogeneity (p = 0).

Mean Anchorage Loss of the MI Group

The pooled anchorage loss for the MI group was 0.05 mm (95% CI = −0.3 to 0.4 mm, p = 0.794), with high heterogeneity among studies (I^2 = 86%). Anchorage loss was significantly less when the MIs were placed in the mandible than in the maxilla (−0.6 mm *vs.* 0.2 mm), when the MIs were inserted between the second premolar and the first molar than in the palate (−0.2 mm *vs.* 1.3 mm), when 2 MIs were inserted *per* patient instead of 1 (−0.2 mm *vs.* 1.3 mm), when MIs were connected directly rather than indirectly (−0.2 mm *vs.* 0.8 mm), as well as when there was absence of measured loss rather than existing loss (−0.4 mm *vs.* 0.9 mm). In every case, however, heterogeneity was still present; thus, these results should be seen with caution (Appendix Fig. 2, Appendix Table 3).

Furthermore, the location of MI insertion and type of connection should be taken into consideration for the interpretation of the anchorage loss values. Three studies with direct and one with indirect MI connection reported anchorage gain (negative values), translated clinically as distalization or/and intrusion of the anchoring teeth, which may possibly indicate biased results. In the directly connected MIs, molar distalization could be due to the force acting on the archwire through special hooks. In the indirectly connected MIs, these were placed distal to the mandibular first molars and were connected to the molars through ligature wire ties, which exercised an active application of force on the molars, resulting in their distalization.

Mean Difference of Anchorage Loss Ratio between the MI and Conventional Anchorage Groups

The pooled MD of anchorage loss ratio between the MI and conventional anchorage groups was −0.5 (95% CI = −0.6 to 0.3, p = 0), indicating that reinforcement of orthodontic anchorage with MIs decreased loss of anchorage. However, high heterogeneity was present (I^2 = 73%).

Stratification by treatment duration diminished within-groups' heterogeneity. When treatment lasted fewer than 12 mos, the MD of anchorage loss ratio was −0.6, while it was −0.2 when treatment lasted more than 12 mos, with no heterogeneity (p = 0.395 and p = 0.880, respectively) for the two groups. The MD of anchorage loss ratio between groups was of significantly higher magnitude in young than in adult patients (−0.6 *vs.* −0.4), as well as when MIs were inserted into the mandible than into the maxilla (−0.7 *vs.* −0.4), although residual heterogeneity was present (Fig. 3, Appendix Table 3).

Mean Anchorage Loss Ratio of the MI Group

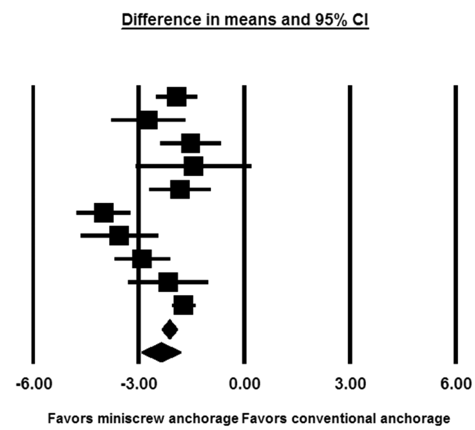
Mean anchorage loss ratio of the MI group could be calculated from only some of the included studies. The mean anchorage

Table 2. Quality Evaluation of Included Studies

Author (yr)	Study Design	Adequate Sample Size	Adequate Selection Description	Valid Measurement Methods	Use of Method Error Analysis	Blinding in Measurement	Adequate Statistics Provided	Confounders Included in Analysis	Score	Quality
Hedayati *et al.* (2007)	1	0	0	1	1	0	1	0	4	Low
Park *et al.* (2008)	1	1	1	1	1	0	1	0	6	Medium
Shi *et al.* (2008)	1	0	1	1	0	0	1	0	4	Low
Upadhyay *et al.* (2008a)	3	1	1	1	1	1	1	0	9	High
Upadhyay *et al.* (2008b)	1	1	1	1	1	0	1	0	6	Medium
Liu *et al.* (2009)	3	1	1	1	1	0	1	0	8	Medium
Wilmes *et al.* (2009)	1	0	1	1	0	0	1	0	4	Low
Basha *et al.* (2010)	3	0	1	1	0	0	1	0	6	Medium
Overall estimate									6	Medium

The following 8 variables were evaluated: Study design (RCT = 3 points; prospective study = 1 point; retrospective study = 0 point); Adequate sample size = 1 point; Adequate selection description = 1 point; Valid measurement methods = 1 point; Use of method error analysis = 1 point; Blinding in measurement = 1 point; Adequate statistics provided = 1 point; Confounders included in analysis = 1 point. In summary, a study could maximally score 10 points and was categorized as presenting low (0–5 points), medium (6–8 points), or high (9-10 points) quality.

Model	Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Hedayati 2007 (Mx)	-1.930	0.299	0.089	-2.516	-1.344	-6.457	0.000
	Hedayati 2007 (Md)	-2.730	0.536	0.287	-3.780	-1.680	-5.096	0.000
	Liu 2009 (Mx)	-1.530	0.439	0.193	-2.391	-0.669	-3.482	0.000
	Park 2008 (Mx)	-1.450	0.832	0.693	-3.081	0.181	-1.742	0.082
	Shi 2008 (Mx)	-1.830	0.446	0.199	-2.704	-0.956	-4.103	0.000
	Upadhyah 2008a (Mx)	-4.000	0.388	0.150	-4.760	-3.240	-10.321	0.000
	Upadhyah 2008a (Md)	-3.560	0.557	0.310	-4.652	-2.468	-6.392	0.000
	Upadhyah 2008b (Mx)	-2.900	0.402	0.161	-3.688	-2.112	-7.216	0.000
	Wilmes 2009 (Mx)	-2.160	0.575	0.330	-3.286	-1.034	-3.760	0.000
	Basha 2010 (Mx)	-1.730	0.163	0.026	-2.049	-1.411	-10.645	0.000
Fixed		-2.142	0.110	0.012	-2.357	-1.928	-19.552	0.000
Random		-2.390	0.279	0.078	-2.936	-1.843	-8.573	0.000



Model	Heterogeneity: Q-value	df (Q)	P-value	I-squared	Publication bias: tau Squared	tau
Fixed effects	44.277	9	0.000	79.674	0.564	0.751

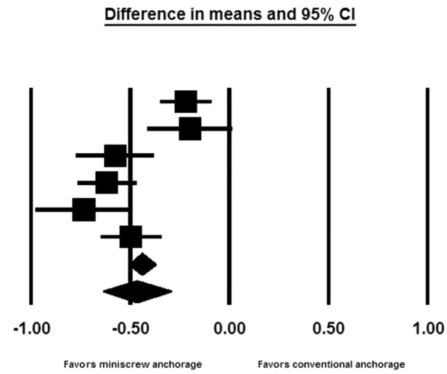
Figure 2. Forest plot for the mean difference of the anchorage loss between the MI and conventional anchorage groups, including the number of source studies, the effect sizes with the 95% confidence intervals, the assessment of heterogeneity, and the statistical significance.

loss ratio in the MI group was 0.05 (95% CI = −0.03 to 0.12, p = 0.252), with high heterogeneity present ($I^2 = 72\%$).

The mean anchorage loss ratio was significantly lower (indicating less gain of anchorage) in adult than in young patients (0.001 *vs.* 0.1) or when the MIs were inserted into the maxilla than into the mandible (0.02 *vs.* 0.1). However, a small amount of anchorage loss was observed when treatment lasted more than 12 mos (−0.009), while anchorage gain was observed when

Model	Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Liu 2009 (Mx)	-0.218	0.065	0.004	-0.346	-0.090	-3.341	0.001
	Park 2008 (Mx)	-0.199	0.108	0.012	-0.411	0.013	-1.842	0.066
	Shi 2008 (Mx)	-0.576	0.100	0.010	-0.772	-0.380	-5.760	0.000
	Upadhyah 2008a (Mx)	-0.617	0.075	0.006	-0.764	-0.470	-8.212	0.000
	Upadhyah 2008a (Md)	-0.733	0.124	0.015	-0.976	-0.490	-5.911	0.000
	Upadhyah 2008b (Mx)	-0.495	0.077	0.006	-0.646	-0.344	-6.426	0.000
Fixed		-0.441	0.035	0.001	-0.509	-0.373	-12.703	0.000
Random		-0.467	0.088	0.008	-0.639	-0.296	-5.334	0.000

Statistics for each study



Model	Heterogeneity Q-value	df (Q)	P-value	I-squared	Publication bias tau Squared	tau
Fixed effects	18.417	5	0.002	72.852	0.489	0.699

Figure 3. Forest plot for the mean difference of the anchorage loss ratio between the MI and conventional anchorage groups, including the number of source studies, the effect sizes with the 95% confidence intervals (CI), the assessment of heterogeneity, and the statistical significance.

treatment lasted fewer than 12 mos (0.07). Nevertheless, residual heterogeneity was present, and these results should be seen with caution (Appendix Fig. 3, Appendix Table 3).

MIs' Success Rate

The pooled MI failure rate in the included controlled studies was 0.123 (95% CI = 0.089 to 0.167, p = 0), with no heterogeneity (I^2 = 0%). This corresponds to a success rate of 87.7% (95% CI = 83.3% to 91.1%), with no significant differences among the three different subgroups that could be included (Appendix Fig. 4, Appendix Table 3).

Sensitivity Analysis

Sensitivity analysis indicated relative robustness of results. Significant differences in the results were found concerning the MD of anchorage loss between the MI and conventional anchorage groups. Higher effect size was found in blind studies, compared with non-blind studies (−3.9 mm *vs.* −2.0 mm) (Appendix Table 4). A 'reversal of effect direction' was noted concerning the anchorage loss ratio of the MI group in RCTs and CCTs (0.1 *vs.* −0.06). While CCTs reported statistically insignificant anchorage loss (p = 0.097), RCTs reported statistically significant anchorage gain (p = 0). For the rest of the outcomes, only minor changes were observed.

Concerning the importance of individual studies, no changes were found. The only possible exception in robustness was observed with the removal of the study by Upadhyay *et al.* (2008a), which seemed to decrease the MD of anchorage loss between the two anchorage types by 0.2 mm.

DISCUSSION

The electronic search yielded few studies appropriate for inclusion, due to the fact that, in this meta-analysis, a precise protocol was followed to minimize possible selection bias. This may be indicative of the lack of original high-quality studies in the currently existing literature. Evidence of heterogeneity existed in some cases, and attempts were made to evaluate it and to incorporate it into the overall estimate.

The results of this investigation indicate that there are differences between anchorage reinforcement derived from MIs and that achieved by conventional orthodontic means. The MD of anchorage loss between these two groups was −2.4 mm (95% CI = −2.9 to −1.8 mm, p=0). Especially in critical cases, more than 2 mm of anchorage loss can undermine the efficacy of treatment (Upadhyay *et al*., 2008a). Thus, MI reinforcement significantly reduces anchorage loss of the posterior teeth compared with conventional anchorage reinforcement.

The pooled anchorage loss for the MI group was 0.05 mm (95% CI = −0.3 to 0.4 mm, p = 0.794). Further, maxillary anchorage loss was greater than mandibular loss (0.2 mm *vs.* −0.6 mm), indicating that mandibular MIs provided more than adequate anchorage, with the pooled effect translated as anchorage gain. This is in agreement with the findings of Hedayati *et al*. (2007) and Upadhyay *et al*. (2008a), which were the only studies included in the analysis that provided data with the corresponding comparisons. In addition, the MD of anchorage loss, as well as the MD of the anchorage loss ratio between the experimental groups, was also lower in the maxilla than in the mandible (−3.1 mm *vs.* −2.2 mm and −0.7 *vs.* −0.4, respectively). All these findings demonstrate the superior anchoring effectiveness of MIs when used in the mandible, which could possibly be attributed to the high density of the mandibular bone.

The anchorage loss observed in the MI group in the current study seems to be less when the MIs were inserted between the second premolar and the first molar than in the palate, when 2 MIs were inserted *per* jaw of the patient, instead of one, and when they were directly rather than indirectly connected.

However, these three categories coincided with each other, and thus their individual evaluation was not possible.

Insignificant anchorage loss (−0.009) was observed when treatment lasted more than 12 mos. This could be attributed to the fact that although MIs are not osseointegrated, some osseointegration phenomena may occur after a prolonged period of use, as can be assumed by the mineral deposits that have been found on their surfaces (Eliades *et al*., 2009), which were reported as "isles of calcification." This partial osseointegration could provide additional stability, increasing MIs' anchorage effectiveness. In contrast, significant molar distalization (anchorage gain) was observed when treatment lasted fewer than 12 mos, possibly due to the biased set-up as mentioned above.

Significantly less anchorage gain was observed in adult than in young patients (0.001 *vs.* 0.1), indicating that MIs were more effective in supporting anchorage when they were used in adult patients. This could be attributed to the fact that adult patients seem to have significantly higher cortical thicknesses at specific sites in the maxilla and mandible compared with young patients (Fayed *et al*., 2010), providing more MI stability.

The males and the older age group had significantly higher buccolingual, buccal, and palatal cortical thicknesses at specific sites and levels in the maxilla and the mandible.

The reported success rates of the MIs in the included studies ranged from 71.4% to 100%. The overall event rate of MI failures according to the current investigation was 0.123, which corresponds to a success rate of 87.7%. This figure is slightly higher than the 83.6% found by a recent meta-analysis of uncontrolled studies (Schätzle *et al*., 2009).

Survival of non-osseointegrated implants seems to be affected by many risk factors. However, only two included studies reported success rates associated with certain characteristics. The first (Hedayati *et al*., 2007) reported higher success rates for MIs placed in the mandible than in the maxilla, agreeing with results from another study (Luzi *et al*., 2007). However, other studies with relatively larger samples reported superiority of the maxilla (Park *et al*., 2006) or no significant differences (Antoszewska *et al*., 2009). The second study (Shi *et al*., 2008) reported no success penalty for reinstalled MIs after failure, and higher success rates for maxillary MIs, agreeing with previous data (Baek *et al*., 2008).

The main limitations of this investigation include the small number of original studies included in the meta-analysis, their medium quality, and the large heterogeneity of the data, which diminishes the power of sensitivity and subgroup analyses. Studies with low quality reported inconsistent results compared with high-quality studies. In detail, less MD of anchorage loss between groups (−2.1 mm *vs.* −2.6 mm), more anchorage loss in the MI group (0.8 mm *vs.* −0.4 mm), greater MD of anchorage loss ratio between groups (−0.6 *vs.* −0.4), smaller anchorage loss ratio (−0.1 *vs.* 0.07), and higher MI failure rates (0.139 *vs.* 0.118) were observed in the low-quality compared with the high-quality studies.

Further, clinical or methodological heterogeneity and missing information limited the extent of statistical data pooling. Finally, the selective reporting of MI failures, patient characteristics, and possible risk factors in the original studies did not allow for assessment of every possible bias.

CONCLUSIONS

The results of this meta-analysis must be interpreted with caution, due to the number and quality of included studies, as well as the heterogeneity of the data, although every attempt was made to avoid misleading errors. Under the current limitations, the following conclusions can be drawn:

- The use of MIs significantly decreased or negated loss of anchorage.
- MIs were found more effective in supporting anchorage when they were used in the mandible, between the second premolar and the first molar, when 2 MIs were inserted into a patient's jaw, when they were directly connected, when they were used in adult patients, as well as when treatment lasted more than 12 mos.
- MIs used for anchorage have a success rate of 87.7%, with no significant differences between the various subgroups.

The investigation of risk factors which may affect the success rates and clinical effectiveness of MIs by well-designed RCTs could be very useful. Such high-quality studies could produce strong evidence to further support the results of the current investigation, as well as to answer the questions that remained unanswered in this investigation due to the lack of appropriate data.

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CONCISE REVIEW

M.A. Papadopoulos[1]*, S.N. Papageorgiou[2], and I.P. Zogakis[2]

[1]Department of Orthodontics, School of Dentistry, Aristotle University of Thessaloniki, GR-54124 Thessaloniki, Greece; and [2]School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece; *corresponding author, mikepap@dent.auth.gr

Clinical Effectiveness of Orthodontic Miniscrew Implants: a Meta-analysis

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APPENDICES

Appendix Table 1. The Electronic Databases Searched and the Search Strategy Used in the Meta-analysis *(as of June 2, 2010)*

Databases of Published Trials	Search Strategy Used	Hits
MEDLINE searched *via* PubMed (1950 – week 1, June 2010) www.ncbi.nlm.nih.gov/sites/entrez/	[(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh]) OR ("clinical trial"[tw]) OR [(singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])] OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study OR evaluation studies OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw])] AND [((orthodont*) OR (tooth movement*) OR (malocclusion*)] AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)])	611
EMBASE searched *via* ScienceDirect (1974 – January, 2010) www.embase.com	[([('phase-4-clinical-trial'/exp OR 'phase-4-clinical-trial') OR ('randomized-control-trial') OR ('randomization'/exp OR 'randomization') OR ('controlled-study'/exp OR 'controlled-study') OR ('multicenter-study'/exp OR 'multicenter-study') OR ('phase-3-clinical-trial'/exp OR 'phase-3-clinical-trial') OR ('double-blind-procedure'/exp OR 'double-blind-procedure') OR ('single-blind-procedure'/exp OR 'single-blind-procedure')] OR (random*:ab OR cross?over*:ab OR factorial*:ab OR placebo*:ab OR volunteer*:ab) OR (random*:ti OR cross?over*:ti OR factorial*:ti OR placebo*:ti OR volunteer*:ti) OR [(singl* OR doubl* OR trebl* OR tripl*) AND near AND (blind*:ti OR mask*:ti)] OR [(singl* OR doubl* OR trebl* OR tripl*) AND near AND (blind*:ab OR mask*:ab)]) NOT [([('animal'/exp OR 'animal') OR ('nonhuman'/exp OR 'nonhuman')]) NOT [([('animal'/exp OR 'animal') OR ('nonhuman'/exp OR 'nonhuman')]) AND ('human'/exp OR 'human')])] AND [((orthodont*) OR (tooth movement*) OR (malocclusion*)] AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)])	205

(continued)

Appendix Table 1. (continued)

Databases of Published Trials	Search Strategy Used	Hits
Cochrane Database of Systematic Reviews searched *via* The Cochrane Library at June 2, 2010 www.thecochranelibrary.com	(orthodont* OR tooth movement* OR malocclusion*) and [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)]	20
Cochrane Central Register of Controlled Trials searched *via* The Cochrane Library at June 2, 2010	(orthodont* OR tooth movement* OR malocclusion*) AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)]	61
Google Scholar Beta searched at June 2, 2010 www.scholar.google.com	orthodont* AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)]	742
Web of Science Searched at June 2, 2010 http://scientific.thomson.com/products/wos/	[((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh]) OR ("clinical trial"[tw]) OR [(singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])] OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study OR evaluation studies OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw])]) AND Topic=(orthodont* OR malocclusion* OR tooth movement*) AND Topic=[((implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)]) Refined by: Subject Areas = (DENTISTRY, ORAL SURGERY & MEDICINE OR MEDICINE, RESEARCH & EXPERIMENTAL OR ENGINEERING, BIOMEDICAL OR SURGERY OR MATERIALS SCIENCE, BIOMATERIALS OR RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING) Timespan = All Years. Databases = SCI-EXPANDED, SSCI, A&HCI.	162
Evidence-Based Medicine Searched at June 2, 2010 http://ebm.bmjjournals.com	(orthodont* OR malocclusion*) AND [(implant*) OR (miniscrew*) OR (mini screw*)]	14
Scopus searched at June 2, 2010 www.scopus.com	(ALL(orthodont* OR malocclusion* OR "tooth movement*") AND ALL(implant* OR miniscrew* OR "mini screw*" OR "mini implant*" OR "miniscrew implant*" OR "mini screw implant*" OR microscrew* OR "micro screw*" OR microimplant* OR "micro implant*" OR microscrew implant* OR "micro screw implant*" OR osseointegrat* OR anchorag)] AND (LIMIT-TO(DOCTYPE, "ar")] AND (LIMIT-TO(SUBJAREA, "DENT") OR LIMIT-TO(SUBJAREA, "MULT")]	820
Windows Live Academic searched at June 2, 2010 *via* search.live.com	(orthodontic OR malocclusion OR tooth movement) and (implant OR miniscrew OR mini screw OR mini implant OR miniscrew implant OR mini screw implant OR microscrew)	17
Databases of Published Trials	Search Strategy Used	Hits

(continued)

Appendix Table 1. (continued)

Databases of Published Trials	Search Strategy Used	Hits
LILACS database searched at June 2, 2010 http://bases.bvs.br	(orthodontic OR malocclusion OR tooth movement) AND (implant OR miniscrew OR mini screw OR mini implant OR miniscrew implant OR mini screw implant OR microscrew OR micro screw OR microimplant OR micro implant OR microscrew implant)	41
Bibliografia Brasileira de Odontolgogia searched at June 2, 2010 http://bases.bvs.br	(orthodontic OR malocclusion OR tooth movement) AND (implant OR miniscrew OR mini screw OR mini implant OR miniscrew implant OR mini screw implant OR microscrew OR micro screw OR microimplant OR micro implant OR microscrew implant)	1231
Ovid database Searched at June 2, 2010 http://ovidsp.ovid.com/autologin.html	[((orthodont*) OR (tooth movement*) OR (malocclusion*)] AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)])	164
	Journal subsets: Clinical medicine, Life and biomedical sciences, Life sciences; Limited to abstracts	
Bandolier searched at June 2, 2010 http://www.jr2.ox.ac.uk/Bandolier	(orthodontic OR malocclusion OR tooth movement) AND (implant OR miniscrew OR mini screw OR mini implant OR miniscrew implant OR mini screw implant OR microscrew OR micro screw OR microimplant OR micro implant OR microscrew implant)	0
Extenza searched at June 2, 2010 www.extenza-eps.com	(orthodont* OR tooth movement* OR malocclusion*) AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage) OR (stationary anchorage) OR (infinite anchorage) OR (temporary anchorage) OR (temporary absolute anchorage) OR (temporary skeletal anchorage) OR (temporary stationary anchorage)]	65
African Journals Online searched at June 2, 2010 www.ajol.info	(orthodontic OR malocclusion OR tooth movement) and (implant OR miniscrew OR mini screw OR mini implant OR miniscrew implant OR mini screw implant OR microscrew OR micro screw OR microimplant OR micro implant OR microscrew implant)	12
Databases of dissertations and conference proceedings		
Digital Dissertations searched *via* UMI ProQuest at June 2, 2010 http://proquest.umi.com/pqdweb?RQT = 302&cfc = 1	(orthodont* OR tooth movement* OR malocclusion*) AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*) OR (absolute anchorage) OR (skeletal anchorage)]	720
Conference Paper Index searched *via* Cambridge Scientific Abstracts (1982 – June 2, 2010) http://journals.cambridge.org/action/search	(orthodont* OR malocclusion*) AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*)]	104
Databases of research registers		
metaRegister of Controlled Trials (all registers active and archived) searched *via* www.controlled-trials.com at June 2, 2010	(orthodont* OR malocclusion*) AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*)]	25
German National Library of Medicine (ZB MED) searched *via* http://www.medpilot.de	[(orthodont*) OR (tooth movement*) OR (malocclusion*)] AND [(implant*) OR (miniscrew*) OR (mini screw*) OR (mini implant*) OR (miniscrew implant*) OR (mini screw implant*) OR (microscrew*) OR (micro screw*) OR (microimplant*) OR (micro implant*) OR (microscrew implant*) OR (micro screw implant*) OR (osseointegrat*)]	16
Sum		5030

Appendix Table 2. Characteristics of the Studies Included in the Meta-analysis

Author (yr)	Source	Quality Score	Study Design	Sample (M/F)	Average Age in Yrs (SD)	Dropouts	Overall Number of Implants (*per* patient)	Treatment Time in Months (SD)	Anchorage Units (MA, CA)	Activation Force	Outcome Measurement	Success Rate Reported	Anchorage Loss Measured at the First Molar in mm (SD)	Active Movement in mm (SD)	Anchorage Loss Ratio (SD)	Authors' Conclusions
Hedayati *et al.* (2007)	Electronic Search (PubMed, Scopus, Embase)	Low	CCT	9	17.4	N/A	27 (3)	5.4	MA: MIs in buccal alveolus & palatal area	NiTi coil springs	Cephalometric analysis	81.5%	Mx: 0.57 (0.39) Md: −0.18 (1.22)	N/A	N/A	MIs can be successfully used for stationary anchorage.
				10	18.2				CA: Conventional means				Mx: 2.5 (0.82) Md: 2.55 (1.12)			
Park *et al.* (2008)	Electronic Search (PubMed)	Medium	CCT	16 (2/14)	22.5 (4.8)	N/A	48 (3)	25.6 (5.5)	MA: MIs in buccal alveolus	NiTi coil springs (retraction), superelastic threads (intrusion)	Cephalometric analysis	87%	Mx: 0.26 (1.84)	Mx: −8.59 (2.62)	Mx: −0.03 (0.21)	Facial profile improved in MI group. Reduction in treatment duration with MIs.
				14 (3/11)	22.9 (4)			29.6 (4.2)	CA: Tweed-Merrifield technique				Mx: 1.71 (2.69)	Mx: −7.47 (2.69)	Mx: −0.229 (0.37)	
Shi *et al.* (2008)	Electronic Search (Embase)	Low	CCT	10	20.7	N/A	28 (2 or 4)	10.5	MA: MIs in buccal alveolus	Elastic springs & traction hooks	Cephalometric analysis	89%	Mx: 0.72 (1.23)	Mx: −6.9 (1.08) Md: −3.98 (1.63)	Mx: −0.104 (0.18)	MIs remained stable during retraction period.
				10					CA: TPA / HG				Mx: 2.55 (0.69)	Mx: −3.75 (1.01) Md: −2.5 (0.82)	Mx: −0.68 (0.26)	
Upadhyay *et al.* (2008a)	Electronic Search (PubMed, Scopus)	High	RCT	19	17.61 (3.56)	1	72 (4)	8.61 (2.2)	MA: MIs in buccal alveolus	NiTi coil springs	Cephalometric analysis	93%	Mx: −0.78 (1.35) Md: −0.89 (1.23)	Mx: −7.22 (2.07) Md: −6.06 (1.76)	Mx: 0.108 (0.19) Md: 0.147 (0.21)	Anchorage gain in MI group (teeth distalized & intruded).
				20	17.38 (2.89)	2		9.94 (2.44)	CA: TPA / HG / BM / DF				Mx: 3.22 (1.06) Md: 2.67 (2.11)	Mx: −6.33 (2.57) Md: −4.56 (1.46)	Mx: −0.509 (0.27) Md: −0.586 (0.5)	
Upadhyay *et al.* (2008b)	Electronic Search (PubMed, Scopus)	Medium	CCT	15 (5/10)	17.17	N/A	30 (2)	9.2	MA: MIs in buccal alveolus	NiTi coil springs	Cephalometric analysis	87%	Mx: −0.83 (1.4)	Mx: −6.23 (2.65)	Mx: 0.133 (0.23)	Intermolar distance decreased in MI group.
				15 (4/11)				10.6	CA: NB / HG / BM/ DF				Mx: 2.07 (0.68)	Mx: −5.72 (2.37)	Mx: −0.362 (0.19)	
Liu *et al.* (2009)	Electronic Search (PubMed, Scopus, Google Scholar)	Medium	RCT	17 (3/14)	21.65 (4.49)	N/A	68 (4)	25.65 (5.06)	MA: MIs in buccal alveolus	Power chain to crimpable hooks & sliding mechanisms	Cephalometric analysis	88%	Mx: −0.06 (1.4)	Mx: −7.03 (1.99)	Mx: 0.009 (0.2)	Better treatment changes can be achieved by MIs, especially in hyper-divergent patients.
				17 (3/14)	19.71 (3.06)			26.88 (6.54)	CA: TPA				Mx: 1.47 (1.15)	Mx: −4.76 (1.67)	Mx: −0.209 (0.18)	
Wilmes *et al.* (2009)	Electronic Search (PubMed, Embase, Cochrane Library, Scopus)	Low	CCT	5	20.9	N/A	10 (1)	N/A	MAa: Midpalatal MI connected to first molars	N/A	3D scan of casts	100%	Mx: 2.05 (1.39)	N/A	N/A	MI anchorage more effective than conventional anchorage. Anterior palate is preferable with correct mechanics.
				5					MAb: Midpalatal MI connected to first molars & TPA							
				10					CA: TPA				Mx: 4.21 (1.17)			
Basha *et al.* (2010)	Electronic Search (PubMed, Scopus)	Medium	RCT	7 (0/7)	17.36 (1.35)	N/A	14 (2)	6.08 (0.32)	MA: MIs in buccal alveolus	Elastomeric chain	Cephalometric analysis	71.4%	Mx: 0	N/A	N/A	Significant differences in treatment duration. Less anchorage loss in MI group.
				7 (0/7)	16 (1.41)			6.03 (1.07)	CA: TPA / BM				Mx: 1.73 (0.43)			

CCT, Controlled Clinical Trial; RCT, Randomized Controlled Trial; M/F, male/female; SD, standard deviation; MA, miniscrew implant anchorage; CA, conventional anchorage; MI, miniscrew implant; TPA, transpalatal arch; HG, headgear; BM, banded molars; DF, differential forces; NB, Nance button; Mx, maxilla; Md, mandible; N/A, not available.

Appendix Table 3. Results of the Meta-analysis Using the Random-effects Model for the Mean Difference of Anchorage Loss between the MI and Conventional Anchorage Groups, the Mean Anchorage loss in the MI Group, the Mean Difference of Anchorage Loss Ratio between the MI and Conventional Anchorage Group, the Mean Anchorage Loss Ratio in the MI Group and the MI Failure Rate with Regard to the Various Subgroups, Including the Number of Source Studies, the Effect Sizes with the 95% Confidence Intervals, the Assessment of Heterogeneity, and the Statistical Significance *(Significant P-values for the differences between subgroups are presented in bold.)*

		No. of Source Studies	Effect Size and 95% Confidence Interval					Heterogeneity		
			Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Q-value	df (Q)	P-value
Subgroups for MD of anchorage loss between the MI and conventional anchorage groups										
Average patient age (yrs)	Young	5	-2.733	0.466	0.217	-3.646	-1.820	37.582	4	0.000
	Adult	5	-2.056	0.291	0.085	-2.626	-1.485	6.632	4	0.157
								0.063	1	0.801
MI connection method	Direct	7	-2.451	0.397	0.157	-3.228	-1.674	42.567	6	0.000
	Indirect	3	-2.127	0.238	0.056	-2.593	-1.661	1.705	2	0.426
								0.005	1	0.941
Jaw of insertion	Maxilla	8	-2.226	0.302	0.091	-2.817	-1.635	36.023	7	0.000
	Mandible	2	-3.131	0.415	0.172	-3.944	-2.318	1.154	1	0.283
								7.101	1	**0.008**
MI insertion site	P2M1	8	-2.484	0.358	0.128	-3.185	-1.784	43.694	7	0.000
	Midpalatal area	2	-1.979	0.265	0.070	-2.499	-1.459	0.126	1	0.722
								0.458	1	0.499
Number of MIs inserted	One	2	-1.979	0.265	0.070	-2.499	-1.459	0.126	1	0.722
	Two or more	8	-2.484	0.358	0.128	-3.185	-1.784	43.694	7	0.000
								0.458	1	0.499
Existence of anchorage loss	Loss	4	-1.906	0.220	0.048	-2.337	-1.475	0.531	3	0.912
	No loss	6	-2.711	0.442	0.195	-3.576	-1.845	42.207	5	0.000
								1.540	1	0.215
Subgroups for mean anchorage loss in the MI group										
Average patient age (in yrs)	Young	5	-0.185	0.218	0.048	-0.612	0.243	35.711	4	0.000
	Adult	5	0.409	0.465	0.216	-0.502	1.321	27.920	4	0.000
								2.880	1	**0.090**
MI connection method	Direct	7	-0.249	0.203	0.041	-0.648	0.149	25.340	6	0.000
	Indirect	3	0.783	0.502	0.252	-0.200	1.766	14.599	2	0.001
								26.572	1	**0.000**
Jaw of insertion	Maxilla	8	0.196	0.206	0.042	-0.207	0.600	56.368	7	0.000
	Mandible	2	-0.595	0.350	0.122	-1.281	0.090	2.058	1	0.151
								8.086	1	**0.004**
MI insertion site	P2M1	8	-0.243	0.183	0.033	-0.601	0.115	25.536	7	0.001
	Midpalatal area	2	1.250	0.738	0.544	-0.195	2.696	10.425	1	0.001
								30.551	1	**0.000**
Number of MIs inserted	One	2	1.250	0.738	0.544	-0.195	2.696	10.425	1	0.001
	Two or more	8	-0.243	0.183	0.033	-0.601	0.115	25.536	7	0.001

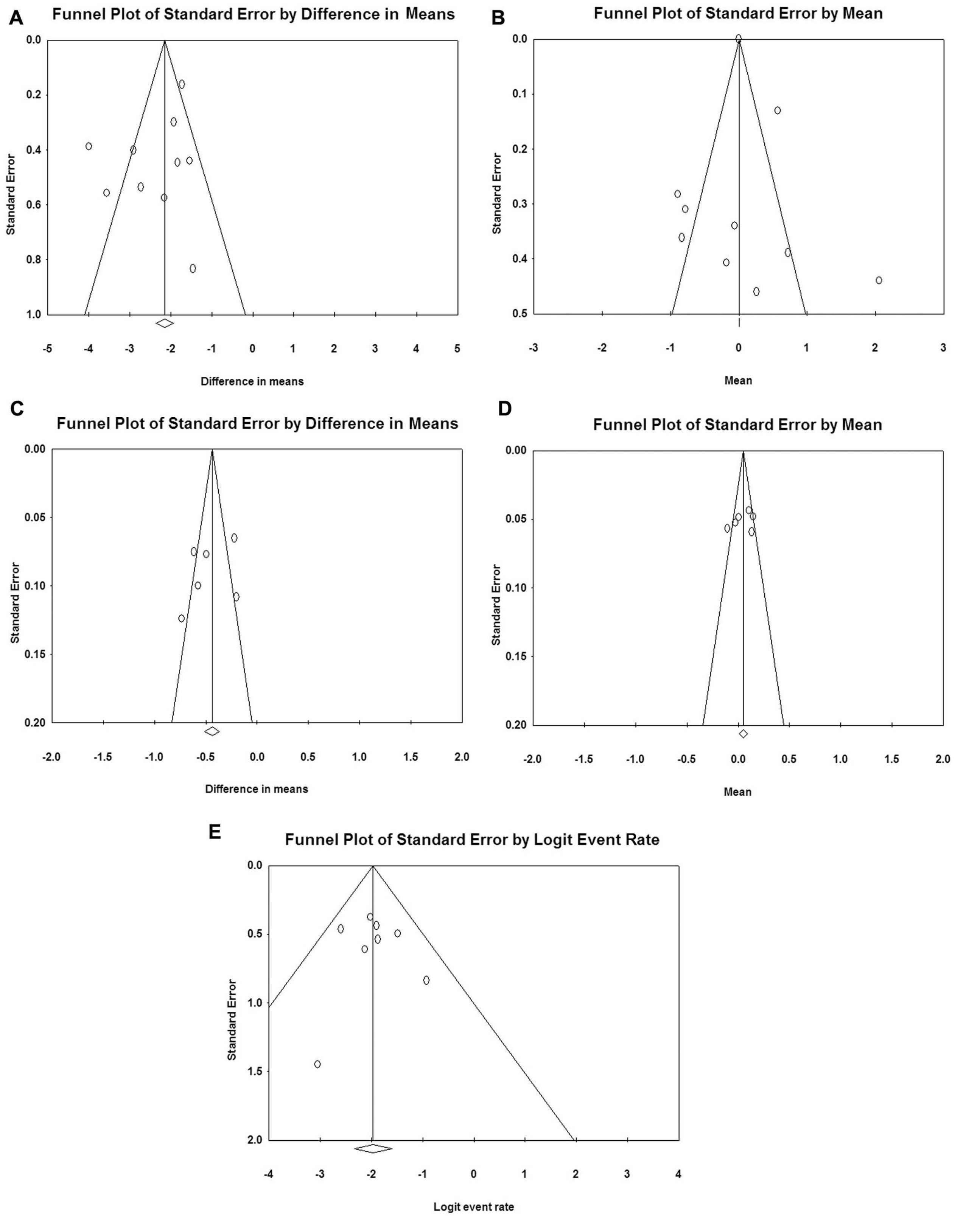
(continued)

Appendix Table 3. (continued)

		No. of Source Studies	Effect Size and 95% Confidence Interval					Heterogeneity		
			Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Q-value	df (Q)	P-value
Existence of anchorage loss	Loss	4	0.861	0.324	0.105	0.226	1.496	11.257	3	0.010
	No loss	6	-0.429	0.213	0.045	-0.846	-0.012	21.790	5	0.001
								33.464	1	**0.000**
Subgroups for MD of anchorage loss ratio between the MI and conventional anchorage groups										
Treatment duration	< 12 mos	4	-0.583	0.044	0.002	-0.670	-0.497	2.978	3	0.395
	>12 mos	2	-0.213	0.056	0.003	-0.322	-0.103	0.023	1	0.880
								27.038	1	**0.000**
Average patient age (yrs)	Young	2	-0.648	0.064	0.004	-0.774	-0.522	14.679	3	0.002
	Adult	4	-0.371	0.094	0.009	-0.556	-0.186	0.640	1	0.424
								14.720	1	**0.000**
Jaw of insertion	Maxilla	5	-0.422	0.091	0.008	-0.600	-0.245	24.008	4	0.000
	Mandible	1	-0.733	0.124	0.015	-0.976	-0.490	0.000	0	1.000
								6.031	1	**0.014**
Existence of anchorage loss	Loss	2	-0.390	0.188	0.036	-0.759	-0.020	6.557	1	0.010
	No loss	4	-0.504	0.113	0.013	-0.726	-0.283	23.127	3	0.000
								0.355	1	0.551
Subgroups for mean anchorage loss ratio in the MI group										
Treatment duration	< 12 mos	4	0.073	0.055	0.003	-0.034	0.181	13.590	3	0.004
	>12 mos	2	-0.009	0.036	0.001	-0.079	0.061	0.298	1	0.585
								4.244	1	**0.039**
Average patient age (in yrs)	Young	2	0.126	0.032	0.001	0.062	0.189	0.360	1	0.548
	Adult	4	0.001	0.046	0.002	-0.090	0.091	8.713	3	0.033
								9.059	1	**0.003**
Jaw of insertion	Maxilla	5	0.024	0.042	0.002	-0.058	0.107	13.244	4	0.010
	Mandible	1	0.147	0.048	0.002	0.053	0.241	0.000	0	1.000
								4.888	1	**0.027**
Existence of anchorage loss	Loss	2	-0.064	0.039	0.001	-0.140	0.012	0.913	1	0.339
	No loss	4	0.098	0.031	0.001	0.036	0.159	4.799	3	0.187
								12.420	1	**0.000**
Subgroups for MI failure rate										
Average patient age (in yrs)	Young	4	0.135	-	-	0.075	0.230	4.347	3	0.226
	Adult	4	0.117	-	-	0.074	0.179	0.606	3	0.895
								0.110	1	0.740
MI connection method	Direct	6	0.116	-	-	0.081	0.164	3.461	5	0.629
	Indirect	2	0.158	-	-	0.065	0.338	1.044	1	0.307
								0.559	1	0.455
Existence of anchorage loss	Loss	4	0.136	-	-	0.083	0.215	1.441	3	0.696
	No loss	4	0.115	-	-	0.072	0.178	3.338	3	0.342
								0.285	1	0.594

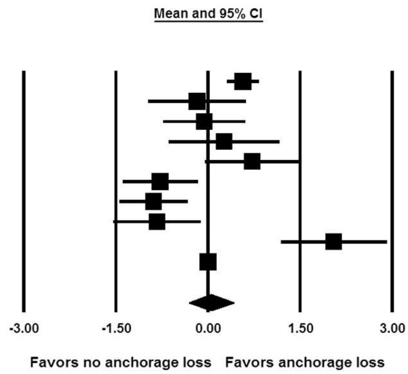
Appendix Table 4. Results of the Meta-analysis Using the Random-effects Model for the Mean Difference of Anchorage Loss between the MI and Conventional Anchorage Groups, with Regard to the Sensitivity Analysis, Including the Number of Source Studies, the Effect Sizes with the 95% Confidence Intervals, the Assessment of Heterogeneity, and the Statistical Significance *(Significant P-values for the differences between subgroups are presented in bold.)*

	Effect Size and 95% Confidence Interval						Test of Null (2-tailed)		Heterogeneity		
	No. of Studies	Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Z-value	P-value	Q-value	df (Q)	P-value
Sample											
Large	5	-2.759	0.515	0.265	-3.769	-1.749	-5.355	0.000	22.212	4	0.000
Small	5	-1.854	0.128	0.017	-2.106	-1.602	-14.434	0.000	3.607	4	0.462
Total Between									18.459	1	**0.000**
Study design											
RCT	5	-2.712	0.509	0.259	-3.710	-1.714	-5.325	0.000	41.249	4	0.000
CCT	5	-2.025	0.203	0.041	-2.423	-1.626	-9.955	0.000	2.556	4	0.635
Total Between									0.472	1	0.492
Blinding											
Yes	2	-3.856	0.318	0.101	-4.480	-3.233	-12.123	0.000	0.421	1	0.517
No	8	-2.002	0.172	0.030	-2.340	-1.664	-11.612	0.000	10.917	7	0.142
Total Between									32.940	1	**0.000**
Year											
Old	7	-2.674	0.362	0.131	-3.383	-1.965	-7.391	0.000	26.472	6	0.000
Recent	3	-1.736	0.147	0.022	-2.025	-1.447	-11.781	0.000	0.766	2	0.001
Total Between									17.039	1	**0.000**
Method error analysis											
Yes	7	-2.626	0.381	0.145	-3.372	-1.880	-6.899	0.000	29.498	6	0.000
No	3	-1.769	0.148	0.022	-2.059	-1.480	-11.989	0.000	0.539	2	0.764
Total Between									14.240	1	**0.000**
Quality											
Low	4	-2.061	0.210	0.044	-2.472	-1.650	-9.827	0.000	2.049	3	0.562
Medium & High	6	-2.555	0.463	0.215	-3.464	-1.647	-5.515	0.000	42.022	5	0.000
Total Between									0.206	1	0.650



Appendix Figure 1. Funnel plot analysis **(A)** for the mean difference of anchorage loss between the MI and conventional anchorage groups, **(B)** for the anchorage loss in the MI group, **(C)** the anchorage loss ratio mean difference between the MI and conventional anchorage groups, **(D)** for the anchorage loss ratio in the MI group, and **(E)** for the MI failure rate.

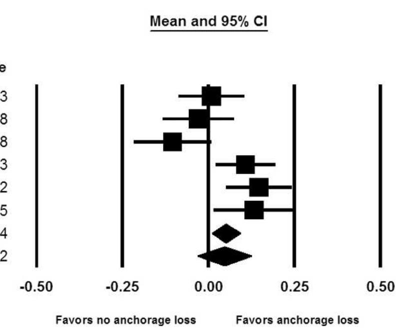
Model	Study name	Mean	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Hedayati 2007 (Mx)	0.570	0.130	0.017	0.315	0.825	4.385	0.000
	Hedayati 2007 (Md)	-0.180	0.407	0.165	-0.977	0.617	-0.443	0.658
	Liu 2009 (Mx)	-0.060	0.340	0.115	-0.726	0.606	-0.177	0.860
	Park 2008 (Mx)	0.260	0.460	0.212	-0.642	1.162	0.565	0.572
	Shi 2008 (Mx)	0.720	0.389	0.151	-0.042	1.482	1.851	0.064
	Upadhyah 2008a (Mx)	-0.780	0.310	0.096	-1.387	-0.173	-2.518	0.012
	Upadhyah 2008a (Md)	-0.890	0.282	0.080	-1.443	-0.337	-3.154	0.002
	Upadhyah 2008b (Mx)	-0.830	0.361	0.131	-1.538	-0.122	-2.296	0.022
	Wilmes 2009 (Mx)	2.050	0.440	0.193	1.188	2.912	4.664	0.000
	Basha 2010 (Mx)	0.000	0.000	0.000	-0.000	0.000	0.000	1.000
Fixed		0.000	0.000	0.000	-0.000	0.000	0.001	0.999
Random		0.048	0.184	0.034	-0.313	0.409	0.261	0.794



Model	Heterogeneity: Q-value	df (Q)	P-value	I-squared	Publication bias: tau Squared	tau
Fixed effects	66.512	9	0.000	86.469	0.238	0.487

Appendix Figure 2. Forest plot for the mean anchorage loss in the MI group, including the number of source studies, the effect sizes with the 95% confidence intervals (CI), the assessment of heterogeneity, and the statistical significance.

Model	Study name	Mean	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Liu 2009 (Mx)	0.009	0.049	0.002	-0.086	0.104	0.186	0.853
	Park 2008 (Mx)	-0.030	0.053	0.003	-0.133	0.073	-0.571	0.568
	Shi 2008 (Mx)	-0.104	0.057	0.003	-0.216	0.008	-1.827	0.068
	Upadhyah 2008a (Mx)	0.108	0.044	0.002	0.023	0.193	2.478	0.013
	Upadhyah 2008a (Md)	0.147	0.048	0.002	0.053	0.241	3.051	0.002
	Upadhyah 2008b (Mx)	0.133	0.059	0.004	0.017	0.249	2.240	0.025
Fixed		0.051	0.021	0.000	0.010	0.091	2.456	0.014
Random		0.046	0.040	0.002	-0.032	0.123	1.147	0.252

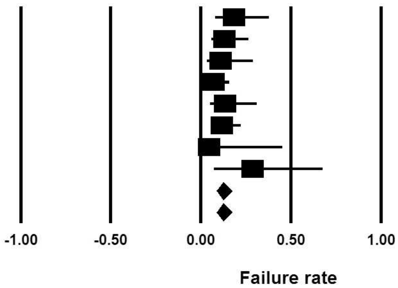


Model	Heterogeneity: Q-value	df (Q)	P-value	I-squared	Publication bias: tau Squared	tau
Fixed effects	18.132	5	0.003	72.425	0.007	0.082

Appendix Figure 3. Forest plot for the mean anchorage loss ratio in the MI group, including the number of source studies, the effect sizes with the 95% confidence intervals (CI), the assessment of heterogeneity, and the statistical significance.

Model	Study name	Event rate	Upper limit	Lower limit	Z-Value	p-Value
		Statistics for each study				
	Hedayati 2007	0.185	0.375	0.079	-2.991	0.003
	Park 2008	0.130	0.261	0.060	-4.333	0.000
	Shi 2008	0.107	0.284	0.035	-3.470	0.001
	Upadhyah 2008a	0.069	0.156	0.029	-5.598	0.000
	Upadhyah 2008b	0.133	0.306	0.051	-3.485	0.000
	Liu 2009	0.118	0.218	0.060	-5.353	0.000
	Wilmes 2009	0.045	0.448	0.003	-2.103	0.035
	Basha 2010	0.286	0.673	0.072	-1.095	0.273
Fixed		0.123	0.167	0.089	-10.605	0.000
Random		0.123	0.167	0.089	-10.605	0.000

Event rate and 95% CI



Model	Heterogeneity: Q-value	df (Q)	P-value	I-squared	Publication bias: tau Squared	tau
Fixed effects	5.064	7	0.652	0	0.000	0.000

Appendix Figure 4. Forest plot for the MI failure rate, including the number of source studies, the effect sizes with the 95% CIs, the assessment of heterogeneity, and the statistical significance.