

# Hypnosis/Relaxation Therapy for Temporomandibular Disorders: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

## Yuqing Zhang, MD, MS(c)

Medical Doctor, Guang'anmen Hospital  
China Academy of Chinese Medical Science,  
Beijing, China  
Doctoral Candidate, Department of Clinical  
Epidemiology and Biostatistics  
McMaster University  
Hamilton, Ontario, Canada

## Luis Montoya, DDS, MSc

Endodontist, Department of Dentistry  
Santo Tomas University  
Bogotá, Distrito Capital, Colombia

## Shanil Ebrahim, PhD, MSc

Assistant Professor, Department of Clinical  
Epidemiology and Biostatistics  
Postdoctoral Fellow, Department of  
Anesthesia  
McMaster University, Ontario, Canada

## Jason W. Busse, DC, PhD

Assistant Professor  
Departments of Anesthesia and Clinical  
Epidemiology and Biostatistics  
McMaster University  
Hamilton, Ontario, Canada

## Rachel Couban, MS, MIST

Librarian, Institute for Work and Health  
Hamilton, Ontario, Canada

## Randi E. McCabe, PhD

Director, Anxiety Treatment & Research Centre  
Psychologist-in-Chief, St. Joseph's Healthcare  
Associate Professor, Department of Psychiatry  
and Behavioural Neurosciences  
McMaster University  
Hamilton, Ontario, Canada

## Peter Bieling, MA, PhD

Director, Mental Health and Addictions  
Services  
Psychologist, St. Joseph's Hospital  
Associate Professor, Psychiatry &  
Behavioural Neurosciences  
McMaster University  
Hamilton, Ontario, Canada

## Alonso Carrasco-Labra, DDS, MSc, PhD

Doctoral Candidate, Department of Clinical  
Epidemiology and Biostatistics  
McMaster University  
Hamilton, Ontario, Canada  
Lecturer, Evidence-Based Dentistry Unit  
Faculty of Dentistry, Universidad de Chile  
Santiago, Chile

## Gordon H. Guyatt, MD, MSc, FRCPC

Distinguished Professor  
Departments of Medicine and Clinical  
Epidemiology and Biostatistics  
McMaster University  
Hamilton, Ontario, Canada

## Correspondence to:

Dr Yuqing Zhang  
Department of Clinical Epidemiology and  
Biostatistics  
McMaster University  
1280 Main Street  
Hamilton, Ontario, L8S 4K1, Canada  
Email: Madisonz1220@gmail.com

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**Aims:** To conduct a systematic review and meta-analysis to evaluate the effectiveness of hypnosis/relaxation therapy compared to no/minimal treatment in patients with temporomandibular disorders (TMD). **Methods:** Studies reviewed included randomized controlled trials (RCTs) where investigators randomized patients with TMD or an equivalent condition to an intervention arm receiving hypnosis, relaxation training, or hyporelaxation therapy, and a control group receiving no/minimal treatment. The systematic search was conducted without language restrictions, in Medline, EMBASE, CENTRAL, and PsycINFO, from inception to June 30, 2014. Studies were pooled using weighted mean differences and pooled risk ratios (RRs) for continuous outcomes and dichotomous outcomes, respectively, and their associated 95% confidence intervals (CI). **Results:** Of 3,098 identified citations, 3 studies including 159 patients proved eligible, although none of these described their method of randomization. The results suggested limited or no benefit of hypnosis/relaxation therapy on pain (risk difference in important pain  $-0.06$ ; 95% CI:  $-0.18$  to  $0.05$ ;  $P = .28$ ), or on pressure pain thresholds on the skin surface over the temporomandibular joint (TMJ) and masticatory muscles. Low-quality evidence suggested some benefit of hypnosis/relaxation therapy on maximal pain (mean difference on 100-mm scale =  $-28.33$ ; 95% CI:  $-44.67$  to  $-11.99$ ;  $P = .007$ ) and active maximal mouth opening (mean difference on 100-mm scale =  $-2.63$  mm; 95% CI:  $-3.30$  mm to  $-1.96$  mm;  $P < .001$ ) compared to no/minimal treatment. **Conclusion:** Three RCTs were eligible for the systematic review, but they were with high risk of bias and provided low-quality evidence, suggesting that hypnosis/relaxation therapy may have a beneficial effect on maximal pain and active maximal mouth opening but not on pain and pressure pain threshold. Larger RCTs with low risk of bias are required to confirm or refute these findings and to inform other important patient outcomes. *J Oral Facial Pain Headache* 2015;29:115–125. doi: 10.11607/ofph.1330

**Key words:** *hypnotics and sedatives, pain, temporomandibular disorders (TMD), temporomandibular dysfunction syndrome, temporomandibular joint disorder*

Temporomandibular disorders (TMD) refer to a cluster of conditions characterized by pain in the temporomandibular joint (TMJ) or surrounding tissues, functional movement limitations of the mandible, or clicking in the TMJ during motion.<sup>1,2</sup> Cross-sectional surveys suggest that TMD are the second most commonly occurring musculoskeletal conditions resulting in pain and disability, affecting approximately 5% to 12% of the population in Sweden,<sup>3</sup> England,<sup>4</sup> Hong Kong,<sup>5</sup> Spain,<sup>6</sup> Canada,<sup>7</sup> and United States.<sup>8</sup> The incidence and prevalence range widely<sup>9,10</sup> depending on sex and age distributions of the patient populations.<sup>11–13</sup>

No therapy has emerged as optimal for the management of TMD. Investigators have reported evidence supporting various approaches, including exercise, cognitive behavioral therapy, hypnosis, relaxation training, pharmacologic therapy (eg, nonsteroidal anti-inflammatory drugs, muscle relaxants, or narcotic analgesics), and splint therapy.<sup>14–16</sup>

Hypnosis is defined as “a procedure during which a health professional or researcher suggests that a patient or healthy individual experiences changes in sensations, perceptions, thoughts, or behavior

that normally involves relaxation.<sup>17</sup> Hypnosis therapy relieves pain during and after surgical procedures<sup>18–20</sup> and reduces discomfort associated with various chronic pain conditions.<sup>21–23</sup>

Relaxation therapy shares common elements with hypnosis and involves self-regulation techniques intended to reduce muscle tension around the jaw.<sup>24</sup> Therapy includes the adoption of a relaxed, passive mode of thinking, brought about by focusing of attention on some neutral target or set of targets, such as parts of the body or breathing, while ignoring distracting thoughts.<sup>25</sup>

Relaxation therapy may reduce sensory features<sup>26</sup> and affective aspects of pain,<sup>27</sup> as well as narcotic intake,<sup>28,29</sup> in postoperative patients. A narrative review<sup>30</sup> suggests relaxation may result in a similar therapeutic effect to hypnosis on pain syndromes such as chronic back pain, headache, fibromyalgia, gastrointestinal pain in children, and TMD.

A narrative review for TMD management with hypnosis/relaxation therapy suggested the use of biobehavioral interventions in the management of TMD may be appropriate<sup>31</sup>; however, this approach appears to be rarely used in practice. A survey of 700 dentists from three dental practice-based research networks conducted in 2013 in the United States and Scandinavia (72% response rate) found that respondents treated an average of three patients with TMD-related pain per month, and no respondent endorsed the use of hypnosis or relaxation therapy.<sup>32</sup>

No systematic review has explored the impact of hypnosis/relaxation versus no/minimal treatment in patients with TMD. Therefore, this systematic review and meta-analysis aimed to evaluate the effectiveness of hypnosis/relaxation therapy compared to no/minimal treatment in patients with TMD.

## Materials and Methods

This systematic review followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.<sup>33</sup>

### Eligibility Criteria

1. Inclusion of patients with TMD or an equivalent condition with any of the following characteristics (a or b or c): (a) myofascial pain, meaning discomfort or pain in the muscles that control jaw function and the neck and shoulder muscles; (b) internal derangement of the joint, meaning a dislocated jaw or displaced disc, or injury to the condyle; or (c) degenerative joint disease, defined as reporting of a degenerative disease by the primary study authors that was confirmed by at least

an imaging technique (radiography, computed tomography [CT] scan, others); for example, osteoarthritis or rheumatoid arthritis in the TMJ. The following conditions meet these criteria: TMD, craniomandibular dysfunction, myofascial pain dysfunction syndrome, myofascial pain, facial arthromyalgia, masticatory myalgia, and mandibular dysfunction.

2. Random allocation to an intervention arm receiving hypnosis, relaxation therapy or hyporelaxation therapy, and a control group receiving no/minimal therapy (a clinician visit without treatment).

### Information Sources and Search

An experienced medical librarian (R.C.) conducted electronic searches to identify eligible studies, in any language, through a systematic search of Medline, EMBASE, PsycINFO, Allied and Complementary Medicine (AMED), the Cochrane Library including CENTRAL, Database of Abstracts of Reviews of Effects (DARE), and the National Health Service Economic Evaluation Database (NHS EED), from inception of each database to June 30, 2014. In addition, the Cochrane Database of Systematic Reviews (CDSR) was searched for relevant systematic reviews; additional relevant randomized controlled trials (RCTs) from the systematic reviews were audited for potential inclusion. Searched terms included: temporomandibular joint, temporomandibular joint disorder, masticatory muscle, mandible condyle, relaxation training, hypnosis, muscle relaxation, etc. An example of the search strategy applied for PsycINFO is presented in Table 1. Reviewers scanned the reference lists of all eligible RCTs and review articles to identify additional studies.

### Eligibility Adjudication and Data Collection

Two reviewers (Y.Z. and L.M.) used a standardized form to screen titles and abstracts of all citations identified in the search. The same reviewers independently applied eligibility criteria to the full text of all potentially eligible studies, and they extracted data from each eligible study. Data extracted included study characteristics (ie, sample size, country where the study was conducted, age and sex distribution of patients), diagnostic system used to confirm TMD, intervention and control group details, follow-up time, and all reported patient-important outcomes. Akl et al<sup>34</sup> have defined patient-important outcomes as “an outcome for which one would answer with ‘yes’ the following question: ‘If the patient knew that this outcome was the only thing to change with treatment, would patient consider receiving this treatment if associated with side effects or cost?’” Two clinical specialists, an endodontist and a general dentist (L.M. and A.C.), independently determined outcomes classified as patient-important.

Reviewers resolved discrepancies by discussion to reach consensus, and an arbitrator (S.E.) adjudicated unresolved disagreements.

### Assessment of Risk of Bias in Individual Studies

The Cochrane Risk of Bias Tool assesses the following six sources of biases: sequence generation; concealment of allocation; masking of participants, study personnel and outcome assessors; loss to follow-up; selective outcome reporting; and other potential sources of bias (eg, trial stopped early, extreme baseline imbalance, etc). A modified and previously validated risk of bias tool was used in this review. The modified tool excluded the option for assessors to endorse “unsure” for any risk category and assessed the following additional components: blinding of health care providers, data collectors, and data analysts. Reviewers determined each source of bias in the studies as “low risk of bias” with the response options of “yes” or “probably yes” and as “high risk of bias” with the response options of “probably no” and “no”.<sup>35</sup> Reviewers also attempted to contact authors whose study did not provide explicit information for assessment of risk of bias or to acquire other missing information; however, the authors did not reply to such inquiry.

### Statistical Analyses

Agreement between reviewers was assessed on full text eligibility by using an unweighted kappa. The kappa values were interpreted as slight agreement (0.21 to 0.40), moderate agreement (0.41 to 0.60), substantial agreement (0.61 to 0.80), or almost perfect agreement (greater than 0.80).<sup>36</sup> For all outcomes, the longest follow-up time point was chosen for the pooled analysis, as patients and clinicians are most likely to be interested in sustained effects of hypnosis/relaxation therapy. In cases where the same continuous outcome measure was reported by more than one eligible study, weighted mean differences (MDs) and their associated 95% confidence intervals (CIs) were calculated. For dichotomous outcomes, pooled risk ratios (RRs) and their associated 95% CIs were calculated using a Mantel-Haenszel random-effects model, as it takes both within-study and between-study variability into account in calculation of random error in the analysis<sup>37,38</sup> (and hence is more conservative than a fixed-effects model).

All data analyses were conducted using Review Manager (RevMan [Mac OS X]. Version 5.1.7. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011).

Eligible studies reported a mix of change scores (change from baseline to longest follow-up time point) and posttreatment scores. For their analysis, both the differences in change scores and difference in post-

**Table 1 Search Strategies for PsycINFO Database**

1	musculoskeletal disorders/
2	jaw/
3	joint disorders/
4	temporo?mandibular.mp.
5	or/1-4
6	exp biofeedback/
7	exp relaxation therapy/
8	behavior therapy/
9	cognitive therapy/
10	cognitive behavior therapy/
11	brief psychotherapy/
12	hypnosis/
13	pain management/
14	psychotherapeutic processes/
15	psychotherapeutic techniques/
16	counseling/
17	behavior modification/
18	electromyography/
19	biopsychosocial approach/
20	or/6-19
21	biofeedback.mp.
22	electromyography.mp.
23	counseling.mp.
24	hypnosis.mp.
25	relaxation.mp.
26	or/21-25
27	20 or 26
28	5 and 27

treatment scores were pooled between groups.<sup>39</sup> In a sensitivity analysis of studies that provided both pretreatment scores and posttreatment scores but no change scores, the baseline scores were subtracted from the posttreatment scores to calculate the mean change scores and used a correlation coefficient of 0.5 to calculate the associated standard deviations (SDs).<sup>40</sup> To test the robustness of the correlation coefficients, further sensitivity analyses were conducted using correlation coefficients of 0.2 and 0.8. The difference between the results of the pooled analysis of change and posttreatment scores and the pooled analysis of reported change scores with imputed change scores was tested using the estimated correlation.

The minimal important difference (MID) was defined as “the smallest difference in score in the outcome of interest that informed patients or informed proxies perceive as important, either beneficial or harmful, and which would lead the patient or clinician to consider a change in the management.”<sup>41</sup> To facilitate interpretation for clinicians and other stakeholders, the MID to contextualize the effect of hypnosis/relaxation therapy on TMJ or muscle pain was provided. In a study that included 2,724 patients suffering from various types of chronic pain, Farrar et al<sup>42</sup> concluded a 30% pain reduction on a visual analog scale (VAS) as the MID

based on patient global impression of change as the anchor. National Health Service (NHS) Primary Care Guidelines for the Management of Chronic Pain<sup>43</sup> also state that a 30% improvement in chronic pain on a VAS or numeric rating scale (NRS) represents a “good outcome.” Therefore, to estimate the MID for TMD patients, 30% of the median VAS score of the control groups at baseline was used among the eligible studies.

Even if the average effect is smaller than the MID, there is still the possibility that a worthwhile proportion of patients experience an effect greater than or equal to the MID.<sup>44</sup> Therefore, the proportion of patients experiencing a treatment effect greater than or equal to the MID was calculated. For the control group and intervention group in each study, the probability ( $P_{Ci}$  and  $P_{Ei}$ , respectively) of obtaining a treatment effect greater than or equal to the MID was first calculated:

$$p_{Ci} = 1 - \Phi\left(\frac{MID - m_{Ci}}{sd_{Ci}}\right) \quad \text{and} \quad p_{Ei} = 1 - \Phi\left(\frac{MID - m_{Ei}}{sd_{Ei}}\right)$$

where  $\Phi$  denotes the standard normal cumulative distribution function,  $m_{Ci}$  and  $m_{Ei}$  the control and intervention mean, and  $sd_{Ci}$  and  $sd_{Ei}$  the control and intervention standard deviation for the given study  $i$ .<sup>45</sup> Then, the risk difference (RD) for each study was calculated using the formula  $RD_i = p_{Ei} - p_{Ci}$  and the associated standard errors (SE) using

$$SE(RD_i) = \sqrt{\frac{(p_{Ei} * (1 - p_{Ei}))}{n_{Ei}} + \frac{(p_{Ci} * (1 - p_{Ci}))}{n_{Ci}}}$$

where  $n_{Ei}$  and  $n_{Ci}$  represent the intervention and control sample size for the given study  $i$ . Subsequently, a standard meta-analysis was performed using the inverse variance method to pool the RDs, in order to obtain a proportion of patients who have an important improvement from the hypnosis/relaxation therapy.<sup>45</sup>

### Assessment of Publication Bias

The review intended to assess publication bias by visually observing asymmetry of the funnel plot for each outcome, only if there were at least 10 studies in a particular meta-analysis.<sup>46</sup>

### Assessment of Heterogeneity

Chi-squared ( $\chi^2$ ) and  $I^2$  tests were used to investigate heterogeneity associated with pooled effects,<sup>47,48</sup> and a priori hypotheses were formulated to explain heterogeneity. To avoid a high risk of spurious subgroup findings, subgroup analyses were performed only when there were at least five studies.

### Confidence in Effect Estimates

Reviewers independently and in duplicate assessed the confidence in effect estimates (quality of evi-

dence) for each outcome by using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system, which addresses precision, consistency, risk of bias, directness of evidence, and publication bias.<sup>49</sup> The confidence in pooled effect estimates were categorized into the following four levels<sup>50</sup>: (1) high quality of evidence, indicating that reviewers are very confident that the true effect lies close to that of the estimate of the effect; (2) moderate quality of evidence, indicating that reviewers are moderately confident in the effect estimate and that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; (3) low quality of evidence, indicating that reviewers' confidence in the effect estimate is limited and that the true effect may be substantially different from the estimate of the effect; (4) very low quality of evidence, indicating that reviewers have very little confidence in the effect estimate and that the true effect is likely to be substantially different from the estimate of effect. Reviewers resolved discrepancies by discussion to reach consensus, and an arbitrator (S.E.) adjudicated unresolved disagreements.

## Results

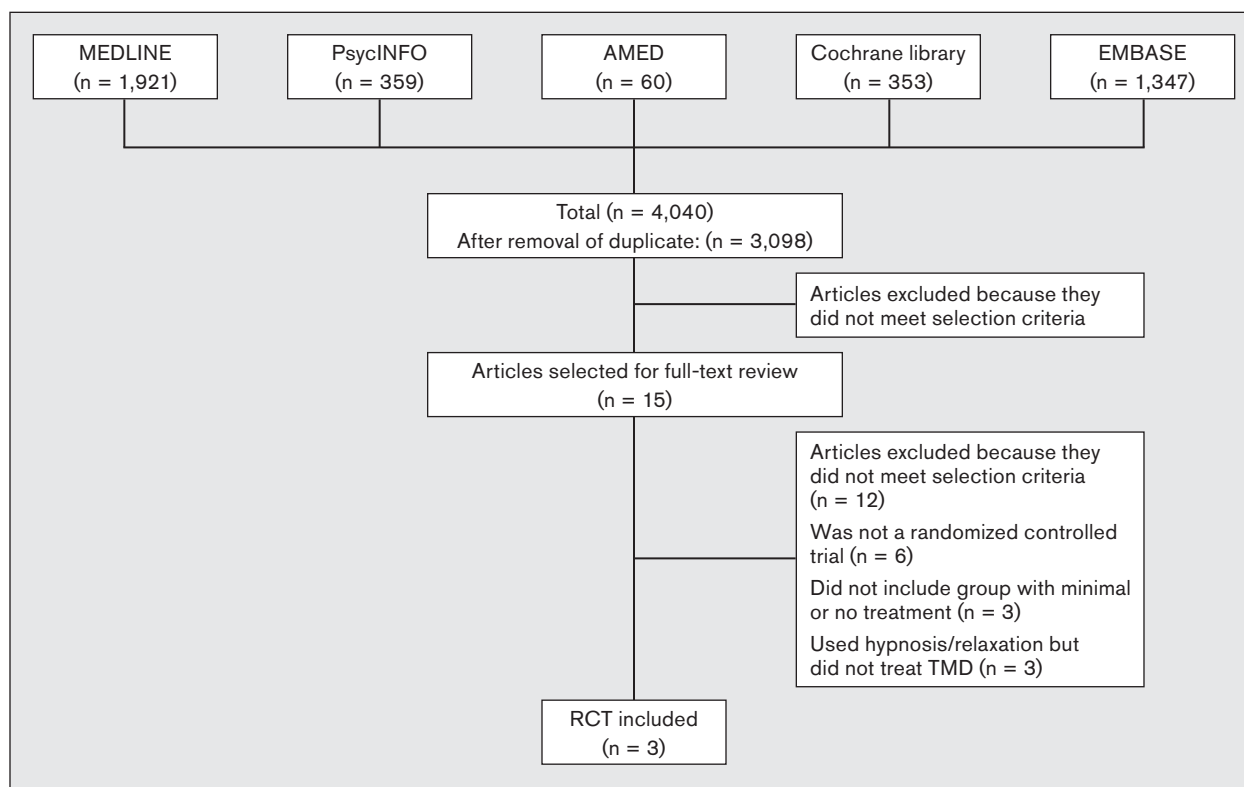
### Description of Included Studies

The search strategy generated a total of 3,098 unique citations; 15 were retrieved in full text and 3 proved eligible for this review (Fig 1).

Table 2 summarizes the study characteristics of the three eligible RCTs.<sup>51–53</sup> There was perfect agreement in the full-text review stage ( $\kappa = 1.0$ ). Two studies<sup>52,53</sup> used the Research Diagnostic Criteria (RDC) for TMD<sup>54</sup> for diagnosing TMD. One study<sup>51</sup> indicated that all participants reported their diagnosis of TMD and experienced TMD syndromes for at least one year but without mentioning specific diagnostic criteria. Two studies<sup>51,52</sup> did not mention adverse events, and one study<sup>53</sup> reported no adverse events.

One study<sup>52</sup> stated clearly that a licensed senior faculty member from the institution with a medical hypnosis license administered the relaxation therapy. One study claimed that “a trained therapist” conducted the study but provided no details on the qualification.<sup>53</sup> One study used a therapist who has a Master of Social Work in psychotherapy and a PhD from the Department of Applied Psychology at New York University.<sup>51</sup>

One study<sup>51</sup> described the hypnosis exercise in details with three components (hypnotic induction, deep relaxation, specific instruction on pain reduction). One study specified that the relaxation therapy was working specifically for relaxation of the facial



**Fig 1** Study selection process.

**Table 2** Characteristics of Included Studies

Study	Location	Sample size		Sex (M/F)		Age in years, mean/range (SD)		Treatment	Control	Follow-up time (longest)	Outcome reported
		TG	CG	TG	CG	TG	CG				
Angelone <sup>51</sup> (2008)	USA	19	20	3/16	5/15	41.89 (12.60)	43.35 (10.44)	Hypnosis exercise	Attention Control	2 weeks	Pain (VAS%)
Winocur et al <sup>52</sup> (2002)	Israel	15	10	0/15	0/10	21–49 (31)	22–42 (28.1)	Hypno-relaxations	No treatment	2 mo	Press pain; AMO; PMO; DAP; MS; TS; SMS
Wahlund et al <sup>53</sup> (2003)	Norway	41	39	6/35	12/27	15.4 (2.0)	14.8 (1.9)	BI+RT	BI	6 mo	PPT; PMO; self-evaluation

TG = treatment group; CG = control group; VAS = visual analog scale; AMO = active maximal mouth opening; PMO = passive maximal mouth opening; DAP = difference between AMO and PMO; MS = mean masseter sensitivity to palpation; TS = mean temporalis sensitivity to palpation; SMS = mean superficial masseter sensitivity to palpation; PPT = TMJ and/or muscle pressure pain threshold.

musculature,<sup>52</sup> and another stated that the relaxation therapy was focused on teaching patients to apply the method in everyday situations when bodily tension and pain increased.<sup>53</sup>

Reviewers attempted to contact the corresponding author from one study<sup>53</sup> to obtain missing information but received no response.

### Methodological Quality of Included Studies

Risk of bias in eligible studies was high due to the limited reporting of allocation concealment, blinding of participants, health care providers, data collectors, outcome assessors, and data analysts. None

of the studies described their method of randomization. Two studies blinded outcome assessors.<sup>52,53</sup> No study reported missing data or explicitly declared an intention-to-treat analysis. Table 3 presents the risk of bias within studies. Due to the limited amount of studies, reviewers were unable to assess publication bias.

Two clinical specialists who were part of the systematic review team determined the following outcomes to be patient-important: TMD-related pain, maximal pain, active (voluntary) maximal mouth opening, pressure pain threshold, patient subjective evaluation of the treatment, and school absence.

**Table 3 Risk of Bias Within Included Studies**

Study	Type of bias								
	Allocation concealment (selection bias)	Masking of participants	Masking of health care providers	Masking of data collectors	Masking outcome assessment (detection bias)	Masking of data analysts	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Angelone <sup>51</sup> (2008)	+	-	+	+	+	+	-	-	-
Winocur et al <sup>52</sup> (2002)	+	+	+	+	-	+	-	-	-
Wahlund et al <sup>53</sup> (2003)	+	+	+	+	-	+	-	-	-

+ Indicates presence of bias; - indicates absence of bias.

**Table 4 Confidence in Estimates of Effect (Quality of Evidence) Assessment by GRADE System**

No of studies	Quality assessment						Quality
	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
3	Randomized trials	Serious*	Serious <sup>†</sup>	No serious indirectness	Serious <sup>‡</sup>	None	Very low
1	Randomized trials	Serious <sup>§</sup>	No serious inconsistency	No serious indirectness	Serious <sup>‡</sup>	None	Low
1	Randomized trials	Serious <sup>§</sup>	No serious inconsistency	No serious indirectness	Serious <sup>‡</sup>	None	Low
1	Randomized trials	Serious <sup>  </sup>	No serious inconsistency	No serious indirectness	Serious <sup>‡</sup>	None	Low
1	Randomized trials	Serious <sup>  </sup>	No serious inconsistency	No serious indirectness	Serious <sup>‡</sup>	None	Low
1	Randomized trials	Serious <sup>  </sup>	No serious inconsistency	No serious indirectness	Serious <sup>‡</sup>	None	Low
1	Randomized trials	Serious <sup>  </sup>	No serious inconsistency	No serious indirectness	Serious <sup>‡</sup>	None	Low

\*None of these three studies reported allocation concealment. Only one study reported blinding of participants and two studies reported blinding of outcome assessment. Moreover, none of the studies reported blinding of data collectors and data analysts.

<sup>†</sup>I-squared value of 76% and chi-squared value of 8.17 with the pooled effect of MD = -9.16 mm; 95% CI: -23.47 to 5.14 mm.

<sup>‡</sup>Total population size is less than 400 (a threshold rule-of-thumb value; using the usual  $\alpha$  and  $\beta$ , and an effect size of 0.09 SD, representing a minimal effect).

<sup>§</sup>The authors did not report on allocation concealment or blinding of participants, health care providers, data collectors, or data analysts.

<sup>||</sup>No report of allocation concealment or blinding of participants and outcome assessors.

The methodological quality varied by outcome (Table 4). It was low for maximal pain, active (voluntary) maximal mouth opening, pressure pain threshold (TMJ), pressure pain threshold (muscles), patients' subjective evaluation of the treatment, and school absence, and very low for pain.

### Pain

All three studies used a 100-mm visual analog scale (VAS) to assess the intensity of TMD-related pain at intervals ranging from 2 weeks to 6 months. Very low-quality evidence showed a nonsignificant benefit of hypnosis/relaxation therapy for reducing pain compared to no/minimal treatment (mean difference [MD] = -9.16 mm; 95% CI: -23.47 to 5.14 mm;  $P = .21$ ); the median pain represented by the VAS score in the control group at baseline was 51 mm and 30% was considered as the estimate of the MID (15.3 mm) (Fig 2, Table 4). The pooled result showed considerable statistical heterogeneity ( $\chi^2 = 8.17$ ,  $P = .42$ ;  $I^2 = 76\%$ ).

### Maximal Pain

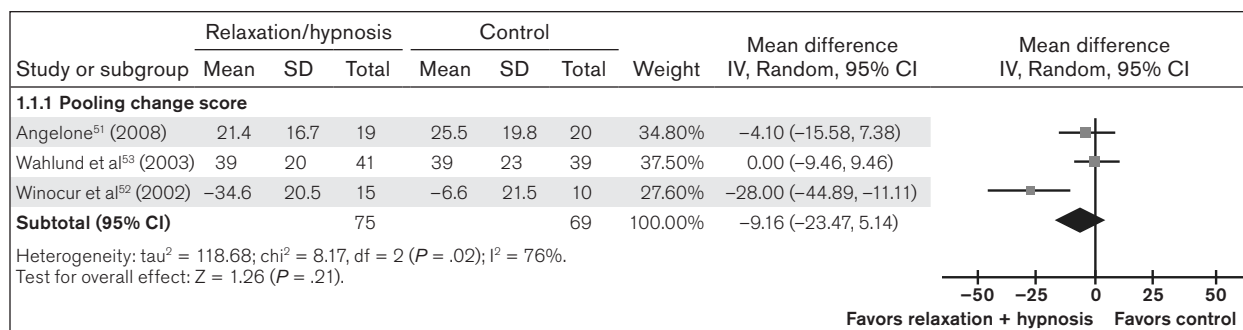
One study<sup>52</sup> reported maximal pain (the worst pain patients experienced during the last 6 months on VAS). Low-quality evidence found a significant benefit of hypnosis/relaxation therapy for reducing maximal pain compared to no/minimal treatment (MD = -28.33; 95% CI: -44.67 to -11.99;  $P = .007$ ).

### Active (Voluntary) Maximal Mouth Opening

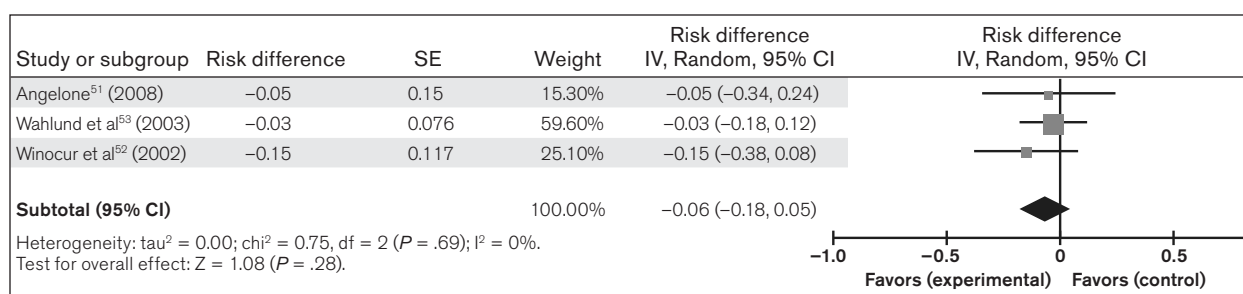
One study<sup>52</sup> reported the effect of relaxation/hypnosis on active (voluntary) maximal mouth opening. Low-quality evidence from this study showed a significant benefit of relaxation/hypnosis compared to no/minimal treatment (MD = -2.63 mm; 95% CI: -3.30 to -1.96 mm;  $P < .001$ ).

### Pressure Pain Threshold

One study<sup>53</sup> reported on the pressure pain threshold on the skin surface over the TMJ and over the masticatory muscles. Relaxation therapy showed no



**Fig 2** Relaxation/hypnosis therapy versus minimal/no treatment in reducing pain.



**Fig 3** Relaxation/hypnosis therapy versus minimal/no treatment on proportion of patients who have an important improvement in pain.

significant effect compared to minimal treatment on increasing the pressure pain threshold for the TMJ (MD = 18.30 kPa; 95% CI: -8.08 to 44.68;  $P = .17$ ) or for the masticatory muscles (MD = 11.80 kPa; 95% CI: -35.30 to 58.90;  $P = .62$ ).

### Patient Subjective Evaluation of the Treatment

One study<sup>53</sup> reported on patients' subjective evaluation of treatment outcome. This measure was composed of six response alternatives: completely well, much better, somewhat better, unchanged, somewhat worse, much worse. Completers who experienced a subjective improvement obtained a pre-post improvement rate ranging between 38% and 68% (mean value 53%) on the pain index score (pain intensity multiplied by pain frequency). The hypnosis/relaxation therapy group had a 35% mean subjective improvement compared to 26% for the no/minimal treatment group. No specific scores were reported at baseline or posttreatment.

### School Absence

One study<sup>53</sup> reported the number of days of patient absence from school during the previous month because of TMD pain. Relaxation therapy reduced school absences per month from  $0.86 \pm 0.98$  to  $0.38 \pm 0.53$  compared to minimal treatment ( $0.08 \pm 0.41$  to  $0.04 \pm 0.20$ ) on a 0 to 31-point scale.

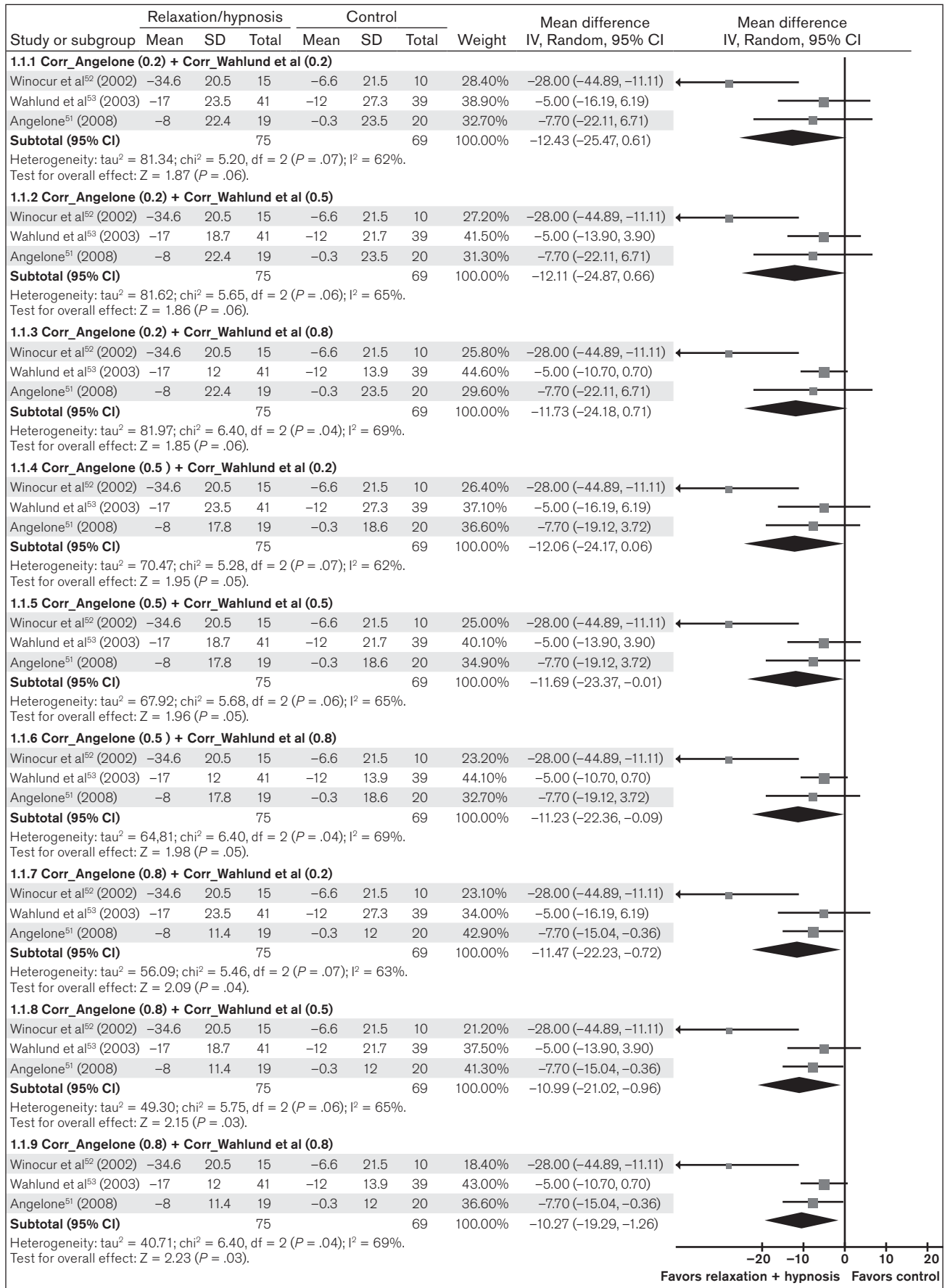
### MID Interpretation

For each eligible study, reviewers dichotomized TMD-related pain by using an MID of 15.3 mm to calculate how many patients experienced a meaningful improvement with hypnosis/relaxation therapy. A meta-analysis pooling RDs derived from the change and posttreatment scores showed 6% of TMD patients experienced a MID in reducing pain with hypnosis/relaxation therapy versus no treatment/minimal treatment (RD = -0.06; 95% CI: -0.18 to 0.05;  $P = .28$ ) (Fig 3).

### Sensitivity Analyses

Hypnosis/relaxation therapy showed a borderline effect on pain reduction compared to no/minimal treatment in the sensitivity analysis using change scores for pooling across studies. Reduction of pain ranged from a MD of -12.43 (95% CI: -25.47 to 0.61;  $P = .06$ ;  $I^2 = 0\%$ ) to a MD of -10.27 (95% CI: -19.29 to -1.26;  $P = .03$ ;  $I^2 = 0\%$ ) with a median MD of -12.06 (95% CI: -24.17 to 0.06;  $P = .05$ ;  $I^2 = 0\%$ ) (Fig 4).

Sensitivity analyses were also performed using the median of the estimated change scores to calculate the proportion of patients who had a meaningful improvement in pain. The meta-analysis showed 8% of individuals experienced an important reduction in pain with hypnosis/relaxation therapy (RD = -0.08; 95% CI: -0.18 to 0.01;  $P = .08$ ;  $I^2 = 0\%$ ).



**Fig 4** Sensitivity analysis of imputed standard deviation and a range of correlation coefficients on relaxation/hypnosis therapy versus minimal/no treatment on the proportion of patients who had an important improvement in pain.



## Discussion

This is the first systematic review and meta-analysis evaluating hypnosis/relaxation in patients with TMD. Low-quality evidence showed that hypnosis/relaxation therapy may reduce maximal pain and improve maximal mouth opening, but not TMJ or masticatory muscle pressure pain threshold. There was low-quality evidence that hypnosis/relaxation therapy does not reduce pain. Hypnosis/relaxation treatment improved both patient subjective evaluation of the treatment and school absence compared to no/minimal treatment.

### Sensitivity Analysis Regarding Pain

The conclusion from the primary analysis showed that hypnosis/relaxation therapy had no effect on reducing pain; however, there was a suggested borderline effect in the sensitivity analysis using change scores for pooling across studies. The discrepancy may have resulted from a number of possibilities:

1. Using correlation coefficient imputation to calculate and pool change scores corrected the baseline imbalances between treatment and control group within studies. On the other hand, however, imputed correlation coefficient caused the imprecision of the estimation on the SDs for change scores in two out of three included studies. The imprecision can substantially influence the pooled result.
2. Since the results did not remain robust under different methods of analysis, the pooled result from the meta-analysis should be interpreted cautiously. It is unclear if hypnosis/relaxation therapy has a potential beneficial effect in reducing pain.
3. There was a discrepancy between the pooled analysis consisting of end scores and change scores and sensitivity analyses of imputed change scores on the significance of benefit. However, when the distribution of important effect was measured, the estimates were virtually identical in that there seemed to be little to no important benefit to patients using relaxation therapy.

### Comparing Findings with Other Studies

Orlando et al<sup>91</sup> conducted a narrative review on biobehavioral therapies in the treatment of TMD, which included hypnosis/relaxation therapy. A nonrandomized study and case report included in the review<sup>55,56</sup> suggested that hypnosis/relaxation therapy could reduce pain, muscle sensitivity to palpation, and anxiety and depression compared to minimal or no treatment. A 2010 overview of all published systematic reviews and meta-analyses in the management of TMD<sup>57</sup> suggested a potential beneficial effect of using hypnosis/relaxation for reducing pain. However, all of the included reviews only synthesized the evidence quali-

tatively and were not specific for hypnosis/relaxation. A Cochrane review of three RCTs suggested a benefit of hypnosis for relieving pain associated with pediatric dentistry but did not complete a meta-analysis due to differences in intervention and control arms among eligible studies.<sup>58</sup>

### Strengths and Limitations of the Systematic Review

Strengths of this systematic review include a comprehensive search, independent and duplicate screening and reviewing of articles, and assessment of confidence in estimates by using the GRADE criteria. This review also reported all patient-important outcomes and presented the proportion of patients who had an important reduction on pain by applying the method of dichotomizing MID on TMD-related pain.

There were also limitations in the systematic review. All included studies suffered from a high risk of bias, including limited descriptions of study design and randomization, and limitations of imprecision and inconsistency, resulting in low or very low confidence in estimates of effect. Blinding patients in studies of hypnosis/relaxation therapy is challenging and it is impossible to blind health care providers. Blinding patients would only be possible if there was a sham treatment as a control and patients were naive to hypnosis/relaxation therapy. Secondly, the small number of studies identified precluded the ability to perform subgroup analyses to explore the heterogeneity across studies, or to explore for the presence of publication bias. Potential sources of variability in study results include length of follow-up times ranging from 2 weeks to 6 months, differences in TMD subtypes, and differences in the therapy administered. Thirdly, the reviewers estimated the MID for TMJ or masticatory muscle pain on the VAS with guidance from the literature,<sup>8,42</sup> since there is no established measure.

### Implications for Clinical Practice and Future Research

The low quality and very low quality of the evidence provided by the included studies reduce confidence in the strength of inferences from the findings. There is a need for RCTs with adequate protection against bias and larger sample sizes to confirm or refute the effectiveness of hypnosis/relaxation treatment in patients with TMD. This systematic review has emphasized the need for improved reporting of randomization generation, allocation concealment, and blinding of participants and personnel, as well as reporting functional outcomes and enrolling larger sample sizes. Included studies in the review reported functional outcomes such as pain, school absence, maximal mouth opening, etc. Although these outcomes could infer functional outcomes, these were

not a direct measure of function. Trialists assessing hypnosis/relaxation therapy for TMD should capture and report patient-important outcomes and measurement of practical functional tasks, such as quality of life and patients' eating ability. Finally, research is required to establish the MID in pain reduction among patients suffering from TMD.

## Conclusions

Three studies rated as having a high risk of bias and providing only low and very low quality of evidence suggest that hypnosis/relaxation therapy has a beneficial effect on reducing maximal pain and improving patients' active maximal mouth opening, but that it does not affect pain or TMJ or masticatory muscle pressure pain threshold in patients with TMD. The impact of hypnosis/relaxation therapy on practical functional tasks remains uncertain.

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