

# The effectiveness of splint therapy in patients with temporomandibular disorders

## A systematic review and meta-analysis

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**T**emporomandibular disorders (TMDs) are characterized by pain in the temporomandibular joint (TMJ) area, masticatory muscles and associated musculoskeletal structures in the head and neck.<sup>1</sup> Patients with these conditions experience pain, functional limitations of the mandible or clicking in the TMJ region during motion.<sup>2,3</sup> The findings of studies addressing the frequency and characteristics of TMD suggest it is not uncommon,<sup>1-4</sup> typically affects people between the ages of 20 and 50 years and occurs more frequently in women than in men.<sup>1,5,6</sup>

Management of TMD varies widely; current strategies include exercise, pharmacological interventions (such as nonsteroidal anti-inflammatory drugs, muscle relaxants or narcotic analgesics), acupuncture, intra-articular injections with anesthetics or corticosteroids, psychological interventions (such as relaxation techniques and stress management), surgery and splint therapy.<sup>2,7,8</sup> A 1990 survey of a random sample of 10,000 members of the American Dental Association (with a 25 percent response rate) identified splint therapy as the most

### ABSTRACT

**Purpose.** The authors conducted a systematic review of all published randomized controlled trials in which investigators compared the effectiveness of splint therapy with that of minimal or no treatment in patients with temporomandibular disorders (TMDs).

**Types of Studies Reviewed.** The authors searched MEDLINE, Embase and the Cochrane Central Register of Controlled Trials for studies published from inception of each database through August 2011. In eligible studies, investigators enrolled adult patients with TMDs and assigned them randomly to splint therapy or a control group receiving minimal or no treatment.

**Results.** Of 1,567 potentially eligible studies, 11 proved eligible and were included. Moderate-quality evidence suggests that splint therapy reduced pain in the temporomandibular joint (TMJ) area (standardized response mean = -0.93, 95 percent confidence interval [CI], -1.33 to -0.53; risk difference for having continued pain = -0.35, 95 percent CI, -0.21 to -0.46; mean change on the 100-millimeter visual analog scale = -11.5 mm, 95 percent CI, -16.5 mm to -6.6 mm). Low to very low quality of evidence showed no significant differences between the splint therapy and control groups in terms of quality of life or depression. None of the trial reports described effect on function.

**Conclusions.** Although overall results are promising for the reduction of pain, establishing the role of splints for patients with TMDs will require large trials with stronger safeguards against bias.

**Key Words.** Temporomandibular disorders; temporomandibular joint; myofascial pain; craniomandibular disorders; splint; appliance; meta-analysis.

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frequently used treatment for TMD by both general practitioners and dental specialists.<sup>9</sup> Using data from 1990, Pierce and colleagues<sup>10</sup> estimated that approximately 3 million splints were made per year, at a cost of approximately \$990 million, in the United States.

Various designs of appliances are used in the management of TMD, including stabilization and anterior repositioning appliances.<sup>11,12</sup> Stabilization splints also are known as Michigan splints, Tanner appliances, Fox appliances or centric relation appliances. They usually are made of processed hard acrylic, are worn on the teeth like a retainer and are designed to provide a temporary and ideal occlusion, improve the alignment of the upper and lower teeth, reduce abnormal muscle function and protect teeth from jaw clenching.<sup>12-15</sup> Less expensive soft stabilization appliances also are available, but they require adjustment for comfort and efficacy, as do hard acrylic appliances.<sup>11</sup> Anterior positioning appliances improve the disk-condyle relationship and biomechanics of joint function by repositioning the mandible and condyle anteriorly.<sup>11</sup> Dentists usually advise patients to wear these splint appliances at night; at regular intervals, dentists evaluate patients to adjust the splint and to ensure that a consistent jaw relationship is reached.<sup>11,12,16</sup>

Authors have published two meta-analyses in which they evaluated splint therapy in patients with TMD. In the first, a search of literature published through 2001, investigators found low-quality evidence from four trials suggesting that the use of occluding splint therapy may be beneficial for reducing pain in the TMJ area compared with receiving minimal treatment (a clinician visit without treatment) or no treatment.<sup>16</sup> Researchers in the second meta-analysis, a search of the literature published through 2006, compared the results of the three trials they evaluated and found no statistically significant difference between splint therapy and minimal or no treatment.<sup>11</sup> Both reviews had important limitations. Investigators in the former review evaluated patients with pain dysfunction syndrome only, those in the latter review excluded three studies owing to their inability to convert effects into comparable summary estimates, and both reviews excluded trials published subsequent to their end-of-search dates.<sup>11,16</sup>

In light of the paucity of systematic reviews in this area, we conducted a systematic review and meta-analysis of published randomized controlled trials (RCTs) to determine the effect of splint therapy in patients with TMD. Our aims were to evaluate whether splint therapy is more effective

than minimal or no treatment in patients with TMD and to produce intuitively understandable and statistically robust summary estimates for the pooled meta-analysis findings that will help inform relevant decision makers about the magnitude of effect of splint therapy.

## METHODS

**Eligibility criteria.** Eligible studies met the following criteria: random allocation of adult patients to a splint therapy arm or a control arm consisting of minimal or no treatment; inclusion of patients with TMD or an equivalent condition. Eligible disorders included cranio-mandibular dysfunction, myofascial pain dysfunction syndrome localized to the jaw, myofascial pain localized to the jaw and mandibular dysfunction. We used the classification system used by Gray and colleagues<sup>12</sup> and, accordingly, classified splint therapy as use of any of the following: stabilization splint, Michigan splint, Tanner appliance, Fox appliance, centric relation appliance, soft appliance or anterior repositioning appliance.

**Information sources and search.** We conducted a computerized search of databases to identify relevant RCTs, in any language, by conducting a systematic search of MEDLINE, Embase and The Cochrane Central Register for Controlled Trials from inception of each database through Aug. 22, 2011. An experienced academic librarian collaborated in the development of the literature search strategy used with each electronic database. Reviewers (S.E. and L.M.) also scanned the reference lists of all eligible RCTs and review articles, then searched [www.clinicaltrials.gov](http://www.clinicaltrials.gov) to identify additional studies.

**Study selection.** Two reviewers (S.E. and L.M.) screened titles and abstracts of identified published citations, independently and in duplicate, using a standardized, pilot-tested screening form. The same reviewers independently applied eligibility criteria to the full text of potentially eligible studies. A general dentist (A.C.-L.), an orthodontist and an endodontist (L.M.) independently reviewed the patient population and splint therapy for each study, masked as to study results, to confirm eligibility.

**Data collection process and data items.** The reviewers (S.E. and L.M.) used standard-

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**ABBREVIATION KEY.** **CRPS:** Complex regional pain syndrome. **GRADE:** Grading of Recommendations, Assessment, Development and Evaluation. **NR:** Not reported. **RCT:** Randomized controlled trial. **TMD:** Temporomandibular disorder. **TMJ:** Temporomandibular joint. **VAS:** Visual analog scale.

ized forms and a detailed instruction manual to extract data independently and in duplicate from each eligible study. Data extracted included demographic information, methodology, splint therapy and control arm details, and all reported patient-important outcomes. We found substantial diversity in the outcome measures used among eligible trials.<sup>17-27</sup> Three reviewers (S.E., L.M. and J.W.B.) independently grouped outcomes into common domains and reached consensus through discussion for three outcome categories: pain, quality of life and depression. They excluded a number of outcomes as not patient-important (jaw range of motion, occlusal contact changes, joint crepitus) or not sufficiently important (TMJ dysfunction, medication use, nonpain somatization).

**Risk of bias in individual studies.** Two reviewers (S.E. and L.M.) assessed risk of bias for each eligible trial by using a modified Cochrane risk-of-bias instrument,<sup>28</sup> with response options of “definitely yes,” “probably yes,” “probably no” and “definitely no.” We ultimately assigned trials in the “definitely yes” and “probably yes” categories a high risk of bias and those in the “probably no” and “definitely no” categories a low risk of bias.<sup>29</sup> The reviewers resolved disagreements by means of discussion, and an arbitrator (J.W.B.) adjudicated unresolved disagreements. We attempted to contact corresponding authors from seven studies in which details regarding the risk of bias (that is, information on allocation concealment, masking and number of participants lost to follow-up) were unclear or not reported.<sup>17-23</sup> The remaining four studies<sup>24-27</sup> did not include contact information for the authors. Table 1<sup>17-27,30-35</sup> shows all the characteristics of the included studies.

**Statistical analysis.** We measured agreement at the stage of full-text review and interpreted the chance-independent agreement ( $\Phi$ ) statistics for selection of eligible studies.<sup>36,37</sup> Values of 0 to 0.20 represented slight agreement, of 0.21 to 0.40 represented fair agreement, of 0.41 to 0.60 represented moderate agreement, of 0.61 to 0.80 represented substantial agreement and of greater than 0.80 represented almost perfect agreement.<sup>38</sup>

We used the means and standard deviations (SDs) of the change scores (change from baseline to longest follow-up time point) for our pooled analysis. When change scores were not provided, we subtracted the baseline score from the end-of-study score to obtain the mean and imputed the SDs by using a correlation coefficient of 0.78. This correlation coefficient was calculated from the SDs of the baseline score, end-of-study score and

change score,<sup>39</sup> available from one of the eligible studies in our review.<sup>17</sup> We conducted sensitivity analyses to investigate the impact of using correlation coefficients of 0.1 and 0.9 on our findings.

We pooled data from all outcome assessments that measured a patient-important outcome category. If investigators had used more than one instrument within a trial to measure the same outcome category, we chose only one assessment based on the following prioritization, in descending order of importance: most commonly used instrument across trials, validated instrument and instrument with the most precise estimation of effect. To compare and pool data across trials, we calculated the standard mean difference (SMD), the difference in the change scores between groups from the longest follow-up time reported to baseline divided by the SD of the change.<sup>40</sup> When outcomes were reported as dichotomies, we calculated the odds ratios (ORs) and converted them to SMDs using this formula:  $SMD = (\sqrt{3}/\pi)(\ln OR)$ .<sup>41</sup> This allowed for comparison between trials in SD of change units. We considered an SMD of 0.2 to represent a small difference, 0.5 a medium difference and 0.8 a large difference.<sup>42</sup>

To facilitate interpretation for clinicians and other stakeholders, we converted the pooled SMD to a risk difference (RD) and, if an anchor-based minimally important difference was available, to natural units on the most familiar instrument to decision makers.<sup>43,44</sup> To calculate the RD, we used 0.6 for the control group risk of continued pain, which we derived from the results of eligible trials in which investigators measured pain as a dichotomous outcome.<sup>18,20,21,25-27</sup> To test this estimate, we performed a sensitivity analysis to compare differences in the RDs by using 0.2 and 0.8 as the control group risk of continued pain. We converted the SMD to natural units using this formula:  $MD = SMD \times SD(MD)$ , where MD stands for the mean difference, SMD the standard mean difference and  $SD(MD)$  the standard deviation of the MD.<sup>41</sup> The visual analog scale (VAS) was the instrument most familiar to decision makers for measuring pain; the  $SD(MD)$  on a 100-mm VAS was 12.4 mm. We obtained the associated measure of precision by converting the confidence limits of the SMD to natural units, using the same formula.

We used random-effects meta-analyses, which are conservative in that they take both within-study and between-study variability into account.<sup>45,46</sup> We examined heterogeneity by using both a  $\chi^2$  test and the  $I^2$  statistic, the percentage of among-study variability that is due to true differences between studies (heterogeneity)

TABLE 1

**Characteristics of included studies.**

SOURCE (COUNTRY OF STUDY)	SAMPLE SIZE		AGE IN YEARS, MEAN (SD*)		CONDITION	SPLINT THERAPY	PATIENT-IMPORTANT OUTCOME MEASURES† RECORDED
	Test	Control	Test	Control			
<b>Lundh and Colleagues, 1985<sup>27</sup> (Sweden)</b>	23	23	NR‡	NR	Disk displacement with reduction	Stabilization splint	Palpatory tenderness laterally over the joint, palpatory tenderness of lateral pterygoid muscle, palpatory tenderness of temporal muscle, palpatory tenderness of superficial masseter muscle
<b>Lundh and Colleagues, 1988<sup>26</sup> (Sweden)</b>	21	22	NR	NR	Temporomandibular disorder (TMD)–associated muscle pain, disk displacement with reduction	Stabilization splint	Pain during chewing, pain during protrusion, palpatory tenderness laterally over the joint, palpatory tenderness of lateral pterygoid muscle, palpatory tenderness of insertion of temporal muscle, palpatory tenderness of anterior portion of temporal muscle, palpatory tenderness of superficial masseter muscle
<b>Johansson and Colleagues, 1991<sup>20</sup> (Sweden)</b>	15	15	NR	NR	TMD with facial pain and headache	Stabilization splint	Changes in facial pain and headache, score on pain intensity visual analog scale <sup>§</sup> (VAS)
<b>List and Colleagues, 1992<sup>24</sup> (Sweden)</b>	30	20	39 (11)	48 (13)	Painful temporomandibular joint (TMJ) disk displacement without reduction	Stabilization splint	Activities of Daily Living Scale, <sup>¶</sup> pain intensity VAS, frequency of pain, pressure pain threshold
<b>Lundh and Colleagues, 1992<sup>25</sup> (Sweden)</b>	25	26	NR	NR	TMD-associated muscle pain	Stabilization splint	Changes in pain at maximal mouth opening, changes in pain at protrusion, changes in pain in affected joints on movements toward other side, changes in palpatory tenderness of masseter muscle

\* SD: Standard deviation.  
 † Assessment measures nonvalidated except for those for which references are cited.  
 ‡ NR: Not reported.  
 § Source: Carlsson.<sup>30</sup>  
 ¶ Source: List and Helkimo.<sup>31</sup>  
 # Source: Radloff.<sup>32</sup>  
 \*\* Source: Pollock and colleagues.<sup>33</sup>  
 †† Source: Ferrans and Powers.<sup>34</sup>  
 ‡‡ Source: Ware and colleagues.<sup>35</sup>

rather than sampling error (chance).<sup>47,48</sup> Using the Cochrane Collaboration guidelines,<sup>49</sup> we considered heterogeneity of 0 to 40 percent to fall into the “might not be important” category, 30 to 60 percent to be moderate heterogeneity, 50 to 90 percent to be substantial heterogeneity and 75 to 100 percent to be considerable heterogeneity. The Cochrane Collaboration has proposed overlapping categories to convey that there are no strict cutoffs for interpreting heterogeneity, and that the decision will depend on the magnitude and direction of effects and the strength of evidence for heterogeneity.<sup>50</sup>

We generated two a priori hypotheses to explain variability between studies:  
 ■ studies with high risk of bias will demon-

strate larger effects than will studies with low risk of bias;

■ treatment effects in studies with longer follow-up times will be fewer than those in studies with shorter follow-up times.

As a threshold for high risk of spurious subgroup findings, we chose five studies (that is, if there were fewer than five studies, we did not conduct subgroup analyses). We conducted tests of interaction to establish if the effect size from the subgroups differed significantly from each other (according to the method described by Guyatt and colleagues<sup>51</sup>). We conducted a posthoc subgroup analysis to evaluate if studies involving the use of different types of splint therapy had variable effects.

TABLE 1 (CONTINUED)

SOURCE (COUNTRY OF STUDY)	SAMPLE SIZE		AGE IN YEARS, MEAN (SD*)		CONDITION	SPLINT THERAPY	PATIENT-IMPORTANT OUTCOME MEASURES† RECORDED
	Test	Control	Test	Control			
<b>Turk and Colleagues, 1993<sup>22</sup> (United States)</b>	30	20	35.9 (9.1)	33.1 (8.0)	TMD muscle pain	Stabilization splint	Pain severity scale; muscle palpation pain index; pain in the following muscle sites examined bilaterally: origin and insertion sites of the masseter, temporalis and internal pterygoid muscles, and one palpation site for the external pterygoid; Epidemiologic Studies- Depression <sup>‡</sup> ; and Profile of Mood States—Depression Scale <sup>**</sup>
<b>Dao and Colleagues, 1994<sup>18</sup> (Canada)</b>	20	19	29.3 (NR)	31.8 (NR)	TMD muscle pain in general population	Stabilization splint	Pain intensity VAS, pain unpleasantness VAS, Quality of Life Index <sup>††</sup>
<b>Wright and Colleagues, 1995<sup>23</sup> (United States)</b>	10	10	34 (NR)	31 (NR)	TMD muscle pain	Soft splint	Pressure algometer score
<b>Al Quran and Kamal, 2006<sup>17</sup> (Jordan)</b>	38	38	31.8 (NR)	36 (NR)	Myogenous TMD	Stabilization splint	Pain severity VAS
<b>Fischer and Colleagues, 2008<sup>19</sup> (Germany)</b>	10	10	51.4 (12.2)	43.5 (15.2)	Complex regional pain syndrome type I, TMD	Stabilization splint	10-point numerical rating pain scale, SF-36 health survey, <sup>‡‡</sup> temporomandibular muscle index
<b>Tecco and Colleagues, 2010<sup>21</sup> (Italy)</b>	20	10	NR	NR	TMD-associated disk displacement with reduction	Anterior repositioning appliance	Pain, muscle pain, subjective relief VAS

**Confidence in effect estimates.** The reviewers, independently and in duplicate, evaluated the confidence in effect estimates (quality of evidence) for all outcomes by using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) rating system.<sup>51</sup> This system categorizes evidence from RCTs as warranting high confidence, but confidence may be downgraded as a result of limitations in one or more of the following categories: risk of bias, consistency, directness, imprecision and reporting bias.<sup>52</sup> After considering these categories, the reviewers categorized the confidence in effect estimates for each outcome as follows: high quality of evidence, implying that they were very confident that the true effect lay close to that of the estimate of the effect; moderate quality of evidence, implying that they were moderately confident in the effect estimate and the true effect was likely to be close to the estimate of the effect, but there was a possibility that it was substantially different; low quality of evidence, implying that their confidence in the effect estimate was limited and the true effect may have been substantially different

from the estimate of the effect; and very low quality of evidence, implying that they had very little confidence in the effect estimate and the true effect was likely to be substantially different from the estimate of effect.<sup>51</sup>

We performed all statistical analyses using The Cochrane Collaboration software Review Manager (RevMan), version 5.1.2 (The Cochrane Collaboration, Oxford, England). We rated quality of evidence by using GRADEpro software, version 3.6 (The Cochrane Collaboration).

## RESULTS

We identified 1,567 potentially eligible studies and retrieved 70 articles in full text. Fifty-five articles did not meet inclusion criteria, four articles were unavailable and 11 trials were eligible and included in our study<sup>17-27</sup> (Figure 1). According to  $\Phi$ , the mean chance-independent agreement was 0.78 (range, 0.46-0.92), representing substantial agreement. We established contact with corresponding authors from three<sup>18,21,23</sup> of the seven trials that provided contact information; all clarified details regarding allocation concealment, masking and loss to

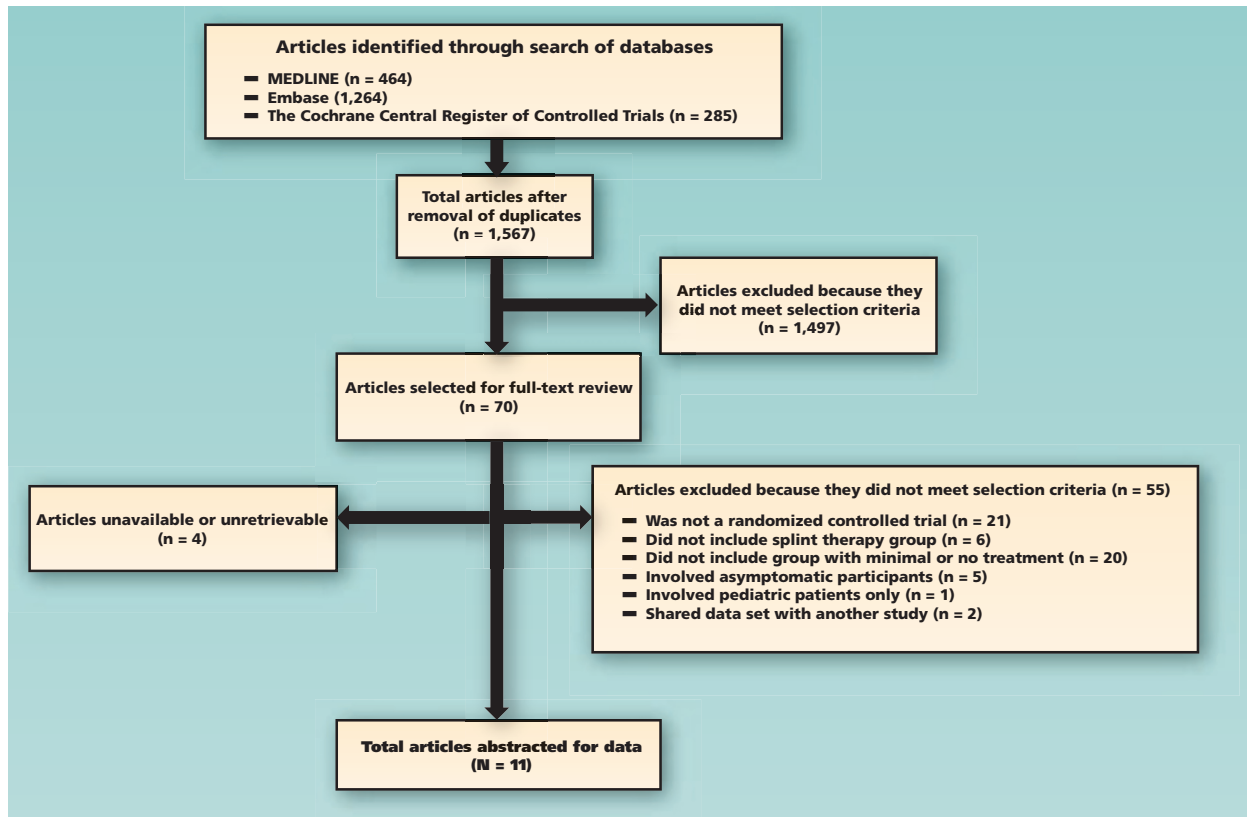


Figure 1. A flow diagram of the literature search process.

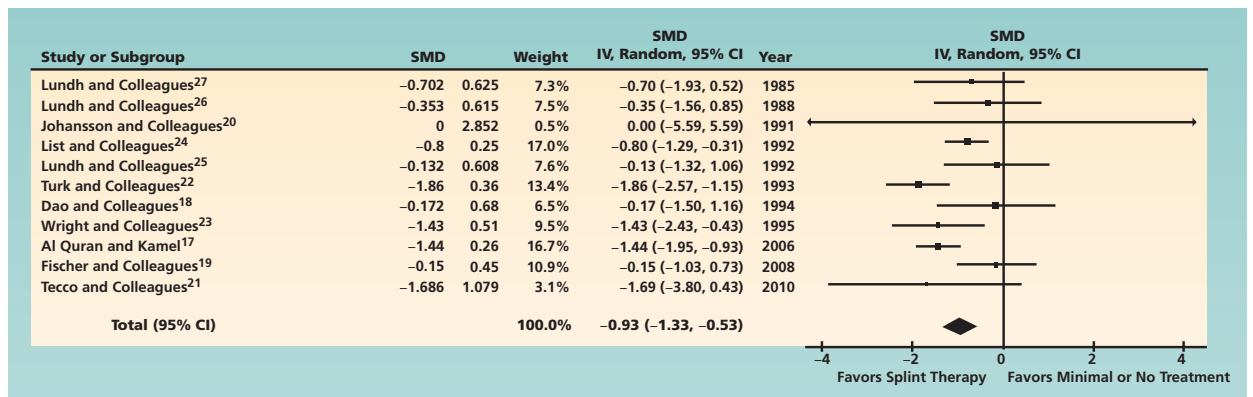


Figure 2. Forest plot of the effect of splint therapy versus minimal or no treatment in reducing pain. CI: Confidence interval. IV: Inverse variance. SMD: Standard mean difference. SE: Standard error. Heterogeneity:  $\tau^2 = 0.18$ ;  $\chi^2_0 = 18.84$ ,  $P = .04$ ;  $I^2 = 47$  percent. Test of overall effect:  $z = 4.53$  ( $P < .01$ ).

follow-up. We received no responses from the authors of the remaining four studies.<sup>17,19,20,22</sup>

Table 1 describes the characteristics and outcome measures reported in the 11 eligible trials. Protection against bias generally was poor. Researchers in two studies reported concealment of allocation. Masking of patients was not always possible. Health care providers were masked in five trials, data collectors in four trials, outcome assessors in five trials and data

analysts in one trial. Authors of three trials reported loss to follow-up (2.5 percent,<sup>22</sup> 3 percent<sup>18</sup> and 4.8 percent,<sup>23</sup>) and the authors of the other eight studies made no specific statement regarding loss to follow-up. No investigators reported outcomes in their methods that were not reported in their results. Reporting of outcomes was inconsistent across trials. We did not downgrade the overall quality on the basis of suspicion of publication bias (Table 2).

TABLE 2

Risk of bias in included studies.									
STUDY AUTHOR, YEAR	TYPE OF BIAS*								
	Allocation Concealment (Selection Bias)	Masking of Participants	Masking of Health Care Providers	Masking of Data Collectors	Masking of Outcome Assessment (Detection Bias)	Masking of Data Analysts	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Other Bias
Lundh and Colleagues, 1985 <sup>27</sup>	—	—	—	—	—	—	+	+	+
Lundh and Colleagues, 1988 <sup>26</sup>	—	—	+	+	+	—	+	+	+
Johansson and Colleagues, 1991 <sup>20</sup>	—	—	+	—	+	—	+	+	+
List and Colleagues, 1992 <sup>24</sup>	—	—	—	—	—	—	+	+	+
Lundh and Colleagues, 1992 <sup>25</sup>	—	—	—	—	—	—	+	+	+
Turk and Colleagues, 1993 <sup>22</sup>	—	—	—	—	—	—	—	+	+
Dao and Colleagues, 1994 <sup>18</sup>	—	—	+	+	+	+	—	+	+
Wright and Colleagues, 1995 <sup>23</sup>	+	—	+	+	+	—	+	+	+
Al Quran and Kamal, 2006 <sup>17</sup>	—	—	—	—	—	—	—	+	+
Fischer and Colleagues, 2008 <sup>19</sup>	+	—	+	+	+	—	+	+	+
Tecco and Colleagues, 2010 <sup>21</sup>	—	—	—	—	—	—	+	+	+

\* + indicates presence of bias; — indicates absence of bias.

**Outcomes. Pain.** The pooled results from 11 trials showed that splint therapy had a substantial effect on reducing pain (SMD = -0.93; 95 percent CI, -1.33 to -0.53;  $I^2 = 47$  percent; heterogeneity  $P = .04$ ) (Figure 2). The RD of having continued pain was -0.35 (95 percent CI, -0.21 to -0.46). The calculated natural units on a 100-mm VAS scale were -11.5 mm (95 percent CI, -16.5 mm to -6.6 mm). Our a priori and posthoc hypotheses failed to explain heterogeneity between studies.

**Quality of life.** The pooled results from two trials showed no significant effect of splint therapy on quality of life (SMD = -0.09; 95 percent CI, -0.51 to 0.32;  $I^2 = 0$  percent; heterogeneity  $P = .77$ ).

**Depression.** The pooled results from two

trials showed no significant effect of splint therapy on depressive symptoms (SMD = -0.20; 95 percent CI, -1.75 to 1.35;  $I^2 = 87$  percent; heterogeneity  $P = .006$ ).

**Sensitivity analyses.** We found no important differences in SMDs when we used 0.1 and 0.9 as the correlation coefficients to calculate change scores. We found important differences in RDs for pain when we substituted 0.2 and 0.8 for the control group risk of continued pain. With a 0.8 control group risk, the RD of continued pain was -0.34; with a 0.2 control group risk, the RD of continued pain was -0.16. We found no important differences in our SMD when we removed a trial in which investigators evaluated patients with complex regional pain syndrome (CRPS) and TMDs.<sup>19</sup>

TABLE 3

**GRADE\* rating system evidence profile: effectiveness of splint therapy versus minimal or no treatment in patients with temporomandibular disorders.**

OUTCOME (TYPE)	QUALITY ASSESSMENT						
	No. of Participants (Study Type), Length of Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence
<b>Pain (Critical)</b>	455 (11 RCT <sup>§</sup> ), six to 52 weeks	Serious <sup>¶</sup> owing to lack of reporting allocation concealment and masking of personnel	No serious inconsistency; $I^2 = 47\%$ ; heterogeneity $P = .04$	No serious indirectness	No serious imprecision	Undetected	Moderate owing to risk of bias
<b>Quality of Life (Critical)</b>	90 (two RCTs), seven to eight weeks	Serious <sup>#</sup> owing to lack of reporting allocation concealment and masking of personnel	No serious inconsistency; $I^2 = 0\%$ ; heterogeneity $P = .77$	No serious indirectness	Serious <sup>‡</sup> owing to less-than-optimal population size	Undetected	Low owing to risk of bias and imprecision
<b>Depressive Symptoms (Important)</b>	82 (two RCTs), seven to eight weeks	Serious <sup>**</sup> owing to lack of reporting allocation concealment and masking of personnel	Serious inconsistency; $I^2 = 87\%$ ; heterogeneity $P = .06$	No serious indirectness	Serious <sup>††</sup> owing to less-than-optimal population size	Undetected	Very low owing to risk of bias, inconsistency and imprecision

\* GRADE: Grading of Recommendations, Assessment, Development and Evaluation (Guyatt and colleagues<sup>51</sup>).

† SMD: Standard mean difference.

‡ CI: Confidence interval.

§ RCTs: Randomized controlled trials.

¶ Investigators in nine of the 11 studies did not report allocation concealment; in six studies did not report masking of health care providers; in seven studies did not report masking of data collectors; in six studies did not report masking of outcome assessors; and in one study reported masking of data analysts.

# Fischer and colleagues<sup>19</sup> had no serious limitations. List and colleagues<sup>24</sup> did not report allocation concealment or masking of health care providers, outcome assessors, data collectors and data analysts.

\*\* Turk and colleagues<sup>22</sup> did not report allocation concealment or masking of health care providers, outcome assessors, data collectors and data analysts.

†† 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 standard deviation, representing a minimal effect).

**DISCUSSION**

Our systematic review and meta-analysis yielded moderate-quality evidence that splint therapy has a substantial effect on reducing pain among patients with TMDs (Table 3). Low-quality and very low-quality evidence showed no significant effect on quality of life or depression, respectively (Table 3).

**Strengths of the review.** The strengths of our review include a systematic and replicable approach and a comprehensive and transparent search strategy. We conducted independent and duplicate eligibility assessment and data extraction, and we developed a priori subgroup hypotheses to explain heterogeneity. Our focus was on patient-important outcomes, for which we provided summaries of effects with specification and rationale for confidence in the estimate of effect.

In addition, before our efforts, the most com-

prehensive systematic reviews were a 2004 Cochrane Collaboration review in which researchers evaluated four RCTs to determine the effectiveness of occluding splint therapy compared with minimal or no treatment in patients with jaw-related pain dysfunction syndromes (under the umbrella of TMDs)<sup>16</sup> and a 2010 review in which the authors conducted a meta-analysis of three RCTs to determine the effectiveness of stabilization appliances compared with no treatment in patients with TMDs.<sup>11</sup> Our review includes seven additional studies.

**Limitations of the review.** Our review has limitations. We pooled the study results by longest follow-up time; this ranged, however, from 6.7 weeks to 12 months. We anticipated this as a potential source of heterogeneity and specified differences in follow-up time as an a priori subgroup hypothesis; we found no differences attributable to length of follow-up.



TABLE 3 (CONTINUED)

SUMMARY OF FINDINGS			
Therapy Received, No. of Participants		SMD <sup>†</sup> (95% CI <sup>‡</sup> )	Risk Difference (95% CI) With Splint Therapy
Splint therapy	Minimal or no treatment		
242	213	-0.93 (-1.33 to -0.53)	-0.35 (-0.21 to -0.46) of having no pain compared with having any pain
50	40	0.09 (-0.51 to 0.32)	No significant effect
43	39	-0.20 (-1.75 to 1.35)	No significant effect

In addition, there were different splint designs used in each study. To ensure that we pooled similar interventions, we had three clinical specialists (a general dentist, an orthodontist and an endodontist) confirm the eligibility of splint therapy in the trials independently. We also conducted a posthoc subgroup analysis of the different type of splints used across trials and failed to find important differences. It remains possible, however, that differences in response exist but that our analysis did not have sufficient power to detect these differences. Additionally, although viewpoints differ,<sup>53</sup> it may be possible to differentiate subtypes of TMD reliably, and that the subtypes will respond differently to splint therapy and to different types of splint therapy. For instance, the study by Fischer and colleagues<sup>19</sup> included only patients with CRPS. We conducted a sensitivity analysis excluding Fischer and colleagues' findings and found similar results with and without exclusion of the study. Thus, the results provide no support for the hypothesis that patients with CRPS respond differently to splints than do other patients with TMD. The data available did not permit other subgroup analyses that addressed other subtypes of TMD. Therefore, although the available data do not support the differential response hypothesis, neither do they

exclude the possibility. Further studies of sufficient size, with clear and reproducible classification of TMD subtypes, would be required to satisfactorily address the issue of possible differential response.

There was a lack of uniformity in the measurement of outcomes across the studies. Although three reviewers independently grouped outcomes according to common domains, there could be important differences between instruments.

Finally, the included studies involved the use of multiple measures assessing the same underlying domain within each study. Although we prioritized use of validated instruments, many of the outcomes used in the studies were nonvalidated measures (Table 1) that may have introduced bias in estimating the pooled effect.

**Findings regarding pain reduction.** We conclude that the findings of the eligible studies provide moderate confidence in estimates for reduction of pain; however, it could be argued that the evidence is of only low confidence. Although we did not downgrade for inconsistency, we found moderate heterogeneity by using the  $I^2$ , and the test for heterogeneity suggested a low likelihood of chance explaining variability in results ( $P = .04$ ). Furthermore, although the SMD suggested a large effect in splint therapy reducing pain, rescaling the SMD to natural units suggested a modest effect, and the apparent large risk difference was sensitive to assumptions about the risk of continued pain in patients not treated with splint therapy. Finally, although pain is a patient-important outcome, large improvements in pain may not necessarily translate to commensurate improvements in function.<sup>54</sup> Investigators in none of the studies in this review, however, evaluated function as an outcome measure.

## CONCLUSIONS

Investigators conducting RCTs to evaluate the effectiveness of splint therapy in patients with TMDs should use standardized instruments with known, satisfactory measurement properties to assess patient-important outcomes, including function, and ensure concealment of randomization, masking of those administering outcome measures and of data analysts, and completeness of follow-up. Given the significant amount of funds allocated to splint therapy annually,<sup>10</sup> the limitations in confidence in estimates of pain reduction and the uncertainty regarding the effect of pain on function and other aspects of well-being, further research is required to confirm the role of splint therapy in patients with TMDs. ■

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