Effectiveness of different psychological interventions in reducing fixed orthodontic pain: A systematic review and meta-analysis

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Background/Objective: Pain induced by tooth movement is a common experience for orthodontic patients. The effectiveness of psychological intervention, as a new approach to control pain, has not been fully explored. Hence, this systematic review and meta-analysis is intended to evaluate the analgesic effect of psychological intervention within the week after fixed orthodontic initial arch wire placement.

Methods: A computerised literature search was conducted in the Medline (1966-2019), Embase (1984-2019), Cochrane Library (Issue 1 of 2019), CBMdisk (1978-2019) and CNKI (1994-2019) databases to identify randomised clinical trials (RCTs), which used psychological interventions to relieve pain during fixed orthodontic treatment. Specific inclusion and exclusion criteria were applied to identify relevant articles. The data were extracted independently by two reviewers and a quality assessment was carried out by using the Cochrane Collaboration ‘risk of bias’ tool. Meta-analyses were conducted with fixed or random effects models as appropriate. Statistical heterogeneity was also examined. The RevMan 5.3 software was used for data analysis.

Results: A total of 472 articles were identified, from which nine RCTs were finally included. A meta-analysis revealed that after initial arch wire placement, cognitive behaviour therapy (CBT) and music therapy could significantly reduce pain within three days compared with a control group. In addition, there were no differences in pain reduction between CBT and music therapy within one week. Furthermore, a structured phone and text follow-up could significantly reduce and control pain and had the same effectiveness in pain reduction.

Conclusions: In the short term after initial arch wire placement, all psychological interventions could significantly reduce the intensity of pain without adverse effects. In the current study, there was no significant difference in pain relief between the different psychological interventions. In the future, more high-quality research with consistency in research design is needed for further evaluation.

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Introduction

Pain induced by tooth movement is a common side-effect of orthodontic treatment (OT).1-2 As a major concern for patients, pain can affect compliance and lead to treatment interruption.3 It is known that orthodontic pain generally occurs after initial arch wire placement and reaches a peak around 24 hours after force application, and subsides within one week.4-6 Therefore, the management of pain within the week after initial arch wire placement has vital clinical significance.
Studies have found that initial and delayed pain was caused by hyperalgesia of the periodontal ligament. When a mechanical force is applied to the teeth, an inflammatory reaction is triggered in the periodontal tissue resulting in the release of inflammatory mediators such as prostaglandins, bradykinin, histamine, and serotonin. Previous studies indicate that the levels of prostaglandin-E2 (PGE2) and interleukin-1 (IL-1) are related to the initial intensity of pain after orthodontic force delivery and the delay of pain after 24 hours, respectively. However, there is no universal recommendation on the means of analgesia. In recent years, non-steroidal anti-inflammatory drugs (NSAIDs) and low-level laser therapy (LLLT) have been used to relieve orthodontic pain. However, it is acknowledged that NSAIDs have side-effects such as gastric ulceration, nausea, bleeding disorders and allergy, amongst others. In addition, it is reported that some NSAIDs may diminish the number of osteoclasts by inhibiting the secretion of prostaglandins, therefore slowing orthodontic tooth movement and prolonging treatment. Furthermore, there is no agreement on whether LLLT can relieve orthodontic pain as the appropriate parameters for LLLT in managing pain and avoiding cell viability inhibition are still unclear.

To seek alternatives for orthodontic pain relief, researchers have adopted psychological interventions such as cognitive behaviour therapy (CBT), music therapy, structured telephone contact, and structured text follow-up. Psychological intervention, as a non-invasive, new and safer approach, is a comprehensive concept, carried out under the guidance of psychological theory which aims to make people move towards an expected goal. Studies have shown that alternative psychological interventions control pain through different mechanisms. To date, no systematic review or meta-analysis has specifically evaluated the effect of psychological interventions on orthodontic pain. Therefore, the aim of the present study was to evaluate the effectiveness of psychological interventions on reducing pain after initial arch wire placement during fixed orthodontic treatment (OT).

**Material and methods**

**Protocol and registration**

The present systematic review protocol was listed under the PROSPERO register with the number CRD42018092560.

**Information sources and search strategy**

An open-ended survey of articles published up to January 2019 was performed to find RCTs that used psychological interventions for fixed appliance orthodontic pain reduction through the following electronic databases: Medline (via Pubmed), Cochrane Library (central), Embase, China Biology Medicine disc (CBMdisc), China National Knowledge Infrastructure (CNKI) with no language limit. The Embase database search strategy is provided in Supplemental Table I.

**Eligibility criteria**

The retrieved articles were processed systematically and separately by two reviewers. Any disagreements were resolved by discussion between the reviewers and a third reviewer to reach a definitive decision. Inclusion and exclusion criteria are shown in Table I.

**Data items and collection**

Two authors independently extracted characteristics and outcomes from the included studies using predefined data extraction forms that were piloted on several articles and modified if required. The collected data included the study design and setting, sample description (sample size, age, and sex distribution) and treatment details (appliance type, the kind of control, intervention type, performer, frequency of treatment and treatment time per point). An attempt to contact the original authors was made for any missing information.

**Risk of bias and quality assessment in individual studies**

The ‘risk of bias’ of the included randomised controlled trials (RCTs) was assessed using the Cochrane Collaboration’s ‘risk of bias’ tool. The following domains were considered: random sequence generation, allocation sequence concealment, blinding of outcome assessment, incomplete outcome data,
Supplementary Table I. Embase search strategy.

1. exp Orthodontic appliances/
2. exp Orthodontics, corrective/
3. Orthodontic$.mp.
4. ((tooth or teeth) adj5 move$).mp.
5. or/1-4
6. exp pain/
7. pain management.mp. or exp pain management/
8. pain measurement.mp. or exp pain measurement/
9. (pain or discomfort or uncomfortable).mp.
10. or/5-9
11. psychotherapy.mp. or exp psychotherapy/
12. ((psychology or psychological) adj3 (therap$ or treatment$ or technique$ or technic$ or intervention$)).mp.
13. exp Counseling/
14. Or/11-13
15. cognitive therapy.mp. or exp cognitive therapy/
16. behavior therapy.mp. or exp behavior therapy/
17. ((cognitive or behavior or cognitive behavior or cognitive-behavior) adj3 (therap$ or treatment$ or technique$ or technic$ or intervention$)).mp.
18. Or/15-17
19. exp music therapy/
20. ((music or musical) adj3 (therap$ or treatment$ or technique$ or technic$ or intervention$)).mp.
21. Or/19-20
22. exp relaxation therapy/
23. (relaxation adj3 (therap$ or treatment$ or technique$ or technic$ or intervention$)).mp.
24. or/12-13
25. (Suggestion therapy or text message or phone call or telephone call or mail or email or e-mail).mp.
26. Or/14,18,21,24,25
27. And/5,10,26

Exp: Mesh terms explosion; mp: free terms; $: replaces one or no letters; adj3: The words must be within three words inclusive of each other in the record.

Table I. Embase search strategy

Inclusion criteria
1. Related human clinical trials (RCTs).
2. All subjects began orthodontic treatment with at least one arch wire placement.
3. For psychological interventions, all the subjects were both physically and mentally healthy regardless of race, age and gender, and currently not taking analgesics.
4. Each experiment group patient received only one kind of psychological intervention.
5. Availability of a suitable control group who underwent fixed orthodontic treatment and had initial arch wire placement but did not receive any kind of analgesic interventions.
6. Follow-up periods were defined as short-term (e.g., 2 hours, 6 hours, 12 hours, 24 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days).
7. The outcomes of pain perception were measured by VAS.

Exclusion criteria
1. Studies that not meet the inclusion criteria.
2. Studies that did not relate to this topic.
3. Studies that were related but had a different aim.
4. Abstracts, laboratory studies, descriptive studies, individual case reports, series of cases, reviews, studies of adult patients, retrospective studies, and meta-analyses.
5. Studies including patients who had received previous orthodontic treatment.
6. Studies designed for pain control after orthodontic separator placement.
7. Studies designed for pain control of orthodontic tooth extraction or mucosa or TMD.
8. Studies using other scales to assess patients’ orthodontic pain instead of VAS.
9. Studies in which experiment group patients received more than one kind of psychological intervention.
10. Studies in which subjects had systemic disease or chronic pain or histories of neurologic and psychiatric disorders.
11. Articles that could not be located.

RCTs, randomised controlled trials; CCTs, controlled clinical trials; VAS, visual analog scale; TMD, temporomandibular disorders
selective outcome reporting, and other sources of bias. For all included trials, the risk of bias for each domain was judged as low risk, high risk, or unclear risk. Each RCT was assigned an overall score: low risk (low for all key domains), high risk (high for ≥1 key domain), and unclear risk (unclear for ≥1 key domain).

**Risk of publication bias assessment**

If more than 10 studies were included in the meta-analysis, standard funnel plots and contoured enhanced funnel plots were drawn to identify publication bias.

**Summary measures and synthesis of results**

Data were combined using Review Manager software, version 5.3. Statistical heterogeneity was explored using the chi-square-based Q statistic method and the I² index, with values of 25%, 50%, and 75% corresponding to low, moderate, and high heterogeneity, respectively. The fixed-effects model and the random-effects model were applied to studies according to the I² test, with less than 50% heterogeneity and greater than 50% heterogeneity, respectively. The Tau² test was also calculated for heterogeneity in the random-effects model. A subgroup analysis was performed according to follow-up time points. The original data were transformed by converting centimetres into millimetres if the VAS scores were measured by centimetres. The combined data of the selected studies were expressed as mean differences (MD) and 95% confidence interval (95% CI), which were calculated using continuous data. VAS scores were combined according to similarity.

**Results**

**Study selection**

Figure 1 shows the flow diagram for the selection of the studies and the excluded articles and explains the reasons for the exclusion. A total of 472 studies were identified from the initial search. Of those, 258 unique citations remained after the removal of duplicates. A total of 246 articles were excluded due to titles and abstracts, and three articles were excluded on the basis of their full texts. The reasons are presented in Supplemental Table II. Finally, nine articles were selected for the qualitative evaluation and meta-analysis.21-29

**Study characteristics**

The characteristics of the included studies are shown in Table II. Several psychological interventions were found and identified as cognitive behaviour therapy (CBT), music therapy, a structured phone call follow-up, or a structured text follow-up.21-29 There were several comparisons related to the effectiveness of pain.
Table II. The characteristics of the included studies.

| Study       | Country | Study design | Sample size(I/C) | Participants' age | Male/female ratio | Orthodontic treatment | Control | Intervention | Performer | Frequency of treatment | Treatment time per point |
|-------------|---------|--------------|------------------|-------------------|-------------------|-----------------------|---------|--------------|-----------|------------------------|--------------------------|
| Bartlett 2005 | America | RCT         | 49/54            | 16.1±0.954[I]     | 49/54             | Fixed appliance       | Control | structured telephone call | primary investigator | One                     | NA                       |
| Cozzani 2015 | Italy    | RCT         | 28/26/30         | 13.6±1.7[I]       | 13.5±1.7[Cl]      | Fixed appliance       | Control | structured text message  | Orthodontists           | One                     | One                     |
| Keith 2013   | America  | RCT         | 20/19            | 12.6[I]           | 14.2[I]           | Fixed appliance       | Control | structured text message  | Orthodontists           | One                     | One                     |
| Huang 2016   | China    | RCT         | 12/12/12         | 22±3              | NA                | Fixed appliance       | Control | CBT customized brainwave music | NA                     | daily, 1-7, 14, 30day   | 5min                    |
| Liu 2017     | China    | RCT         | 44/50            | 55/39             | NA                | Fixed appliance       | Control | structured telephone call | Orthodontists           | one                     | NA                      |
| Xu 2013      | China    | RCT         | 68/73            | 11-35             | 53/88             | Fixed appliance       | Control | music                     | patients               | 2h, 6h, 12h, 1d, 2d, 3d | 1h                       |
| Xue 2017     | China    | RCT         | 21/22/24         | 10-19             | 31/36             | Fixed appliance       | Control | structured text message  | Orthodontists           | One                     | NA                      |
| Zhang 2014   | China    | RCT         | 80/82/74/77/76   | 14.8              | 159/230           | Fixed appliance       | Control | CBT Music relaxation placebo | Patients Orthodontists | 2h, 6h, 12h, 1d, 2d, 3d | NA                      |
| Zheng 2016   | China    | RCT         | 47/43/47/48/41   | NA                | 99/127            | Fixed appliance       | Control | CBT Music relaxation placebo | Patients Orthodontists  | 2h, 6h, 12h, 1d, 2d, 3d | NA                      |
reduction: CBT vs control, music therapy vs control, CBT vs music therapy, structured phone follow-up vs control, structured text follow-up vs control, structured phone follow-up vs structured text follow-up. The follow-up periods were two hours, six hours, 12 hours, once a day and seven days after initial arch wire placement.

Risk of bias in studies
The quality evaluation of RCTs is shown in Figures 2 and 3.

Selection bias
All of the included studies were RCTs. Randomisation and allocation concealment were considered adequate in the publications of Cozzani et al., Huang et al., and Keith et al.22-24 Other included studies were identified as having a high risk or were unclear in relation to allocation concealment.21,25-29

Performance and detection bias
Because of the nature of the interventions in the management of orthodontic pain, blinding of the clinicians or psychiatrists could not be performed and therefore was not assessed. However, in the publications of Bartlett et al.,21 Cozzani et al.,22 Huang et al.,23 and Keith et al.,24 blinding was performed in patients and the associated bias was judged as a low risk. In the remaining studies, the bias remained unclear.25-29 In addition, blinding of the assessors was considered adequate in these studies which were judged as having a low risk of bias.22-24 while the bias of the other papers was judged as unclear.21,25-29

Attrition bias
The withdrawal rates were reported clearly in all the included studies. In general, Cozzani et al., Huang et al. and Keith et al.22-24 were judged as having a low risk of bias. Bartlett et al. and Zhang et al. were judged as having a high risk of bias,21,28 while the remainder were judged as having an unclear risk of bias.25-27,29

Results of meta-analysis
The forest plots are summarised in Tables III–VIII and the original forest plots are presented in Supplemental Figures 1–6.

Cognitive behaviour therapy (CBT) vs control group
Two studies on behaviour therapy were included.23,29 According to different periods of pain observation, the meta-analysis was divided into three subgroups:

| Study       | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) |
|-------------|---------------------------------------------|----------------------------------------|----------------------------------------------------------|------------------------------------------------|----------------------------------------|-------------------------------------|
| Bartlett 2005 | -                                           | +                                      | +                                                        | +                                              | -                                      | +                                   |
| Cozzani 2016 | +                                           | +                                      | +                                                        | +                                              | +                                      | +                                   |
| Huang 2016   | +                                           | +                                      | +                                                        | +                                              | +                                      | +                                   |
| Keith 2013   | +                                           | -                                      | +                                                        | +                                              | +                                      | +                                   |
| Liu 2017     | ?                                            | ?                                      | ?                                                        | +                                              | ?                                      | +                                   |
| Xu 2013      | ?                                            | ?                                      | ?                                                        | +                                              | ?                                      | +                                   |
| Xue 2017     | ?                                            | ?                                      | ?                                                        | +                                              | ?                                      | +                                   |
| Zhang 2014   | ?                                            | ?                                      | ?                                                        | +                                              | ?                                      | +                                   |
| Zheng 2016   | ?                                            | ?                                      | ?                                                        | +                                              | ?                                      | +                                   |

Figure 2. Risk of bias graph: review of the author’s judgment about each risk of bias item presented as percentages.

Figure 3. Risk of bias summary: review of the author’s judgment about each risk of bias item for each included study.
### Supplementary Figure 1.
CBT and control groups for meta-analysis results, reported in mean difference (95% confidence interval), show evidence favouring CBT for pain reduction effectiveness daily within a week after activation of fixed orthodontic treatment.

| Study or Subgroup | Mean Difference | 95% CI |
|-------------------|-----------------|-------|
| Huang 2016        | 12.26           | [12.08, 12.44] |
| Zheng 2016        | 11.07           | [10.87, 11.27] |
| Subtotal (55%)    | 11.13           | [10.94, 11.33] |

Test for overall effect: Z = 7.80 (P < 0.0001)

### Supplementary Figure 2.
Music therapy and control groups for meta-analysis results, reported in mean difference (95% confidence interval), show evidence favouring music therapy for pain reduction effectiveness daily within three days after activation of fixed orthodontic treatment.

| Study or Subgroup | Mean Difference | 95% CI |
|-------------------|-----------------|-------|
| Huang 2016        | 22.44           | [22.08, 22.80] |
| Zheng 2016        | 15.65           | [15.39, 15.91] |
| Subtotal (55%)    | 19.05           | [18.69, 19.41] |

Test for overall effect: Z = 9.84 (P < 0.0001)
Supplementary Figure 3. CBT and Music therapy for meta-analysis results, reported in mean difference (95% confidence interval), show both interventions have similar effectiveness of pain reduction within three days after the activation of fixed orthodontic treatment.

| Study or Subgroup | CBT Mean | SD | Total | CBT Mean | SD | Total | Weight | Music Mean | SD | Total | Music Mean | SD | Total | Mean Difference | IV, Random, 95% CI |
|-------------------|---------|---|-------|---------|---|-------|--------|---------|---|-------|---------|---|-------|------------------|------------------|
| 1.3.1 2 hour      |         |   |       |         |   |       |        |         |   |       |         |   |       |                  |                  |
| Zhang 2014        | 12.41   | 9.35 | 60     | 11.02   | 10.65 | 52     | 96.9%  | 0.59    | 0.39 | [2.50, 5.80]    |                  |                  |
| Zhang 2016        | 13.11   | 13.79 | 47     | 12.37   | 10.34 | 43     | 32.4%  | 0.74    | 0.47 | [1.61, 5.51]    |                  |                  |
| Subtotal (95% CI) | 127     | 125 | 600.0% | 169     | 125 | 600.0% | 0.64   | [1.09, 1.17] |                  |                  |
| Heterogeneity: Tau^2 = 0.00, CHI^2 = 0.00, df = 1 (P = 0.66), I^2 = 0% | Test for overall effect: Z = 2.55 (P = 0.23) |                  |                  |
| 1.3.2 6 hour      |         |   |       |         |   |       |        |         |   |       |         |   |       |                  |                  |
| Zhang 2014        | 17.47   | 13.11 | 60     | 15.49   | 12.33 | 52     | 96.9%  | 1.89    | 1.66 | [5.52, 5.50]    |                  |                  |
| Zhang 2016        | 26.29   | 13.14 | 47     | 17.63   | 12.73 | 43     | 31.7%  | 2.65    | 2.70 | [5.03, 3.29]    |                  |                  |
| Subtotal (95% CI) | 127     | 125 | 600.0% | 169     | 125 | 600.0% | 2.19   | [4.62, 5.20] |                  |                  |
| Heterogeneity: Tau^2 = 0.00, CHI^2 = 0.04, df = 1 (P = 0.84), I^2 = 0% | Test for overall effect: Z = 2.43 (P = 0.11) |                  |                  |
| 1.3.3 12 hour     |         |   |       |         |   |       |        |         |   |       |         |   |       |                  |                  |
| Zhang 2014        | 15.57   | 12.41 | 60     | 15.79   | 12.86 | 52     | 96.9%  | 2.79    | 1.12 | [7.73, 5.74]    |                  |                  |
| Zhang 2016        | 21.91   | 14.42 | 47     | 16.15   | 13.60 | 43     | 30.9%  | 5.61    | 0.66 | [11.70, 0.62]   |                  |                  |
| Subtotal (95% CI) | 127     | 125 | 600.0% | 169     | 125 | 600.0% | 4.44   | [1.20, 7.66] |                  |                  |
| Heterogeneity: Tau^2 = 0.00, CHI^2 = 0.36, df = 1 (P = 0.59), I^2 = 0% | Test for overall effect: Z = 2.68 (P = 0.007) |                  |                  |
| 1.3.4 1 day       |         |   |       |         |   |       |        |         |   |       |         |   |       |                  |                  |
| Huang 2010        | 27.18   | 15.09 | 12     | 22.26   | 14.74 | 12     | 10.4%  | -5.00   | -19.71 | [7.25, 5.78]    |                  |                  |
| Zhang 2014        | 18.95   | 13.37 | 60     | 15.59   | 12.57 | 52     | 55.1%  | 3.28    | 3.66 | [7.33, 7.33]    |                  |                  |
| Zhang 2016        | 20.77   | 13.24 | 47     | 14.74   | 14.37 | 43     | 36.6%  | 0.83    | 0.31 | [11.79, 0.31]   |                  |                  |
| Subtotal (95% CI) | 139     | 137 | 600.0% | 176     | 134 | 600.0% | 3.32   | [1.00, 7.64] |                  |                  |
| Heterogeneity: Tau^2 = 4.23, CHI^2 = 2.69, df = 2 (P = 0.26), I^2 = 31% | Test for overall effect: Z = 1.51 (P = 0.13) |                  |                  |
| 1.3.5 2 day       |         |   |       |         |   |       |        |         |   |       |         |   |       |                  |                  |
| Huang 2010        | 25.18   | 14.86 | 12     | 21.41   | 14.26 | 12     | 4.9%   | 3.77    | 6.00 | [10.19]       |                  |                  |
| Zhang 2014        | 12.65   | 8.96 | 60     | 11.54   | 12.16 | 52     | 55.1%  | 1.11    | 2.16 | [4.32]       |                  |                  |
| Zhang 2016        | 14.04   | 9.34 | 47     | 14.09   | 14.46 | 43     | 27.2%  | -0.05   | 5.14 | [0.04]       |                  |                  |
| Subtotal (95% CI) | 139     | 137 | 600.0% | 176     | 134 | 600.0% | 0.92   | [1.73, 3.57] |                  |                  |
| Heterogeneity: Tau^2 = 0.00, CHI^2 = 0.36, df = 2 (P = 0.84), P = 0% | Test for overall effect: Z = 0.68 (P = 0.50) |                  |                  |
| 1.3.6 3 day       |         |   |       |         |   |       |        |         |   |       |         |   |       |                  |                  |
| Huang 2010        | 19.72   | 14.45 | 12     | 15.25   | 10.67 | 12     | 5.1%   | 4.47    | 5.60 | [14.63]       |                  |                  |
| Zhang 2014        | 8.02    | 7.64 | 62     | 8.61    | 10.58 | 80     | 66.7%  | 0.31    | 2.61 | [3.13]       |                  |                  |
| Zhang 2016        | 9.74    | 7.97 | 47     | 9.81    | 11.94 | 43     | 26.2%  | -0.07   | 4.10 | [4.10]       |                  |                  |
| Subtotal (95% CI) | 141     | 135 | 600.0% | 176     | 134 | 600.0% | 0.44   | [1.08, 2.70] |                  |                  |
| Heterogeneity: Tau^2 = 0.00, CHI^2 = 0.67, df = 2 (P = 0.72), P = 0% | Test for overall effect: Z = 2.50 (P = 0.72) |                  |                  |

Tests for subgroup differences: CHI^2 = 5.54, df = 5 (P = 0.39), I^2 = 9.7%.

At different time points within three days, the pooled MD was between 15.65 and 21.33, with significant differences (overall effect p < 0.05) observed between the CBT group and a control group. The effect of CBT on orthodontic pain was superior to that in the control group, which was statistically significant. It is worth noting that the heterogeneity I^2 was very low (0%) in the subgroup meta-analysis at the observation time points of day 1 and day 2.

**Music therapy vs control group**

Three studies addressing music therapy were included. At different periods of pain observation, the meta-analysis was divided into five subgroups: two hours, six hours, one day, two days, and three days. The meta-analysis of the five subgroups is summarised in Table IV.

At different time points within three days, the pooled MD was between 14.14 and 24.65, with significant differences (overall effect p < 0.05) observed between the music therapy group and a control group. The relief effect of music therapy on orthodontic pain was better than that for the control group, and was statistically significant. It is worth noting that the heterogeneity I^2 was very low (0%) in most of the subgroup meta-analysis.

**Cognitive behaviour therapy vs music therapy**

Three studies assessing cognitive behaviour therapy were included. Three studies were divided into three subgroups, according to different periods of observation.
### Table III. Meta-analysis data summary: Cognitive behavior therapy (CBT) vs control group.

| Time point | Mean difference | 95%CI | Test for heterogeneity | Overall effect |
|------------|-----------------|-------|------------------------|---------------|
|            | Lower           | Upper | χ² | P Value | P Value |
| 1 Day      | 21.33           | 15.44 | 27.23 | 0.9 | 0.34 | 0.00001 |
| 2 Days     | 18.62           | 13.87 | 23.37 | 0.2 | 0.66 | 0.00001 |
| 3 Days     | 15.65           | 10.91 | 20.38 | 1.49 | 0.22 | 0.00001 |

Supplementary Figure 4. Structured phone call follow-up and control for meta-analysis results, reported in mean difference (95% confidence interval), show evidence favouring structured phone call follow-up for pain reduction effectiveness daily within a week after activation of fixed orthodontic treatment.

| Time point | Mean difference | 95%CI | Test for heterogeneity | Overall effect |
|------------|-----------------|-------|------------------------|---------------|
|            | Lower           | Upper | χ² | P Value | P Value |
| 1 Day      | 21.33           | 15.44 | 27.23 | 0.9 | 0.34 | 0.00001 |
| 2 Days     | 18.62           | 13.87 | 23.37 | 0.2 | 0.66 | 0.00001 |
| 3 Days     | 15.65           | 10.91 | 20.38 | 1.49 | 0.22 | 0.00001 |

Table III. Meta-analysis data summary: Cognitive behavior therapy (CBT) vs control group.
Supplementary Figure 5. Structured text follow-up and control for meta-analysis results, reported in mean difference (95% confidence interval), show evidence favouring structured text follow-up for pain reduction effectiveness daily within a week after activation of fixed orthodontic treatment.

Table IV. Metanalysis data summary: Music therapy vs control group.

| Time point | Mean difference | 95%CI | Test for heterogeneity | Overall effect |
|------------|-----------------|-------|------------------------|---------------|
|            | Lower | Upper | χ² | P Value | P Value |
| 2 Hour     | 10.6  | 17.68 | 0.29 | 0.59 | 0.00001b |
| 6 Hour     | 17.27 | 25.08 | 0.0 | 1 | 0.00001b |
| 1 Day      | 20.49 | 28.81 | 0.58 | 0.75 | 0.00001b |
| 2 Days     | 17.02 | 24.31 | 2.02 | 0.36 | 0.00001b |
| 3 Days     | 11.18 | 22.29 | 4.19 | 0.12 | 0.00001b |

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Supplementary Figure 6. Structured phone call follow-up and structured text follow-up for meta-analysis results, reported in mean difference (95% confidence interval), show evidence that both interventions’ pain reduction effectiveness is similar daily within a week after activation of fixed orthodontic treatment.

### Supplementary Figure 6

#### Table V. Meta-analysis data summary: CBT vs music therapy.

| Time point | Mean difference | Test for heterogeneity | Overall effect |
|------------|-----------------|------------------------|---------------|
|            | 95%CI*          | χ² | P Value | P Value |
| 2 Hour     | 0.64            | 1.68 | 3.16       | 0         | 0.96 | 0.62 |
| 6 Hour     | 2.19            | 0.82 | 5.2        | 0.04      | 0.84 | 0.15 |
| 12 Hour    | 4.44            | 0.12 | 7.69       | 0.35      | 0.55 | 0.007 |
| 1 Day      | 0.35            | 0.31 | 6.78       | 2.89      | 0.24 | 0.03 |
| 2 Days     | 0.92            | 1.73 | 3.57       | 0.36      | 0.84 | 0.5 |
| 3 Days     | 0.41            | 1.88 | 2.7        | 0.67      | 0.72 | 0.73 |

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Table V. Meta-analysis data summary: CBT vs music therapy.

| Study or Subgroup | Structured phone call | Text message | Mean Difference | Test for heterogeneity | Overall effect |
|-------------------|-----------------------|--------------|----------------|------------------------|---------------|
|                   | Weight | IV | Random | 95% CI |                   | Weight | IV | Random | 95% CI |
| 1.6.1 1 day       |         |    |        |        |                     |         |    |        |        |
| Cozzone 2015      | 1.2     | 22 | 24     | -1.88  | 3.16                | 0.64    | 0.96 | 0.62 |
| Xu 2017           | 3.52    | 22 | 24     | 0.04   | 0.04                | 0.84    | 0.15 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
| 1.6.2 2 day       |         |    |        |        |                     |         |    |        |        |
| Cozzone 2015      | 28      | 24 | 24     | 3.57   | 6.78                | 0.24    | 0.24 | 0.03 |
| Xu 2017           | 0.35    | 24 | 24     | 1.73   | 34.2                | 0.84    | 0.84 | 0.5 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
| 1.6.3 3 day       |         |    |        |        |                     |         |    |        |        |
| Cozzone 2015      | 15      | 42 | 24     | 0.64   | 3.16                | 0.36    | 0.36 | 0.84 |
| Xu 2017           | 3.52    | 22 | 24     | 0.04   | 0.04                | 0.84    | 0.84 | 0.5 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
| 1.6.4 4 day       |         |    |        |        |                     |         |    |        |        |
| Cozzone 2015      | 10      | 24 | 24     | 0.64   | 3.16                | 0.36    | 0.36 | 0.84 |
| Xu 2017           | 3.52    | 22 | 24     | 0.04   | 0.04                | 0.84    | 0.84 | 0.5 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
| 1.6.5 5 day       |         |    |        |        |                     |         |    |        |        |
| Cozzone 2015      | 9       | 17 | 24     | 0.64   | 3.16                | 0.36    | 0.36 | 0.84 |
| Xu 2017           | 3.52    | 22 | 24     | 0.04   | 0.04                | 0.84    | 0.84 | 0.5 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
| 1.6.6 6 day       |         |    |        |        |                     |         |    |        |        |
| Xu 2017           | 9.5     | 22 | 24     | 0.64   | 3.16                | 0.36    | 0.36 | 0.84 |
| Cozzone 2015      | 5.8     | 17 | 24     | 0.04   | 0.04                | 0.84    | 0.84 | 0.5 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
| 1.6.7 7 day       |         |    |        |        |                     |         |    |        |        |
| Xu 2017           | 5.5     | 22 | 24     | 0.64   | 3.16                | 0.36    | 0.36 | 0.84 |
| Cozzone 2015      | 5.8     | 17 | 24     | 0.04   | 0.04                | 0.84    | 0.84 | 0.5 |
| Total (95% CI)    |         |    |        |        |                     |         |    |        |        |
| Heterogeneity     | ts = 0.24 | df = 1 (P = 0.62); P = 0.38 |
| Test for overall effect | Z = 0.22 (P = 0.89) |
pain observation: two hours, six hours, 12 hours, one day, two days, three days. The meta-analysis of the six subgroups is summarised in Table V.

Most of the time points showed no significant differences (overall effect \( p < 0.05 \)) between the CBT group and music therapy group except at 12 hours. It should be noted that the heterogeneity \( I^2 \) was very low (0%) in all the subgroup meta-analysis. It is therefore considered that the two interventions have a similar effect in reducing orthodontic pain.

**Structured phone call follow-up vs control group**

Four studies that addressed the effects of a structured telephone call were included.\(^{21,22,25,27} \) The pooled data was divided into seven subgroups according to different periods of pain observation: each day in the first week. The meta-analysis of the seven subgroups is summarised in Table VI.

At different time points within the week, compared with the control, a structured telephone call follow-up was more effective in relieving pain after initial arch wire placement. The pooled MD was between 2.45 and 11.68, and the overall \( p \) values showed that the results of the experimental group (structured phone call follow-up) were more popular than the control group. The heterogeneity \( I^2 \) in the most subgroup was low (<25%).

**Structured text follow-up vs control**

Three structured text follow-up studies were included.\(^{22,24,27} \) The pooled data was divided into seven subgroups, according to different periods of pain observation: each day over a week. The meta-analysis of the seven subgroups is summarised in Table VII.

At different time points within the week, compared with the control, a structured text follow-up was more effective in relieving pain after initial arch wire placement. The pooled mean differences were between 3.22 and 15.09. In addition to the \( p \) value on the fifth day, the results were in favour of a structured telephone follow-up compared with the control group (\( p > 0.05 \)).

Although on the fifth day, the pooled MD still favoured the structured text follow-up group, its effects had no statistically significant difference over the control group (\( p > 0.05 \)). On the fifth day, the heterogeneity \( I^2 \) of subgroup meta-analysis was high (77%).

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Table VI. Meta-analysis data summary: Structured phone call follow-up vs control group.

| Time point | Mean difference | 95%CI\(^a\) | Test for heterogeneity | Overall effect |
|------------|----------------|------------|------------------------|---------------|
|            |                | Lower      | Upper      | \( \chi^2 \) | \( P \) Value | \( P \) Value |
| 1 Day      | 8.81           | 4.39       | 13.24      | 1.13         | 0.77          | 0.00001\(^b\) |
| 2 Days     | 9.88           | 5.6        | 14.15      | 3.91         | 0.27          | 0.00001\(^b\) |
| 3 Days     | 11.68          | 7.79       | 15.58      | 0.27         | 0.96          | 0.00001\(^b\) |
| 4 Days     | 8.18           | 4.85       | 11.51      | 2.41         | 0.49          | 0.00001\(^b\) |
| 5 Days     | 6.89           | 4.06       | 9.73       | 4.9          | 0.18          | 0.00001\(^b\) |
| 6 Days     | 5.98           | 3.75       | 8.2        | 1.1          | 0.78          | 0.00001\(^b\) |
| 7 Days     | 2.45           | 0.63       | 4.26       | 0.6          | 0.74          | 0.008         |

Table VII. Meta-analysis data summary: Structured text follow-up vs control group.

| Time point | Mean difference | 95%CI\(^a\) | Test for heterogeneity | Overall effect |
|------------|----------------|------------|------------------------|---------------|
|            |                | Lower      | Upper      | \( \chi^2 \) | \( P \) Value | \( P \) Value |
| 1 Day      | 8.45           | 0.99       | 15.92      | 0.31         | 0.86          | 0.03          |
| 2 Days     | 7.91           | 0.91       | 14.9       | 1.4          | 0.5           | 0.03          |
| 3 Days     | 15.09          | 8.41       | 21.77      | 2.33         | 0.31          | 0.000001\(^b\) |
| 4 Days     | 6.48           | 0.75       | 12.2       | 2.72         | 0.26          | 0.03          |
| 5 Days     | 5.5            | -2.55      | 13.55      | 8.73         | 0.01          | 0.18          |
| 6 Days     | 5.04           | 0.16       | 9.92       | 5.81         | 0.05          | 0.04          |
| 7 Days     | 3.22           | 1.41       | 5.03       | 0.14         | 0.71          | 0.0005        |
Structured phone call follow-up vs structured text follow-up

Only two studies were identified and therefore included.22-27 The pooled data was divided into seven subgroups in accordance with different periods of pain observation: each day over a week. The meta-analysis of the seven subgroups is summarised in Table VIII.

At different time points within the week, the overall effects showed no significant difference between the two groups ($p > 0.05$). On the fifth day, the heterogeneity $I^2$ of subgroup meta-analysis was high (81%) and so it is believed that phone and text follow-up interventions had similar effects on orthodontic pain reduction.

Risk of bias publication studies

Tests for publication bias were not undertaken because fewer than 10 studies were included in each meta-analysis.

Discussion

Tooth movement is a painful inflammatory reaction involving an alveolar bone remodelling process.30 The pain induced by tooth movement is a major complication during orthodontic treatment1-2 and, due to the unwelcome side-effects,13,15-17 psychological interventions became alternatives to NSAIDs and LLLT in reducing orthodontic pain. This is the first meta-analysis to evaluate psychological intervention of pain caused by a fixed orthodontic appliance after initial arch wire placement by exploring the existing best evidence (RCTs).

The current meta-analysis shows that CBT, music therapy, structured telephone call follow-up and structured text follow-up were positive in reducing orthodontic pain intensity in the short term (lasting within a week or three days after OT, respectively). The analgesic effects of cognitive behavioural therapy and music therapy within three days after OT were similar.

Structured phone follow-up and structured text follow-up contact have similar effects on orthodontic pain reduction over a week. The present findings apply to orthodontic patients who are in good mental health and who feel pain after first arch wire placement, without restrictions on age or gender. None of the above interventions shortened the duration of orthodontic pain, but only reduced pain intensity. No side effects of psychological intervention have been reported in the literature. There are still other psychological interventions used to reduce orthodontic pain, such as suggestion therapy and relaxation techniques,24,25 which were not included in the meta-analysis and so no conclusions can be drawn. The reasons are shown in Supplementary Table III.

All of the psychological interventions have different mechanisms of orthodontic pain relief. Huang et al. used EEG (electroencephalography) to evaluate CBT and the brain wave music effect.23 The overall power spectrum of the CBT group was seen to be lower than that of the control group. It was determined that CBT could result in overall neural modulation of pain.

| Time point | Mean difference | 95%CI | Test for heterogeneity | Overall effect |
|------------|-----------------|-------|------------------------|---------------|
|            |                 | Lower | Upper | $\chi^2$ | $P$ Value | $P$ Value |
| 1 Day      | 0.09            | -10.76| 10.94  | 1.63    | 0.2       | 0.99    |
| 2 Days     | 0.77            | -9.49 | 11.03  | 1.51    | 0.22      | 0.93    |
| 3 Days     | 3.15            | -7.12 | 13.42  | 4.15    | 0.04      | 0.54    |
| 4 Days     | 0.16            | -10.03| 10.62  | 3.9     | 0.05      | 0.84    |
| 5 Days     | 3.89            | -8.19 | 15.96  | 11.41   | 0.0007    | 0.46    |
| 6 Days     | 1.26            | -0.88 | 3.4    | 0.21    | 0.65      | 0.29    |
| 7 Days     | 0.98            | -1.86 | 3.82   | 3.34    | 0.51      | 0.24    |

Table VIII. Meta-analysis Data Summary: Structured phone call follow-up vs Structured text follow-up.

Supplementary Table III. The reasons our review did not contain other psychological interventions.

| Psychological interventions | Reasons for exclusion |
|-----------------------------|------------------------|
| Suggestion therapy          | Only Zheng et al.29 have the available outcome |
| Relaxation therapy          | The author thought it was actually the combination of physical and psychological interventions |
perception, which subsequently reduced orthodontic pain perception. It was also found that music therapy could possibly control pain by restoring functional connectivity and brain regularity affected by pain. Cozzani et al. believed that a structured telephone call and a structured text follow-up intervention could reduce a patient’s anxiety and stress, and have a positive impact on the individual perception of pain. It is further contended that the analgesic effect of language or verbal communication may have different results due to cultural differences.

It is known that pain is a highly subjective sensation that defies accurate evaluation because of factors such as age, gender, individual pain threshold, present emotional state, and previous pain experiences. Well-designed RCTs might balance the contributing factors between groups and provide practical information and useful suggestions.

The limitations of the presented meta-analysis were affected by the number of the included studies that had a high or unclear selection or performance bias. It is therefore considered that the present review has a high risk of bias, which has confounding effects. In addition, some studies could not be included due to the lack of the specific estimator required; however, their individual data were consistent with the generated findings.

The limitations of RCTs related to the patient’s gender and personality were important factors in the acceptance of psychological interventions. Given that only few studies have considered these factors, it was not possible to review the effect of psychological interventions on the relief of orthodontic pain in patients with different personalities or genders. In addition, it is unrealistic and unethical to expect that a control group of patients reduce their orthodontic pain without taking any relieving measures. Similarly, even after psychological intervention, some patients might still be sensitive to orthodontic pain and accept the use of analgesic drugs, resulting in a confounding bias. Finally, no studies have compared the effectiveness of pain reduction between CBT vs telephone/text follow-up (also music therapy vs telephone/text follow-up).

Conclusions

It is concluded that, based on relatively weak evidence, the results of the present study support four interventions: cognitive behaviour therapy (CBT), music therapy, structured phone call follow-up and structured text follow-up, which can be judged as effective measures for pain intensity reduction. It was found that CBT vs music therapy together with a structured phone call follow-up vs structured text follow-up had similar effects on pain relief. However, the most effective intervention remains unknown. No side effects were identified in the included studies. In summary, further high-quality RCTs are needed to provide greater levels of evidence regarding the effectiveness of psychological interventions on orthodontic pain reduction.

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