

# **Predictors and Interventions for Intra-Operative and Post-Operative Pain associated with Paediatric Dental Procedures**

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## **Dedication**

*I dedicate this thesis to my parents, my wife, my daughters, and my brothers and sisters.*

## **Acknowledgements**

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## Abstract

**Background:** Pain is an experience that could prevent children from receiving optimal dental care. Painful stimuli in paediatric dentistry are commonly caused by dental caries. Exposing children to painful dental procedures might be associated with different possible consequences. These sequels include anxiety, fear, poor oral hygiene, lack of co-operation, delay in seeking dental care and need for general anaesthesia for dental treatment. A good understanding of predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures could play an important role in preventing loss of co-operation which often leads to the procedure being performed under general anaesthesia which is not always readily available and is associated with risks, albeit small of morbidity and mortality. Therefore, using appropriate pharmacological and non-pharmacological interventions to target these predictors to reduce pain associated with dental procedures might help children cope better with dental care and decrease the number of children requiring general anaesthesia for their dental care.

**Aims:** To identify predictors of intra-operative and post-operative pain associated with routine dental procedures in children, to investigate interventions used to reduce this pain and to combine the findings to develop evidence-based recommendations for managing intra-operative and post-operative pain associated with routine dental procedures in children. The thesis is presented as two systematic reviews with meta-analyses; the

first systematic review identified predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures whereas the second systematic review evaluated pharmacological and non-pharmacological interventions for dental procedures to reduce this pain in children.

### **Methods:**

**The first systematic review:** A systematic review of observational studies was performed using electronic searches such as MEDLINE, EMBASE and PsycINFO, Global Health via OVID, PubMed, Scopus, and SciELO (Web of Science) databases. An adaptation of the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies was used to evaluate the quality of the studies. A meta-analysis of included studies was performed to estimate the impact of dental procedures and anxiety on children's pain perception. A meta-regression analysis was also performed to determine the relative effect of the predictors on children's pain perception compared to a reference category. The analyses used the mean differences (MDs) and 95% confidence intervals (CIs) for continuous outcomes.

**The second systematic review:** A systematic review of randomised controlled clinical trials was performed using electronic searches such as MEDLINE, EMBASE and PsycINFO, Global Health via OVID, Cochrane Library (Wiley), WHO International Clinical Trials Registry Platform, Clinical Trials.gov, PubMed and SciELO (Web of Science) databases. An adaptation of the Cochrane risk-of-bias tool for randomised trials was used to evaluate

the quality of the studies. A meta-analysis of included studies was performed to determine the effectiveness of the interventions using the Cohen's d standardised mean differences (SMDs) and 95% confidence intervals (CIs) for continuous outcomes. The GRADE tool was also used to assess the quality and certainty of the body of evidence and make recommendations.

### **Results:**

**The first systematic review:** The search identified 532 articles; 53 were retrieved for full-text screening; 6 studies were included in the review; 4 were eligible for the meta-analysis. The meta-analysis showed types of procedure that predicted intra-operative pain, with dental extractions being the most painful (Mean Difference [MD] Visual Analogue Scale [VAS] 46.51, 95% confidence interval [CI] 40.40 to 52.62) followed by drilling (MD VAS 41.83, 95% CI 33.38 to 50.28). The meta-regression showed the pain scores for dental extraction and drilling were significantly higher than polishing (the least painful procedure (reference category)) by 23.80 MD VAS, 95% CI 5.13 to 42.46, P-value = 0.012 and 19.64 MD VAS, 95% CI 0.001 to 39.28, P-value = 0.05, respectively. It also showed that highly anxious children reported significantly higher pain scores during dental procedures by 12.31 MD VAS, 95% CI 5.23 to 19.40, P-value = 0.001 than those with low anxiety levels.

**The second systematic review:** The search identified 2261 articles; 153 were retrieved for full-text screening; 45 studies were included in the review, and 37 articles were eligible for the meta-analysis. The meta-analysis

showed significant effects for improvement in intra-operative pain perception associated with local anaesthesia for mechanoreceptor and thermal receptor stimulation (Standardised Mean Difference [SMD] -1.38, 95% CI -2.02 to -0.73) and with local anaesthesia and drilling for behavioural interventions (SMD -0.50, 95% CI -0.83 to -0.18) in comparison with the control groups. Also, there was a significant effect in relieving post-operative pain associated with extraction when pre-emptive analgesics were given (SMD -0.77, 95% CI -1.21 to -0.33). The GRADE assessed the certainty of evidence for these interventions as IB moderate and low risk = strong recommendation.

### **Conclusion:**

The first systematic review demonstrates that the strongest predictors of intra-operative pain associated with routine paediatric dental procedures were dental extractions followed by drilling. Children with high anxiety also reported more pain for similar procedures. Tailoring interventions to reduce pain associated with paediatric dental procedures should be a priority for future research as reducing pain can impact compliance and reduce the need for GA. The second systematic review provides moderate evidence with strong recommendations for the effectiveness of behavioural interventions, mechanoreceptor and thermal receptor stimulation, and pre-emptive oral analgesics in reducing pain associated with routine dental care in children. These interventions can be used early in primary care to improve the number of children accepting treatment in the dental chair and reduce



the number of children requiring general anaesthesia for their dental treatment.

## Table of Contents

<b>Dedication</b> .....	<b>iii</b>
<b>Acknowledgements</b> .....	<b>iv</b>
<b>Abstract</b> .....	<b>v</b>
<b>Table of Contents</b> .....	<b>x</b>
<b>List of Tables</b> .....	<b>xvi</b>
<b>List of Figures</b> .....	<b>xvii</b>
<b>Thesis layout</b> .....	<b>xviii</b>
<b>List of Abbreviations</b> .....	<b>xix</b>
<b>Chapter 1: Introduction and Background</b> .....	<b>1</b>
1.1 Introduction .....	1
1.2 Background.....	3
1.2.1 Child oral health .....	3
1.2.2 Child pain perception .....	4
1.2.2.1 Pain .....	4
1.2.2.2 Toddlers and pre-schoolers (1-5 years-of-age) .....	5
1.2.2.3 School-age children (6-12 years-of-age) .....	6
1.2.2.4 Assessing pain in children.....	6
1.2.3 Dental treatment in children.....	7
1.2.4 General anaesthesia for dental treatment.....	7
1.2.4.1 Benefits of using general anaesthesia for dental treatment in children .....	8
1.2.4.2 Risks of using general anaesthesia for dental treatment in children .....	9
1.2.5 Predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures.....	12
1.2.5.1 Age .....	12
1.2.5.2 Developmental stage.....	12
1.2.5.3 Gender .....	13
1.2.5.4 Inflammation/infection.....	13
1.2.5.5 Injection and its technique.....	14
1.2.5.6 Dental procedures .....	16
1.2.5.7 Anxiety\feared\Previous dental experience \Previous medical experience .....	17
1.2.5.8 Dentists' knowledge and attitudes.....	18

1.2.6 Intervention options to reduce intra-operative and post-operative pain associated with routine paediatric dental procedures .....	19
1.2.6.1 Pharmacological interventions .....	19
<b>1.2.6.1.1 Oral analgesics .....</b>	<b>19</b>
<b>1.2.6.1.1.1 Non-steroidal anti-inflammatory drugs (NSAIDs)</b> .....	<b>21</b>
<b>1.2.6.1.1.2 Paracetamol</b> .....	<b>22</b>
<b>1.2.6.1.1.3 Opioids</b> .....	<b>22</b>
<b>1.2.6.1.1.4 Inhalation sedation with nitrous oxide and oxygen</b> .....	<b>23</b>
1.2.6.2 Non-pharmacological interventions.....	24
<b>1.2.6.2.1 Preparatory information</b> .....	<b>25</b>
<b>1.2.6.2.2 Non-verbal communication</b> .....	<b>25</b>
<b>1.2.6.2.3 Voice control</b> .....	<b>25</b>
<b>1.2.6.2.4 Tell-Show-Do (TSD)</b> .....	<b>26</b>
<b>1.2.6.2.5 Enhancing control</b> .....	<b>27</b>
<b>1.2.6.2.6 Behaviour shaping</b> .....	<b>27</b>
<b>1.2.6.2.7 Positive reinforcement</b> .....	<b>27</b>
<b>1.2.6.2.8 Negative reinforcement</b> .....	<b>28</b>
<b>1.2.6.2.9 Modelling</b> .....	<b>28</b>
<b>1.2.6.2.10 Distraction</b> .....	<b>29</b>
<b>1.2.6.2.11 Systematic desensitisation</b> .....	<b>29</b>
<b>1.2.6.2.12 Cognitive behaviour therapy (CBT)</b> .....	<b>30</b>
1.2.7 Conclusion.....	31
<b>Chapter 2: Methodologies, Aims and Objectives .....</b>	<b>32</b>
2.1 Suggested methodologies.....	32
2.1.1 Observational studies .....	32
2.1.2 Randomised controlled trials (RCTs) .....	34
2.1.3 Systematic reviews .....	35
2.2 Aims and objectives.....	37
2.2.1 Aims.....	37
2.2.2 Specific objectives.....	37

<b>Chapter 3: The First Systematic Review and Meta-analysis.....</b>	<b>38</b>
3.1 Aim .....	38
3.2 Methods .....	38
3.2.1 Criteria for considering studies for this review .....	39
3.2.1.1 Types of studies.....	39
3.2.1.2 Types of participants.....	39
3.2.1.3 Types of predictors .....	39
3.2.1.4 Types of outcome measures .....	40
3.2.1.5 Search methods for identification of studies .....	40
3.2.2 Data collection and analysis .....	41
3.2.2.1 Selection of studies.....	41
3.2.2.2 Data extraction and management.....	41
3.2.3 Quality assessment of the included studies .....	42
3.2.4 Data synthesis and analysis .....	43
3.3 Results .....	45
3.3.1 Study selection.....	45
3.3.2 Study characteristics.....	46
3.3.2.1 Study design .....	46
3.3.2.2 Sample size .....	47
3.3.2.3 Settings .....	47
3.3.2.4 Participants .....	47
3.3.2.5 Predictors.....	48
3.3.2.6 Outcomes.....	48
3.3.3 Quality assessment of included studies .....	51
3.3.4 Meta-analysis of intra-operative pain outcome .....	53
3.3.5 Meta-regression of intra-operative pain outcome .....	54
3.3.5.1 Dental procedures .....	54
3.3.5.2 Anxiety levels.....	55
3.4 Discussion.....	56
3.5 Conclusion .....	61
<b>Chapter 4: The Second Systematic Review and Meta-analysis.....</b>	<b>63</b>
4.1 Aim .....	63
4.2 Methods .....	63
4.2.1 Criteria for considering studies for this review .....	64
4.2.1.1 Types of studies.....	64

4.2.1.2	Types of participants.....	64
4.2.1.3	Types of interventions .....	65
<b>4.2.1.3.1</b>	<b>Computer Driven LA Versus Conventional LA .....</b>	<b>65</b>
<b>4.2.1.3.2</b>	<b>Intra-osseous/Intra-ligamentary LA Versus Conventional LA .....</b>	<b>66</b>
<b>4.2.1.3.3</b>	<b>LA Agent (Articaine Versus Lidocaine) .....</b>	<b>66</b>
<b>4.2.1.3.4</b>	<b>Topical Anaesthesia .....</b>	<b>67</b>
<b>4.2.1.3.5</b>	<b>Mechanoreceptor and thermal receptor stimulation</b>	<b>67</b>
<b>4.2.1.3.6</b>	<b>Pharmacological Interventions .....</b>	<b>68</b>
<b>4.2.1.3.7</b>	<b>Behavioural Interventions .....</b>	<b>68</b>
4.2.1.4	Types of outcome measures .....	68
4.2.1.5	Search methods for identification of studies .....	69
4.2.2	Data collection and analysis .....	69
4.2.2.1	Selection of studies.....	69
4.2.2.2	Data extraction and management.....	70
4.2.3	Quality assessment of the included studies .....	71
4.2.4	Data synthesis and analysis .....	72
4.2.5	Quality of evidence.....	73
4.3	Results .....	74
4.3.1	Study Selection .....	74
4.3.2	Study characteristics.....	76
4.3.2.1	Study design .....	76
4.3.2.2	Sample size .....	77
4.3.2.3	Settings .....	77
4.3.2.4	Participants .....	77
4.3.2.5	Outcomes.....	77
4.3.3	Quality assessment of the included studies .....	78
4.3.3.1	Allocation (selection bias).....	80
<b>4.3.3.1.1</b>	<b>Sequence generation .....</b>	<b>80</b>
<b>4.3.3.1.2</b>	<b>Concealment of allocation .....</b>	<b>81</b>
4.3.3.2	Blinding .....	82
<b>4.3.3.2.1</b>	<b>Blinding of participants and personnel (performance bias) .....</b>	<b>82</b>
<b>4.3.3.2.2</b>	<b>Blinding of outcome assessment (detection bias) ..</b>	<b>82</b>

4.3.3.3	Incomplete outcome data (attrition bias).....	83
4.3.3.4	Selective reporting (reporting bias) .....	83
4.3.3.5	Other potential sources of bias.....	83
4.3.3.6	Overall risk of bias .....	84
4.3.4	Effect of interventions and meta-analyses .....	85
4.3.4.1	Intra-operative pain outcome.....	85
<b>4.3.4.1.1</b>	<b>Computer Driven LA Versus Conventional LA .....</b>	<b>85</b>
<b>4.3.4.1.2</b>	<b>Intraosseous/Intra-ligamentary LA Versus Conventional LA.....</b>	<b>87</b>
<b>4.3.4.1.3</b>	<b>LA Agent (Articaine Versus Lidocaine) .....</b>	<b>89</b>
<b>4.3.4.1.4</b>	<b>Topical Anaesthesia .....</b>	<b>90</b>
<b>4.3.4.1.5</b>	<b>Mechanoreceptor and thermal receptor stimulation</b>	<b>92</b>
<b>4.3.4.1.6</b>	<b>Pharmacological Interventions .....</b>	<b>94</b>
<b>4.3.4.1.7</b>	<b>Behavioural Interventions .....</b>	<b>95</b>
4.3.4.2	Post-operative pain outcome.....	98
<b>4.3.4.2.1</b>	<b>LA Agent (Articaine Versus Lidocaine) .....</b>	<b>98</b>
<b>4.3.4.2.2</b>	<b>Pharmacological Interventions .....</b>	<b>99</b>
<b>4.3.4.2.3</b>	<b>Behavioural Interventions .....</b>	<b>100</b>
4.3.4.3	Anxiety outcome .....	101
<b>4.3.4.3.1</b>	<b>Computer Driven LA Versus Conventional LA .....</b>	<b>101</b>
<b>4.3.4.3.2</b>	<b>Mechanoreceptor and thermal receptor stimulation .....</b>	<b>101</b>
<b>4.3.4.3.3</b>	<b>Pharmacological Interventions .....</b>	<b>101</b>
<b>4.3.4.3.4</b>	<b>Behavioural Interventions .....</b>	<b>102</b>
4.3.5	Quality of evidence.....	103
4.4	Discussion.....	104
4.5	Conclusion .....	113
<b>Chapter 5:</b>	<b>Summary of Findings and Recommendations .....</b>	<b>114</b>
5.1	Summary of main findings.....	114
5.2	Implications and recommendations for dental care for children .	115
5.3	Implications for further research .....	118
5.4	Conclusion .....	120

<b>References .....</b>	<b>121</b>
<b>Appendix 1: Search strategy for the first systematic review .....</b>	<b>156</b>
<b>Appendix 2: The data extraction form for the meta-analysis of the first systematic review .....</b>	<b>172</b>
<b>Appendix 3: Meta-regression of the first systematic review .....</b>	<b>173</b>
<b>Appendix 4: List of studies excluded from the first systematic review following full text article assessment showing exclusion reasons and references .....</b>	<b>174</b>
<b>Appendix 5: Search strategy for the second systematic review .....</b>	<b>183</b>
<b>Appendix 6: The data extraction form for the meta-analysis of the second systematic review .....</b>	<b>197</b>
<b>Appendix 7: List of studies excluded from the second systematic review following full text article assessment showing exclusion reasons and references .....</b>	<b>203</b>
<b>Appendix 8: Characteristics of included studies of the second systematic review .....</b>	<b>224</b>
<b>Appendix 9: GRADE assessment for the certainty of evidence of the second systematic review .....</b>	<b>271</b>

## List of Tables

<b>Table 1. The characteristics of included studies.....</b>	<b>50</b>
<b>Table 2. Quality assessment summary.....</b>	<b>52</b>
<b>Table 3. Random-effects meta-regression evaluation of pain associated with dental procedures.....</b>	<b>55</b>
<b>Table 4. Random-effects meta-regression evaluation of pain associated with anxiety level.....</b>	<b>56</b>
<b>Table 5. The GRADE recommendations. ....</b>	<b>104</b>



## List of Figures

Figure 1. PRISMA flowchart of the study selection process. ....	46
Figure 2. Random-effects meta-analysis evaluation of pain associated with dental procedures.....	53
Figure 3. PRISMA flowchart of the study selection process. ....	75
Figure 4. Overall risk of bias. ....	78
Figure 5. Risk of bias for individual studies.....	79
Figure 6. Random-effects meta-analysis evaluation of intra-operative pain for comparison 1: computer driven LA versus conventional LA.....	86
Figure 7. Random-effects meta-analysis evaluation of intra-operative pain for comparison 2: intra-ligamentary LA versus conventional LA.....	87
Figure 8. Random-effects meta-analysis evaluation of intra-operative pain for comparison 3: intraosseous LA versus conventional LA.....	89
Figure 9. Random-effects meta-analysis evaluation of intra-operative pain for comparison 4: LA agent (Articaine versus Lidocaine). ....	90
Figure 10. Random-effects meta-analysis evaluation of intra-operative pain for comparison 5: topical anaesthesia. ....	91
Figure 11. Random-effects meta-analysis evaluation of intra-operative pain for comparison 6: mechanoreceptor and thermal receptor stimulation.....	94
Figure 12. Random-effects meta-analysis evaluation of intra-operative pain for comparison 7: behavioural interventions. ....	98
Figure 13. Random-effects meta-analysis evaluation of post-operative pain for comparison 8: pharmacological interventions (oral analgesics versus placebo). ....	100
Figure 14. Random-effects meta-analysis evaluation of anxiety for comparison 9: behavioural interventions. ....	103

## **Thesis layout**

The thesis is presented in a chapter format. The first chapter presents an introduction and background, and the second chapter presents the methodologies, aims and objectives. The third chapter presents the first systematic review and meta-analysis, and the fourth chapter presents the second systematic review and meta-analyses. The third and fourth chapters include the aim, methods, results, discussion, and conclusion. Finally, a summary of findings and recommendations is presented in the fifth chapter.

## List of Abbreviations

GA: General Anaesthesia

GDP: General Dental Practitioner

DGA: Dental General Anaesthesia

DFA: Dental Fear and Anxiety

NHS: National Health Service

COX: Cyclooxygenase

CNS: Central Nervous System

NSAIDs: Non-Steroidal Anti-inflammatory Drugs

N<sub>2</sub>O/O<sub>2</sub>: Nitrous oxide – oxygen

TSD: Tell-Show-Do

CBT: Cognitive Behaviour Therapy

GRADE: The Grading of Recommendations Assessment, Development and Evaluation

RCT: Randomised Controlled Trial

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: Prospective Register of Systematic Reviews

LA: Local Anaesthesia

VAS: Visual Analogue Scale

MD: Mean Difference

CI: Confidence Intervals

SD: Standard of Deviation

N: Number of Participants

SE: Standard of Error

MCDAS: Modified Child Dental Anxiety Scale

SFP: Smiley Faces Programme

DFS: Dental Fear Survey

FIS: Facial Image Scale

SMD: Standardised Mean Difference

AV: Audio-Visual

VR: Virtual Reality

VEES: Video Eyeglasses/Earphones System

TSD-T: Tell-Show-Do Technique

HDN-T: Hiding Dental-Needle Technique

WITAUL: Writing In The Air Using Leg

## Chapter 1: Introduction and Background

### 1.1 Introduction

Pain is one of the main reasons that prevents children from receiving optimal dental care. It has been defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (International association for the study of pain, 1994). Dental caries in children is commonly causing painful stimulation that can be expressed in different ways (Versloot, 2007). This pain may interfere with children’s eating, sleeping and/or make them behave negatively (Versloot, 2007). It has been shown that the child’s quality of life seems to be significantly improved after complete treatment of dental caries under general anaesthesia (Thomas and Primosch, 2002; Anderson et al., 2004; Park et al., 2018). Children might describe dental procedures as painful and unpleasant experiences (Ghanei et al., 2018). According to the definition of pain that has been previously mentioned, it can be clearly seen that a dental procedure could have the potential to cause pain as a result of its actual or potential tissue damage. Management of pain during dental care can be normally achieved through the use of local anaesthesia (Ashley et al., 2016). However, a study conducted by Ashkenazi et al. in 2007 evaluating the incidence of post-operative dental pain in children receiving routine dental

treatment, found that 34% of those children still reported post-operative pain despite having had local anaesthesia.

Exposing children to painful dental stimuli might be associated with different possible consequences. These sequelae include anxiety, fear, poor oral hygiene, lack of co-operation, delay in seeking dental care and need for general anaesthesia for dental treatment. Arntz et al. (1990) stated that fear of pain might represent the source of anxiety that could postpone seeking further dental treatment. Moreover, Savanheimo et al. (2005) reported that repeated unpleasant experiences during dental care could be one of the most important factors leading to the provision of dental treatment under general anaesthesia (GA) due to loss of co-operation. Although there are some benefits of having dental treatment under general anaesthesia, there are associated risks and complications with dental treatment under GA – the greatest risk, albeit small, being that of mortality.

A good understanding of the predictors of intra-operative and post-operative pain associated with routine paediatric dental treatment could play an important role in preventing loss of co-operation which often leads to the procedure being performed under general anaesthesia which is not readily available and associated with risks, albeit small of morbidity and mortality. Therefore, using appropriate pharmacological and non-pharmacological interventions to target these predictors to reduce pain associated with dental procedures might decrease the number of children requiring GA for their care.

The aims of this study were therefore to identify predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures, to assess interventions used to reduce this pain and to combine the findings to develop evidence-based recommendations for managing intra-operative and post-operative pain associated with routine dental procedures in children.

## **1.2 Background**

### **1.2.1 Child oral health**

Child oral health is a fundamental and integral part of general health (Alshehri and Nasim, 2015; Public Health England, 2017). It has been defined as “a state of being free from chronic mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss, and other diseases and disorders that limit an individual’s capacity in biting, chewing, smiling, speaking, and psychosocial wellbeing” (WHO, 2003). It has been shown that good oral health positively impacts children’s ability to flourish physically, mentally, and socially (Alshehri and Nasim, 2015). Furthermore, primary teeth can provide valuable benefits which play a vital role in a child’s life for eating, phonetics, aesthetics, and socialising (Alshehri and Nasim, 2015; Setty and Srinivasan, 2016). For these reasons, it has been highly recommended that children need to be seen by a dentist within six months of having the first tooth, then followed by regular dental visits (American Academy of Pediatric Dentistry, 2012). This

provides parents/carers with appropriate preventive advice regarding teeth brushing, fluoridated toothpaste and diet advice, makes the child more familiar with the dental environment and enables the identification of caries at an earlier stage (Welbury et al., 2018).

## **1.2.2 Child pain perception**

### **1.2.2.1 Pain**

The definition of pain clearly states that the experience of pain is multi-dimensional with the physiological pathways being influenced by psychological, genetical, cultural and environmental factors (Pozos-Guillen, 2007; Reaney, 2007; Melzack and Katz, 2013).

It is generally thought that pain begins with a stimulus that is nociceptive in nature and is followed by experiencing pain (Versloot, 2007). Creating a specific pain sensation depends on the characteristics of the stimulus then is expressed in verbal, behavioural and physiological signs (Versloot, 2007). In addition, the individual's characteristics such as age, gender, and temperament, were found to influence these signs (Hdjistavropoulos and Craig, 2002; Versloot, 2007).

As children get older, they can understand and describe pain better (Gaffney et al., 2003; Schechter et al., 2003). A study conducted by Harbeck and Peterson in 1992 assessing children's concepts of specific pains, suggested



that developing children's ability to conceptualise pain has been influenced by age. They compared age with developmental stage and explained that age includes both cognitive factors and experiences of pain. Thus, the progression of understanding of pain causality varies from the child's inability to verbalise a reason why pain hurts to physiological or psychological causes (Versloot, 2007).

#### **1.2.2.2 Toddlers and pre-schoolers (1-5 years-of-age)**

Young children are susceptible to everyday incidents that could cause pain (Versloot, 2007). This pain might teach them how to avoid danger as a normal growth process (Versloot, 2007). A study conducted by Fearon et al. (1996) assessing everyday pain among young children (aged 3-7 years) during free play time in daycare, found that those children, who were exposed to falling, bumping into things or interactions with others, have one painful incident about every three hours. Thus, these personal experiences could educate them on how to cope with pain (Versloot, 2007).

Children (3-5 years-of-age) believe and understand their surrounding environment as they see it and start using associated adjectives and emotions in addition to phenomenological terms (Craig & Grunau, 1991; Versloot, 2007). Likewise, visible external events are more likely used by children to describe the cause of pain (McGrath & Pisterman, 1991; Versloot, 2007).

### **1.2.2.3 School-age children (6-12 years-of-age)**

Cognitive coping skills and associating pain with non-visible physical and psychosocial variables are used by children of school age (Versloot, 2007). In addition, their ability to understand and explain pain concepts improves as they grow (Harbeck & Peterson, 1992).

### **1.2.2.4 Assessing pain in children**

There are different methods for measuring pain in children such as self-report, behavioural observation and physiological measurements (Reaney 2007; Versloot 2007). The self-report measure of pain has been considered as the gold standard for assessing pain in children (Abdellatif 2011; Versloot 2007). A variety of self-report measures have been used to assess pain in children including the Visual Analogue Scale (VAS), the Faces Pain Scale-Revised (FPS-R), Poker Chip Tool and Colour Scales (Abdellatif 2011; Reaney 2007; Versloot 2007). The VAS has been shown in the literature to be a reliable and valid self-report measure of pain (McGrath et al., 1996; Sherman et al., 2006). Behavioural observation measures associate certain types of behaviour with the presence of pain, and they are used when the self-report of pain is not applicable (Reaney 2007; Versloot 2007). Examples of behavioural observation measures are the Face, Legs, Activity, Cry, Consolability scale (FLACC) and Venham scales (Crosta 2014; Reaney 2007; Versloot 2008). There are a number of physiological measures for assessing pain in children through changes in physiological variables such as heart and respiratory rate and blood pressure (Reaney 2007; Versloot 2007).

### **1.2.3 Dental treatment in children**

Children's dental caries is still considered one of the major health problems that may have a negative impact on the child's and the parent's life (Kassebaum et al., 2017; Public Health England, 2020). Globally, it has affected 60-90% of schoolchildren (Freeman et al., 2020). In the UK, childhood dental caries has affected 23.4% of 5-year-old children (Public Health England, 2020). It has also been found that dental caries of the primary dentition is most severe in children aged 1 to 4 years-of-age (Kassebaum et al., 2017).

Most paediatric dental procedures are carried out to treat dental caries in primary care and are conducted by general dental practitioners (GDPs) (Freeman et al., 2020). These procedures may comprise prevention, restorations, pulp treatments, extractions, and other dental care. These dental procedures may cause discomfort, pain, anxiety, and management difficulties which may require a pharmacological intervention (Threlfall et al., 2005; Adewale, 2012). It has been found that dental caries is considered one of the most common reasons for exposing children to general anaesthesia for dental treatment (Knapp et al., 2017).

### **1.2.4 General anaesthesia for dental treatment**

Several studies have investigated the most common factors leading to the use of general anaesthesia for dental treatment (Smallridge et al., 1990; Vermeulen et al., 1991; Holt et al., 1992; Savanheimo et al., 2005; Davis et

al., 2008). They found that early childhood caries, behaviour management issues, severe pulpitis, dental fear, and repeated unpleasant experiences during dental care are recognised as the most important reasons for referring children for general anaesthesia. Moreover, it has been found that a significant proportion of children requiring general anaesthesia for dental care are medically compromised patients (Wong et al., 1997; Harrison and Roberts, 1998; Camilleriu et al., 2004; Davis et al., 2008). Therefore, the aim of dental general anaesthesia (DGA) is to do the whole dental treatment in one session in a way that the child can cope with. This is important for the child who cannot manage in the dental chair and helps avoid repetitive GAs.

#### **1.2.4.1 Benefits of using general anaesthesia for dental treatment in children**

Dental treatment under general anaesthesia can be beneficial for both the child and parents. Some parents have considered general anaesthesia for dental treatment an acceptable and convenient method of therapy addressing their child's oral health needs (Knapp et al., 2017). Children with severe caries affecting multiple teeth can receive the whole treatment in a single session (Knapp et al., 2017). Furthermore, there are positive outcomes following dental general anaesthesia recorded by those children who being pleased and proud that their oral health problems are treated (Rodd et al., 2014; Knapp et al., 2017). Moreover, it can provide other benefits such as alleviation of pain, anxiety and reduction of infection (Adewale, 2012). Therefore, it has been shown that those reasons generally

increase the level of parental satisfaction (Anderson et al., 2004; Goodwin et al., 2015; Knapp et al., 2017).

#### **1.2.4.2 Risks of using general anaesthesia for dental treatment in children**

The use of general anaesthesia for paediatric dental procedures might be associated with the risk of morbidity and mortality. While there is a minimal risk of death from general anaesthesia for dental treatment, approximately 1 in 250,000, morbidities such as nausea, vomiting, post-operative pain, and injuries to adjacent teeth and structures are significantly more common (Knapp et al., 2017; Adewale, 2012). It has been found that 40 to 90% of children having dental general anaesthesia experienced pain, headache, nausea, vomiting, sore throat, sleepiness, and bleeding (Rodd et al., 2014).

Dental general anaesthesia (DGA) is a serious emotional event that children may experience (Aldossari et al., 2019). It has been found that dental treatment under general anaesthesia might be a traumatic experience for children due to the stressful procedures associated with general anaesthesia such as induction, relative loss of control, sequencing of events or the unfamiliar environment and personnel (Hosey et al., 2006; Aldossari et al., 2019). General anaesthesia for dental treatment has been thought as a contributing factor to dental fear and anxiety (DFA) both in the short term and long term (Aldossari et al., 2019). A study carried out by Aldossari et al. (2019) compared the DFA between children who had previously undergone DGA for more than one year and children who had not. They reported that

higher levels of DFA were associated with those children who had previously undergone GA for dental treatment at an earlier time in their childhood. Likewise, Haworth et al. (2017) investigated the impact of using DGA in childhood on dental caries or dental anxiety in adolescence. Their study revealed that children who had received DGA were more likely to have anxiety at age 17 years by over 2.5 times. Moreover, Cantekin et al. (2014) assessed the change in dental anxiety in young children following DGA and found that there was an increase in the level of dental fear among children who had undergone DGA. DFA is considered a risk factor for dental caries in adolescents that may prevent them from seeing a dentist; therefore, this potentially leads to a further need for DGA (Seppa et al., 1989; Kruger et al., 1998; Haworth et al., 2017). A study carried out by Kakaounaki et al. (2011) investigated the number of children who required a further GA for dental treatment within the following six years of having their first GA for dental extractions. They reported that irregular dental clinic attendees after DGA for extractions were four times more likely to have another DGA.

Dental treatment under GA is considered expensive and resource intensive which places a considerable financial burden on the National Health Service (NHS) in the UK and other countries (Knapp et al., 2017; Fox et al., 2022). For example, it has been found that about 43,700 children aged  $\leq 16$  years were admitted to hospitals in England in 2015-2016 for the extraction of multiple teeth under GA which was costed at £30 million (Knapp et al., 2017). In 2018–2019, 44,685 surgical procedures were carried out in English

hospitals to remove more than one tooth in children aged 18 years and under which was costed at £41.5 million (Fox et al., 2022).

Long waiting times for paediatric dental procedures under GA is another significant issue (Knapp et al., 2017; Fox et al., 2022). It has been found that children may be waiting over a year to be treated under GA (Paterson and Tahmassebi, 2003). These children may therefore experience multiple episodes of pain, distress, and infection during this time (North et al., 2007; Fox et al., 2022). Multiple visits to primary dental care may be necessary for placing several temporary dressings or prescribing courses of antibiotics to relieve pain and infection during this period (North et al., 2007; Fox et al., 2022).

As discussed above, because of the risks, costs and availability, GA for dental care should only be used when other options have failed or are not appropriate for the above reasons. Understanding and reducing intra-operative and post-operative pain associated with dental procedures can improve the dental experience and avoid the need for GA. Therefore, it is crucial to understand predictors of intra-operative and post-operative pain so that they can be appropriately targeted.

## **1.2.5 Predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures**

### **1.2.5.1 Age**

Several studies have investigated the influence of age on child pain perception. Two studies, conducted by Arts et al. (1994) investigating the relationship between age and pain experience and another carried out by Bachanas and Roberts (1995) assessing children's health care attitudes to medical procedures, have been reported. They suggested that age can play a vital factor for assessing child pain perception. These studies found that younger children (4-6 years) are more likely to display distress and report pain to be higher than older groups (P-value <0.001). Likewise, the dental literature has documented that pain tends to be more highly perceived by younger children (younger than 14 years) than older children (Krekmanova, 2017).

### **1.2.5.2 Developmental stage**

The capability of a child to understand and cope with a painful experience can be influenced by the stage of development (McGrath, 1995; Versloot, 2007). It has been shown that infants aged six months begin exhibiting some memory of previous pain resulting from their immunizations (McGrath, 1995). Toddlers can use words for pain description, and as well as they can seek comfort as their non-cognitive coping skills, whereas the young school-aged group begin using cognitive coping skills (Craig & Grunau, 1991;



McGrath, 1995; Versloot, 2007). Older adolescents can understand and describe complex concepts of pain such as pain value (Harbeck and Peterson, 1992; McGrath, 1995; Versloot, 2007).

### **1.2.5.3 Gender**

A number of studies have discussed the influence of gender on child pain perception. For example, Krekmanova et al. (2009) evaluated the frequency and intensity of general and oral pain in Swedish children (aged 8 to 19 years) and found that girls significantly reported a higher intensity of pain related to dental injection than boys ( $P < 0.05$ ). However, Almeida et al. (2016) evaluated the influence of gender on dental pain perception in children (aged 3 to 11 years) and found that there was no significant difference between gender and pain perception after different dental treatments ( $P = 0.64$ ). This finding was in agreement with another study conducted by Ghanei et al. (2018) who investigated pain and discomfort in children (aged 3 to 19 years) receiving routine dental treatment ( $p > 0.05$ ). Therefore, it can be seen that the relationship between gender and pain perception is still unclear which might need combining data to evaluate the effect of gender on pain perception.

### **1.2.5.4 Inflammation/infection**

The effectiveness of local anaesthesia can be influenced by inflammation with infection. Inflammation can increase patient sensitivity to pain by inducing a primary area of hyperesthesia, whereas infection can interfere with local anaesthetic dissociation by generating an acid pH (Wong and

Jacobsen, 1992; Lopez and Diago, 2006). It has been shown that pulpitis and apical periodontitis may result in anaesthetic failure or difficulty in obtaining satisfactory analgesia in adult patients (Lopez and Diago, 2006). Likewise, in a study conducted by Nusstein et al. (1998), determining the anaesthetic efficacy of the intra-osseous injection in irreversible pulpitis, it was found that 81% of the lower teeth and 12% of the upper teeth diagnosed with irreversible pulpitis required supplemental intra-osseous anaesthesia. Therefore, the presence of inflammation is known to alter the clinical effects of local anaesthesia.

#### **1.2.5.5 Injection and its technique**

Although local anaesthesia should eliminate pain in dental procedures, it can provoke pain and anxiety in young dental patients (Ram and Peretz, 2002). It has been found that needle insertion and anaesthetic solution deposition can stimulate pain and anxiety (Milgrom et al., 1997; Versloot, 2007). Furthermore, it has been shown that dental injections can stimulate negative responses in children, and these responses can increase over a series of four or five injections (Dean et al., 2011). Moreover, Nakai et al. (2005), Krekmanova et al. (2009) and Naoumova et al. (2012) have recognised dental injection as one of the most painful dental procedures.

Additionally, the site of local anaesthesia can influence pain and discomfort reported after dental injection. Some studies have shown that giving nerve block local anaesthesia in the mandible is more likely to be uncomfortable than those in the maxilla. A study carried out by Jones et al. (1995) assessing children's ratings of dental injection (aged 4 to 10 years), reported

that children rated inferior alveolar nerve block (IANB) significantly more painful than maxillary buccal infiltrations ( $P < 0.0001$ ). Likewise, Versloot et al. (2008) who evaluated self-reported pain for children (aged 4–11 years) at the dentist over two sequential dental visits and found that mandibular injections (Mean  $4.17 \pm$  SD  $3.82$ ) were more painful than maxillary injections (Mean  $2.17 \pm$  SD  $2.88$ ) at the first visit for children younger than 6 years of age. However, other research has reported contradictory findings. A study conducted by Ram and Peretz (2001) assessed the reactions of children (aged 4-10 years) to maxillary infiltration and mandibular block injections and noticed that more children were rated positively during IANB injection than with maxillary infiltration ( $p=0.004$ ). Similarly, another study carried out by Aminabadi et al. (2009) investigated pain reactions to maxillary and mandibular infiltration anaesthesia in children (aged 5-6 years) and reported that local anaesthesia injections were more painful in the maxilla than into the mandible ( $P < 0.05$ ).

A new concept of delivering local anaesthesia through a Computer Controlled Anaesthetic Device (Wand System) has been designed to minimise pain perception during the injection of local anaesthesia (Versloot, 2007). A study conducted by Mittal et al. (2015) evaluating and comparing pain perception rates in paediatric patients (aged 8-12 years) with a computerised system and traditional methods found that children experienced less painful palatal infiltration ( $p<0.05$ ) through using the Wand system whereas there was no difference in pain perception during buccal infiltration ( $p>0.05$ ). Likewise, another study carried out by Baghlaf et al. in

2018, reviewing computerised intra-ligamental anaesthesia in children, concluded that lower pain perception scores and lower pain-related behaviour were associated with using the Wand system. In contrast to the above studies, Tahmassebi et al. (2009) and Kandiah and Tahmassebi (2012) did not find a significant difference between pain experience with the Wand system as compared with conventional injection techniques ( $p>0.05$ ). However, it is difficult to compare studies without knowing what behavioural management techniques were used and knowing the experience and skills of the dentists conducting the injections. Therefore, the efficacy of the Wand device in reducing pain perception is still unclear which might need combining data to evaluate its effectiveness on pain perception.

#### **1.2.5.6 Dental procedures**

A number of studies have investigated the influence of different dental procedures on child pain perception. For instance, in a study conducted by Ghanei et al. (2018), investigating pain and discomfort in children (aged 3 to 19 years) receiving routine dental treatment, it was reported that dental injection and extraction have emerged as the most common causes of pain in paediatric dentistry, while drilling has been recognised as the second common source of pain. This agrees with other studies considering dental injection as the procedure causing the highest pain (Nakai et al., 2005; Krekmanova et al., 2009; Naoumova et al., 2012). Furthermore, in a recent study (Krekmanova, 2017), investigating the frequency and intensity of general and oral pain in Swedish children (aged 8 to 19 years), it was found that dental injection, drilling, or extraction were experienced as painful by

half the young participants receiving invasive dental procedures. Because of the varying evidence for what are the most painful procedures in children, a systematic review would therefore be helpful to determine if more accurate guidance for dentists could be developed.

#### **1.2.5.7 Anxiety\feard\Previous dental experience \Previous medical experience**

Anxiety and fear are considered normal aspects of the developmental process that allow children to react to unknown situations (Krekmanova, 2017). Dental fear (DF) has been defined as “a normal emotional reaction to one or more specific threatening stimuli in the dental situation” (Klingberg and Broberg, 2007, pp.391-392), whereas dental anxiety (DA) has been known as “a state of apprehension that something dreadful is going to happen in relation to dental treatment, and it is coupled with a sense of losing control” (Klingberg and Broberg, 2007, p.392).

Several dental studies have investigated the influence of fear and anxiety on pain perception in children. For instance, a recent study carried out by Lamarca et al. (2018) assessing the role of general psychological disorders on dental pain perception in children (aged 9 to 12 years) suggested that highly anxious children are more likely to report pain. Likewise, Krekmanova (2017) who evaluated the frequency and intensity of general and oral pain in Swedish children (aged 8 to 19 years) and found that children with higher levels of dental fear and anxiety were highly sensitive to pain in their study. Furthermore, it has been shown that pain thresholds can be reduced by fear

and anxiety (Naoumova et al., 2012). Therefore, it would be worthwhile to have a systematic review of the impact of fear and anxiety on pain reports in children to help dentists understand this more accurately.

#### **1.2.5.8 Dentists' knowledge and attitudes**

Few dental studies have assessed dentists' knowledge and attitudes to children's pain perception and pain management in children and adolescents. For instance, a study carried out by Murtomaa et al. in 1996, evaluating dentists' perceptions and management of pain in children receiving dental treatment in the USA and Finland, it was found that a considerable number of general dental practitioners did not routinely ask their young patients about their pain. Similarly, Versloot et al. (2004) analysed the assessment of pain by the child, dentist, and independent observers and concluded that dentists were less likely to observe that the child was in pain than children and observers. Furthermore, Wondimu and Dahllof (2005) found that Swedish general dentists underused local anaesthesia during paediatric dental procedures. Therefore, they recommended that dental surgeons needed to assess pain more and provide appropriate pain management for their young patients.

## **1.2.6 Intervention options to reduce intra-operative and post-operative pain associated with routine paediatric dental procedures**

### **1.2.6.1 Pharmacological interventions**

#### **1.2.6.1.1 Oral analgesics**

Pre-operative analgesics in dentistry refer to the administration of analgesic medication prior to dental treatment with the goal of decreasing intra-operative and post-operative pain (American Academy of Pediatric Dentistry, 2018). Management of post-operative pain in adults through using of pre-operative analgesia is well established in medicine (Toms et al., 2009; Ashley et al., 2016). In dentistry, pre-emptive analgesia is commonly used as an adjunct to the analgesic effect of local anaesthesia in oral surgery for adults (Weil et al., 2007; Ashley et al., 2016).

The use of pre-operative analgesics for paediatric dental patients having dental treatment under GA is also routinely prescribed in many places, but their value is still unclear (Ashley et al., 2016). However, pre-operative analgesia for children undergoing dental procedures under local anaesthesia does not appear to be routinely used, and no guidelines or recommendations are currently available (Ashley et al., 2016). A recent systematic review of pre-emptive analgesia that was given to children having routine dental treatment conducted by Ashley et al. in 2016 concluded that

further randomised clinical trials are recommended to determine the benefit of pre-operative analgesics for paediatric dental patients. The most common analgesics used for relieving pain in children are paracetamol, ibuprofen, and opioids (Lee et al., 2014; Hartling et al., 2016).

Several dental studies have investigated the use of pre-emptive analgesics such as paracetamol and ibuprofen on post-operative pain in children. For instance, a study carried out by Primosch et al. (1993) investigated the efficacy of pre-operative administration of paracetamol on the prevalence of post-operative pain-related behaviours and the frequency of post-operative analgesic use in children (aged 4 to 10 years) following different dental procedures. They reported that there was no significant decrease in post-operative pain between children who received pre-treatment paracetamol and those in the placebo group ( $P=0.46$ ). Likewise, a study carried out by Primosch et al. in 1995 comparing the efficacy of the pre-operative administration of ibuprofen, acetaminophen, or a placebo in reducing post-operative pain associated with primary teeth extraction in children (aged 2-10 years), found that none of the analgesics provided benefits compared to the placebo solution ( $P>0.05$ ). However, McGaw et al. (1987) found that there was superior analgesia associated with using ibuprofen compared with either paracetamol or a placebo for post-operative pain in children undergoing permanent tooth extraction ( $P<0.05$ ). Baygin et al. (2011) also conducted a study comparing pre-emptive ibuprofen, paracetamol, and a placebo in reducing post-operative pain in children (aged 6-12 years) having a primary tooth extraction and showed that there was a significant decrease



in reported post-operative pain scores associated with the use of pre-emptive analgesics ( $P < 0.05$ ). Similarly, an orthodontic study carried out by Bernhardt et al. (2001) comparing the effectiveness of pre-operative and post-operative ibuprofen therapies, and a combination of the two therapies after separator placement in children (aged 9 to 16 years) found that there were beneficial effects on administering pre-emptive ibuprofen on relieving post-operative pain associated with separator placement ( $P < 0.05$ ).

It is not clear if the time when the pain was measured was while the LA was still working or whether the time may have been too long. Pre-emptive analgesics may have more effect during the procedure, and that the procedure may need to be followed by post-operative analgesics to manage the later pain. Therefore, it would be worthwhile to have a systematic review of the effectiveness of pre-emptive analgesics on pain perception in children having routine dental treatment to help dentists justify using pre-operative analgesics in children.

#### **1.2.6.1.1.1 Non-steroidal anti-inflammatory drugs (NSAIDs)**

NSAIDs represent the most common medications that are used in medicine and dentistry for having anti-inflammatory, analgesic, antipyretic, and antiplatelet properties (Kokki, 2003; American Academy of Pediatric Dentistry, 2018). NSAIDs such as ibuprofen can inactivate cyclooxygenase (COX) which is important for the modulation of transformation of prostaglandins - responsible for pain, from arachidonic acid in the cellular plasma membrane (De Carlos et al., 2006; Laskarides, 2016; Monk, 2016).

Therefore, suppressing prostaglandin synthesis can reduce pain (Monk, 2016). However, there are some adverse effects associated with NSAIDs, generally when used over prolonged periods, including problems in bone growth, healing process, platelet function, gastric pain, and bleeding, reduced renal blood flow and increased cardiovascular and respiratory problems (Hartling et al., 2016; Zeltzer et al., 2016; American Academy of Pediatric Dentistry, 2018).

#### **1.2.6.1.1.2 Paracetamol**

Paracetamol or Acetaminophen is an analgesic and antipyretic medication that is used to manage mild to moderate pain (Becker, 2010; American Academy of Pediatric Dentistry, 2018). It is available in different forms such as tablets, capsules, liquid, and for oral, rectal and IV routes (Laskarides, 2016; American Academy of Pediatric Dentistry, 2018). It has the same mechanism of action as NSAIDs but does not have anti-inflammatory properties and has no known effects on gastric mucosal lining or platelets (Becker, 2010; Monk, 2016; Rang et al., 2016).

#### **1.2.6.1.1.3 Opioids**

Opioids have been defined as “any substance, whether endogenous or synthetic, that produces morphine-like effects that are blocked by antagonists such as naloxone” (Rang et al., 2016, p.517). Opioid analgesics are prescribed to manage acute moderate to severe pain in all age groups (American Academy of Pediatric Dentistry, 2018). They are commonly used

to relieve pain in children having cancer, sickle cell disease, osteogenesis imperfecta, epidermolysis bullosa, or neuromuscular disease (Fortuna et al., 2010; Schechter and Walco, 2016; Cooper et al., 2017; American Academy of Pediatric Dentistry, 2018). They are also used for children having dental treatment under general anaesthesia (Laskarides, 2016). However, they are rarely used in children undergoing dental treatment under local anaesthesia (Laskarides, 2016; American Academy of Pediatric Dentistry, 2018).

#### **1.2.6.1.1.4 Inhalation sedation with nitrous oxide and oxygen**

There are different routes of administration of sedative drugs used in Paediatric Dentistry such as oral, inhalation, intranasal, intramuscular, rectal, intravenous and transmucosal. Nitrous oxide - oxygen ( $N_2O/O_2$ ) inhalation sedation is often employed in paediatric dentistry as the first choice for conscious sedation in the UK (Hosey, 2002). Conscious sedation has been defined by the British Standing Dental Advisory Committee (2003) as “A technique in which the use of a drug or drugs produces a state of depression of the central nervous system enabling treatment to be carried out, but during which verbal contact with the patient is maintained throughout the period of sedation”. Therefore, it can be clearly seen that the main target of conscious sedation is to use a pharmacological agent in order to improve behavioural management and to reduce anxiety levels while the patient remains responsive, the patient is maintained throughout the dental procedure.

N<sub>2</sub>O/O<sub>2</sub> inhalation sedation is a widely accepted and used technique for paediatric dental patients (Hosey, 2002). It is a mixture of nitrous oxide and oxygen gases which is colourless and virtually odourless with a slightly sweet smell (Paterson and Tahmassebi, 2003). It has been reported as a safe and effective method of reducing fear, anxiety and pain levels and improving patient cooperation as it can be titrated to the patient's needs (Paterson and Tahmassebi, 2003; SDCEP, 2017). A study carried out by Hammond and Full in 1982 investigated the analgesic properties of nitrous oxide in children (aged 4 to 10 years) having cavity preparation of Class I in the primary molars. They found that the intensity of pain perceived during cavity preparation of Class I in the primary molars was significantly decreased with using N<sub>2</sub>O/O<sub>2</sub>. Furthermore, it has been found that N<sub>2</sub>O/O<sub>2</sub> inhalation sedation raises the pain threshold and that it is used for this in emergency trauma management (Paterson and Tahmassebi, 2003).

#### **1.2.6.2 Non-pharmacological interventions**

Non-pharmacological interventions may play an effective role in managing procedure related-pain, anxiety, and distress with minimal risks of adverse effects (Lewin and Dahl, 1999; Landier and Tse, 2010; Fein et al., 2012; Dostrovsky, 2014; American Academy of Pediatric Dentistry, 2018). It has been shown that pain can be facilitated by fear and anxiety through activating circuits within the central nervous system (CNS) (American Academy of Pediatric Dentistry, 2018). Therefore, providing a safe and comfortable environment may help a young patient feel less stressed and

accept treatment (Fein et al., 2012; Ruest and Anderson, 2016; American Academy of Pediatric Dentistry, 2018).

#### **1.2.6.2.1 Preparatory information**

Giving preparatory information about what will happen during a dental visit can decrease parental anxiety and, in turn, a child's anxiety. It has been shown that pre-appointment letters can help the child cope with the dental visit (Rosengarten, 1961; Bailey et al., 1973; Wright et al., 1973; Chadwick, 2002).

#### **1.2.6.2.2 Non-verbal communication**

Non-verbal communication is a method of socialising that occurs continuously during a dental visit and may emphasise or oppose verbal signals (Chadwick, 2002). This can be achieved by providing a child-friendly environment and a happy dental team (Wright et al., 1987). Furthermore, it has been found that distress associated with dental care can be reduced by physical touching such as gentle pats and squeezes on the shoulder (Weinstein et al., 1982, Chadwick, 2002).

#### **1.2.6.2.3 Voice control**

It has been found that young children are more likely to respond to the tone of voice than the actual words (Wright et al., 1987; Chadwick, 2002).

Children's behaviour can be influenced and directed through using a controlled alteration of voice, volume, tone, and pace (Chadwick, 2002). This

approach aims to improve attention and compliance and establish behaviour (Chadwick, 2002). For instance, the attention of an uncooperative child would be gained when his/her dentist suddenly changes his/her voice from soft to firm (Chadwick, 2002). It has been shown that voice control may reduce disruptive behaviour without generating long-term adverse effects (Greenbaum et al., 1990; Chadwick, 2002).

Although voice control is widely used by dentists, some parents or clinicians may not accept it (Murphy et al., 1984; McKnight-Hanes et al., 1993; Roberts, 1995; Chadwick, 2002). Moreover, it may not be appropriate to be used in children who are too young to understand or for those with intellectual or emotional impairment (Chadwick, 2002).

#### **1.2.6.2.4 Tell-Show-Do (TSD)**

TSD is commonly used in dental practice to familiarise young patients with new dental procedures. Most young patients may have little idea of what dental treatment involves which could raise their dental anxiety (Welbury et al., 2018). The idea of this technique is to explain what will happen at each step of the visit in simple words that children can understand then demonstrate each procedure and immediately do it (Chadwick, 2002). Although the acceptability of this method is established, only a few studies have suggested that it may be a beneficial way to reduce anticipatory anxiety in new patients (Welbury et al., 2018). It still seems to be highly effective for children with low anxiety levels (Welbury et al., 2018).

#### **1.2.6.2.5 Enhancing control**

Enhancing control is a helpful method that gives a child a degree of control over each stage of a dental procedure through using a stop signal such as raising a hand (Thrash, 1982; Chadwick, 2002). The child should practice this stop signal before starting dental treatment, and it is important to be responded to quickly by the dentist when it is used (Thrash, 1982; Chadwick, 2002; Fayle and Tahmassebi, 2003).

#### **1.2.6.2.6 Behaviour shaping**

Behaviour shaping has been defined as “developing appropriate behaviour by reinforcing successive approximations to the desired behaviour until the desired behaviour is achieved” (Lencher and Wright, 1975). This technique usually involves a basic TSD approach but with the desired behaviour being encouraged by praising it and any undesired behaviour being discouraged by ignoring it (Fayle and Tahmassebi, 2003). Thus, the child can learn step by step what is expected in the dental surgery (Wright and Kupietzky, 2014).

#### **1.2.6.2.7 Positive reinforcement**

Positive reinforcement is an effective technique for rewarding a desired child’s appropriate behaviour in order to strengthen its recurrence (Wright and Kupietzky, 2014). It can be expressed in the form of social reinforcers such as positive voice modulation, facial expression, verbal praise, and appropriate physical demonstrations of affection by the dental team (Gupta et al., 2014). Another form of positive reinforcement uses non-social

reinforcers such as tokens and toys (American Academy of Pediatric Dentistry, 2005–06). It has been shown that children behave well when they are praised and encouraged (Gupta et al., 2014). Therefore, it is imperative to praise and positively reinforce the child immediately after demonstrating an appropriate behaviour (Gupta et al., 2014).

#### **1.2.6.2.8 Negative reinforcement**

The idea of negative reinforcement is to apply an unpleasant stimulus to a child exhibiting an undesirable behaviour, and it is removed immediately once the child has shown a desired appropriate behaviour, thus reinforcing that behaviour (Fayle and Tahmassebi, 2003). It includes hand-over-mouth and selective exclusion of the parent (Levitas et al., 1974; Stokes and Kennedy, 1980). However, hand-over-mouth is not supported in many countries, and selective exclusion of the parent requires their agreement that this is appropriate for their child (Chadwick, 2002; Fayle and Tahmassebi, 2003).

#### **1.2.6.2.9 Modelling**

Modelling is a process in which children learn much about their environment by observing the consequences of other individuals' behaviour (Stokes and Kennedy, 1980). It has been shown that modelling can be effective when the model is someone who is a relative of the child or a friend of similar age (Fayle and Tahmassebi, 2003). Also, it has been reported that watching



children having their dental treatment on videotape can be helpful (Fayle and Tahmassebi, 2003).

#### **1.2.6.2.10 Distraction**

Distraction techniques can be used to divert a child's attention from a potentially stressful situation to a totally different sensation or action without breaching trust by deliberately trying to deceive the child (Chadwick, 2002; Fayle and Tahmassebi, 2003). For example, verbal distractors such as talking to the patient while undertaking examination or treatment can help distract the patient's attention (Wright et al., 1987 & Chadwick, 2002).

Moreover, it has been found that audio-visual devices can be more effective in distracting the child's attention (Chadwick, 2002; Fayle and Tahmassebi, 2003). In addition, lip pulling during local anaesthesia, deep breathing or lifting legs during the taking of dental impressions are other effective distractors (Chadwick, 2002; Fayle and Tahmassebi, 2003).

#### **1.2.6.2.11 Systematic desensitisation**

The basic principle of this technique consists of gradually exposing patients to their anxiety, starting with the least anxiety-evoking stimulus and working upward step-by-step to the most anxiety-evoking stimulus until it no longer causes anxiety (Wolpe, 1969; Wright and Kupietzky, 2014). It is a technique for older children and adolescents who can identify and understand the things that cause their anxiety (Chadwick, 2002). Although there are advantages of using systematic desensitisation with anxious patients, it has

been shown that it may be impractical for use in the dental office as it is time-consuming and very costly (Wright and Kupietzky, 2014).

#### **1.2.6.2.12 Cognitive behaviour therapy (CBT)**

CBT has been defined as a talking therapy that combines both behavioural and cognitive intervention in order to treat anxiety in children and adolescents (James et al., 2013; Wang et al., 2017). It has been found that CBT can be an effective way of reducing dental anxiety (Gomes et al., 2018). A randomised controlled clinical trial carried out by Kebriaee et al. (2015) compared the efficacy of inhalation sedation with N<sub>2</sub>O/O<sub>2</sub> and CBT in reducing dental anxiety in children (aged 3 to 6.5 years) having pulp treatment in primary mandibular molars. They reported that CBT significantly improved children's cooperation and reduced their anxiety ( $p=0.00$ ). Likewise, Wang et al. (2017) conducted a systematic review and meta-analysis evaluating CBT and pharmacotherapy's comparative effectiveness and adverse events for anxiety disorders in children (5.4-16.1 years). They supported that CBT can be effective in reducing childhood anxiety symptoms. Furthermore, a recent systematic review of CBT for anxious paediatric dental patients aged 41 months to 18 years, carried out by Gomes et al. (2018), concluded that lower anxiety levels and better cooperation were associated with CBT compared to other behavioural management approaches.

### **1.2.7 Conclusion**

From the literature discussed previously, there was research carried out on predictors of pain associated with routine dental procedures in children and on interventions used to relieve this pain. For predictors of pain, some studies showed effects of age, developmental stage, gender, inflammation/infection, dental injection and its technique, dental procedures, anxiety and dentists' knowledge and attitudes on children's pain perception. Similarly for intervention, studies showed variable findings with some showing pre-emptive oral analgesics and behavioural interventions worked and others showing no effect. However, the evidence is still unclear for certain predictors such as age, dental injection and its technique and dental procedures, and for certain interventions such as pre-emptive analgesics and behavioural interventions. In addition, the direction and strength of the effect of predictors and interventions remain unclear as does the internal and external validity of the research.

## **Chapter 2: Methodologies, Aims and Objectives**

### **2.1 Suggested methodologies**

This section describes the various types of study design available to fulfil the study objectives and hence determines which of these was the most appropriate for the present study which investigated predictors of intra-operative and post-operative pain associated with routine dental procedures in children and assessed interventions that may be effective in relieving this pain.

#### **2.1.1 Observational studies**

For investigating predictors of intra-operative and post-operative pain associated with dental procedures in children, observational study designs can be used to answer the research question. Observational studies have been defined as studies where investigators can observe, collect, and analyse data without intervention or manipulation that may affect the outcome (Butani et al., 2006; Thiese, 2014). It has been found that observational studies can be useful for studying the cause-effect relationship of a specific oral disease, describing or monitoring clinical or epidemiological issues related to oral health in children or measuring risk factors (Petrie et al., 2002; Krithikadatta, 2012; Garrocho-Rangel et al., 2017). In addition, observational studies are less costly, can be completed more quickly, do not require to randomise patients or providers who are willing to different

treatments and are often more satisfactory in terms of practicality and ethics (Sutherland, 2001; Butani et al., 2006). For these reasons, the majority of paediatric dental studies have been conducted through using observational studies (Bader and Shugar, 1995; Bader et al., 1999; Nainar, 2000; Butani et al., 2005). However, they may give invalid or misleading results if multiple factors that can influence outcomes such as confounders are not carefully considered during the study stages (Butani et al., 2006; Althubaiti, 2016).

There are two designs of observational study that can answer the research question about predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures. These are cross-sectional and cohort studies. Cross-sectional study designs enable investigators to measure the outcomes and the exposures in the study participants at a specific point in time, whereas cohort study designs allow researchers to identify a group of individuals based on their exposure status and then follow them over a period of time to evaluate for the occurrence of the outcome (Setia 2016).

The dental literature from the background review showed that there are a number of observational studies on predictors of intra-operative and post-operative pain associated with routine paediatric dental procedures. However, the direction and size of the effect and quality of the studies are unclear.

### **2.1.2 Randomised controlled trials (RCTs)**

For investigating interventions used to relieve intra-operative and post-operative pain associated with routine dental procedures in children, RCTs can be used to answer the research question. Randomised controlled trials have been defined as prospective studies where investigators can measure the effectiveness of a new intervention or treatment (Hariton and Locascio, 2018). They have been considered as the gold standard for clinical research and the best study designs for investigating the efficacy of medical and dental interventions (West et al., 2008; Cioffi and Farella, 2011; Hariton and Locascio, 2018). It has been found that the results of RCTs can help define a treatment protocol for populations who are affected by the same condition of the research sample or to choose among the different therapies available (Pocock, 1996). Furthermore, randomisation in RCTs can prevent selection biases during group allocation (Cioffi and Farella, 2011). However, RCTs can require significant numbers of participants and have high cost in terms of the length of time the study must run and funding. In addition, RCTs may have problems with generalisability and following up participants to ensure they are all accounted for.

The background review chapter has shown that there are sufficient RCT studies on interventions used to relieve intra-operative and post-operative pain associated with routine paediatric dental procedures. However, the direction and size of the effect and quality of the studies are unclear.

### 2.1.3 Systematic reviews

There are over two million journal articles published annually in the biomedical literature resulting in a huge amount of information (Mulrow, 1994). Most healthcare professionals will undoubtedly be unable to read every published article in their area of interest, speciality, or expertise (Watkinson, 2014). Therefore, they may need a research method that allows integrating existing information efficiently and provides data for rational decision-making (Mulrow, 1994). A relative form of publication type, systematic review, was then generated to enable researchers to answer a specific research question by identifying, appraising, and synthesising all available evidence which meets pre-specified eligibility criteria through using explicit and selected systematic methods to minimise bias and provide more reliable results to inform decision-making (Higgins and Green, 2011). Furthermore, it can give a greater generalisability of scientific findings by including studies that address similar questions using different eligibility criteria (Mulrow, 1994). Moreover, the data from multiple studies can be combined into a single meta-analysis to generate a more precise result (Higgins and Green, 2011). Likewise, systematic reviews can be positioned at the top of the hierarchy of evidence depending on the quality and types of studies (Green, 2005). In addition, a systematic review is less costly and can sometimes be completed quicker than conducting a new study (Mulrow, 1994).

In addition to the above advantages, the background literature showed that there are a number of studies on predictors and interventions for pain

associated with routine paediatric dental procedures albeit with different findings which some of them were significant, and others were not. These studies addressed similar questions using different eligibility criteria for participants (different age ranges of participants), different dental procedures (extraction, drilling, local anaesthesia, restoration, scaling, probing, radiograph, and polishing), different methods of measuring outcomes (intra-operative and post-operative pain and anxiety), different interventions (pharmacological and non-pharmacological interventions), and different study designs (observational studies and RCTs). Therefore, a logical step forward to investigate was to carry out two systematic reviews without wasting resources, one review to combine the results of observational studies to determine the effect size and direction of effect of each predictor and the other review to combine the results of RCTs studies to determine the effect size and direction of effect of each intervention. Also, it would not be cost-effective to conduct further research but rather combine the results of existing research to determine if there is an effect.



## **2.2 Aims and objectives**

### **2.2.1 Aims**

The aims of this research were:

1. To identify predictors of intra-operative and post-operative pain associated with routine dental procedures in children.
2. To evaluate interventions used to reduce intra-operative and post-operative pain associated with routine dental procedures in children.
3. To use the findings to develop evidence-based recommendations for managing intra-operative and post-operative pain associated with routine dental procedures in children.

### **2.2.2 Specific objectives**

1. Conduct a systematic review of predictors of intra-operative and post-operative pain associated with routine dental procedures in children through appraising the available evidence.
2. Conduct a systematic review of pharmacological and non-pharmacological interventions used to reduce intra-operative and post-operative pain associated with routine dental procedures in children through appraising the available evidence.
3. Use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to evaluate the certainty of evidence and then recommend based on risks versus benefits of each intervention.

## **Chapter 3: The First Systematic Review and Meta-analysis**

### **Predictors of intra-operative and post-operative pain associated with routine dental procedures in children: A systematic review and meta-analysis**

#### **3.1 Aim**

The aim of this review was to identify predictors of intra-operative and post-operative pain associated with routine dental procedures in children.

#### **3.2 Methods**

This systematic review and meta-analysis were undertaken following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009; Moher et al., 2009). The protocol was registered and published in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42020177746).

The protocol is available at:

[https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD420201777](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD420201777)

[46.](#)

### **3.2.1 Criteria for considering studies for this review**

#### **3.2.1.1 Types of studies**

As discussed in chapter 2, the best study designs that can investigate risk factors 'predictors' are observational studies (Petrie et al., 2002; Krithikadatta, 2012; Garrocho-Rangel et al., 2017). Therefore, observational studies were included.

#### **3.2.1.2 Types of participants**

Studies involving children and adolescents who were old enough to be able to answer the pain evaluation (3 years) aged up to 19 years were included. Children aged 19 years were included as World Health Organisation (WHO) considers this age as adolescence. Children and adolescents having routine dental treatment with or without local anaesthesia (LA) were included.

Children and adolescents receiving dental treatment under N<sub>2</sub>O/O<sub>2</sub> inhalation sedation or general anaesthesia (GA) were excluded according to the aim of this review and because these interventions may have an influence on children's pain threshold as discussed previously in the background.

#### **3.2.1.3 Types of predictors**

Routine paediatric dental procedures such as diagnostic examination, probing, scaling, polishing, radiograph, local anaesthesia, drilling,

restoration, pulpotomy/pulpectomy and extraction were included. Other predictors such as age, gender, infection, anxiety, previous dental and medical experience and dentists' knowledge and attitudes to pain were also included.

#### **3.2.1.4 Types of outcome measures**

The outcomes that were considered for this review were intra-operative and post-operative pain measured using a visual analogue scale (VAS) or other validated scales. The VAS has been shown in the literature to be a reliable and valid self-report measure of pain (McGrath et al., 1996; Sherman et al., 2006).

#### **3.2.1.5 Search methods for identification of studies**

This review used electronic searches with detailed search strategies developed for each database searched to identify eligible studies. The search strategies were formulated by the author (Mohammed Alzubaidi) under the supervision of a specialist librarian at the University of Leeds (Appendix 1). A combination of controlled vocabulary and free text terms was considered for the search strategy to identify eligible studies with no restrictions regarding language or date of publication. If there were non-English studies, they would be translated into English. The following electronic databases were searched up to the 22nd of October 2020: MEDLINE via OVID, EMBASE via OVID and PsycINFO via OVID, Global Health via OVID, PubMed, Scopus and SciELO (Web of Science). These databases were selected to ensure that as many related studies as possible

are identified and to minimise the risk of selection bias (Higgins et al., 2019). The included studies' references were also checked to identify more additional eligible studies. Hand searching in the related dental journals was considered when electronic copies were not available.

## **3.2.2 Data collection and analysis**

### **3.2.2.1 Selection of studies**

All references were exported into EndNote version X9 then the studies were imported into Covidence systematic review software where duplicated records were identified and removed. Covidence is a custom-built data system designed for assisting reviewers to use a structured data collection form for online form building, data entry, data sharing, and efficient data management (Veritas Health Innovation, 2014; Li et al., 2015). This software was therefore used to mitigate the effect of Covid-19 as it allowed data extraction and consensus to be done remotely. Titles and abstracts of relevant articles were independently assessed by the two review authors (Mohammed Alzubaidi and Dr Adam Jones). Discussion and consensus were considered to resolve any disagreement; however, a third reviewer was consulted (Dr Vishal Aggarwal) when consensus was not achieved.

### **3.2.2.2 Data extraction and management**

Any study that met the eligibility criteria regardless of the study quality was included. Study authors were contacted for more details when there was

missing data or inconsistent reporting. The required information was extracted in duplicate by the two reviewers (Mohammed Alzubaidi and Dr Adam Jones) using Covidence systematic review software. The following study characteristics were obtained:

- Name of the first author.
- Journal of publication.
- Year of publication.
- Country.
- Sitting.
- Study design.
- Population and participants characteristics.
- Sample size.
- Predictors.
- Type of outcome.
- Methods of measurement.

### **3.2.3 Quality assessment of the included studies**

The quality assessment of the included studies was undertaken independently by the same reviewers (Mohammed Alzubaidi and Dr Adam Jones). The NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies was considered because the included studies in this systematic review used observational (cohort and cross-sectional) designs as stated in the protocol (National Heart, 2014). This tool consists of 14 questions which are designed to assist reviewers in focusing on concepts that are important to a study's internal validity such as the sample

characteristics, recruitment process, and the level of in-depth reported information on the exposure and outcome measures (National Heart, 2014). Following the assessment, the studies were then assessed as 'Good', 'Fair' and 'Poor'. A numeric score was created to facilitate the rating of overall quality for each study based on the number of 'Yes' to the assessment's questions. The grading was then decided on the total score: 0-4 (Poor), 5-9 (Fair) and 10-14 (Good). None were excluded based on their quality rating. Discussion and consensus were considered to resolve any disagreement; however, a third reviewer was consulted (Dr Vishal Aggarwal) when consensus was not achieved. The NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies is available at: <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>.

### **3.2.4 Data synthesis and analysis**

All extracted data were exported and managed in an Excel file (Microsoft Inc, USA). The data extraction form was then modified to facilitate the process of data analysis (Appendix 2).

Meta-analysis was carried out if there were sufficient studies reporting the same outcomes to give more power to combine the results of these studies. The mean differences (MDs) and 95% confidence intervals (CIs) were considered for continuous outcomes that were measured with the same scale to estimate the impact of predictors on children's pain perception. Data collection for the meta-analysis included the following information:

- Name of the first author.
- Dental procedures included.
- Mean age.
- Gender.
- Age group.
- Anxiety levels (High/Low).
- Pain outcomes (Mean, Standard of Deviation (SD), Number of Participants (N), and Standard of Error (SE)).

Forest plots were generated using Stata 16 statistical software (StataCorp LLC, Texas, USA) with using a random-effects model. The random-effects model was considered because of the large heterogeneity that was expected to be found across studies and later was corroborated in the analysis. Meta-regression analysis using a random-effects model was also performed to determine the relative effect of the predictors on children's pain perception compared to a reference category which was chosen to the least painful procedure for dental procedures and low anxiety levels for anxiety (Appendix 3).

Clinical heterogeneity of included studies was accounted for by inclusion criteria for studies, participants, components of the predictors and outcome measures.  $I^2$  statistics were used for statistical heterogeneity;  $I^2$  statistics with values of 50% or greater represented substantial heterogeneity. A p-value  $\leq 0.05$  was considered statistically significant.



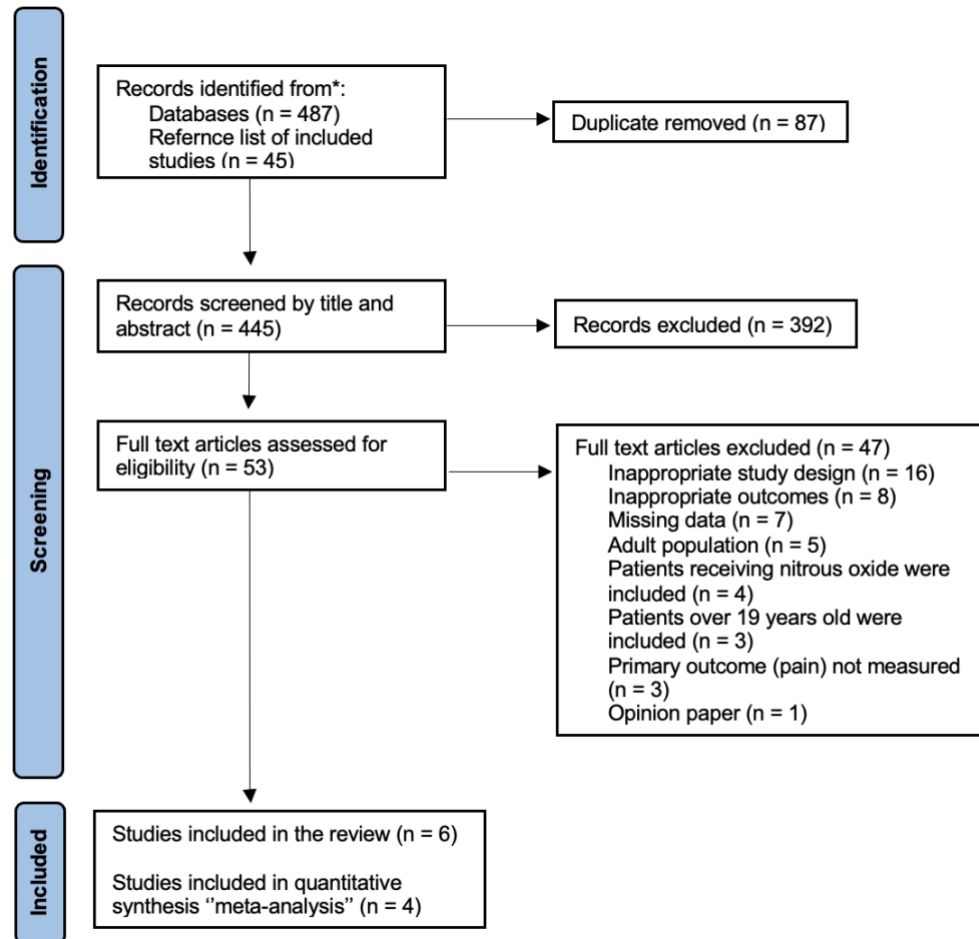
The clinically important difference in pain intensity was determined by a change of 10 for the 100 mm pain VAS according to a study carried out by Powell et al. in 2001 who determined the minimum clinically significant difference in the VAS pain score for children. The study asked the patients when they felt better and a change of 10 mm on the VAS indicated a change when the patient reported they felt a bit better or a bit worse, hence it was clinically significant. Therefore, if the MD VAS score was 10 mm or more, it would be considered clinically significant.

### **3.3 Results**

#### **3.3.1 Study selection**

Initially, a total of 532 studies were identified after the electronic and manual searches, with 445 remaining after excluding duplicates. Following the title and abstract screening, 53 articles were selected for full-text review and examined against the eligibility criteria in detail. Forty-seven studies were excluded (Appendix 4). Sixteen studies had an inappropriate study design. Moreover, eight other studies had inappropriate outcomes, and three studies did not measure pain. Five studies involved an adult population, and three studies included patients over 19 years of age. Furthermore, four studies included patients receiving dental treatment under N<sub>2</sub>O/O<sub>2</sub> inhalation sedation. Seven studies had missing data and although the seven authors were contacted, this was not able to be provided (response rate: 14.29%), and one more study was also excluded because it was an opinion paper.

Consequently, six studies were identified and included in the review, and four studies were eligible for the meta-analysis (Figure 1).



**Figure 1.** PRISMA flowchart of the study selection process.

### 3.3.2 Study characteristics

The characteristics of included studies are summarised in Table 1 and described as follows:

#### 3.3.2.1 Study design

Three included studies adopted a cross-sectional study design, Mathias et al. (2020), Pala et al. (2016) and Versloot et al. (2008), whereas the other

three studies were cohort studies, Krekmanova et al. (2009), Rocha et al. (2009) and Ghanei et al. (2018) (Table 1).

### **3.3.2.2 Sample size**

The sample size ranged from 36 to 2363. Krekmanova et al. (2009) included 368 patients while Rocha et al. (2009) included 36 patients, and Ghanei et al. (2018) included 2363 patients. Furthermore, Mathias et al. (2020), Pala et al. (2016) and Versloot et al. (2008) included 192, 107 and 147 patients, respectively. Only four studies provided a sample size calculation (Table 1).

### **3.3.2.3 Settings**

Two studies were carried out in Sweden, three public dental service clinics were used by Krekmanova et al. (2009), and seven public dental service clinics were used by Ghanei et al. (2018). One study in Canada, six dental practices serving families from both urban and rural settings were used by Rocha et al. (2009), and one study in India, university dental clinics were used by Pala et al. (2016). One study in Brazil, university dental clinics were used by Mathias et al. (2020) and one study in the Netherlands, a special dental care clinic was used by Versloot et al. (2008) (Table 1).

### **3.3.2.4 Participants**

Children aged from three to nineteen years-of-age were included in the studies, and a different age range of children was considered for each study (Table 1).

### **3.3.2.5 Predictors**

A range of different dental procedures was included. Krekmanova et al. (2009) involved extraction, drilling, local anaesthesia, restoration, scaling, probing, radiograph, and polishing whereas Versloot et al. (2008) only assessed local anaesthesia. Likewise, Rocha et al. (2009) studied check-ups, diagnostic examinations, polishing, fillings, and extractions while Ghanei et al. (2018) assessed local anaesthesia, extraction, drilling, and radiographs (the type of radiograph was not reported). Furthermore, Mathias et al. (2020) involved polishing, restoration, and extraction whereas Pala et al. (2016) investigated local anaesthesia and extraction (Table 1).

### **3.3.2.6 Outcomes**

All studies reported on intra-operative pain with three studies, Versloot et al. (2008), Krekmanova et al. (2009) and Rocha et al. (2009), assessed anxiety levels before the dental procedures. In addition, one study, Versloot et al. (2008), compared intra-operative pain between two different age groups (Table 1).

Two studies, Krekmanova et al. (2009) and Ghanei et al. (2018), used a visual analogue scale (VAS) to measure pain intensity during dental procedures (McGrath et al., 1996; McGrath et al., 2000) while one study, Versloot et al. (2008), used a modified version of the visual analogue scale (Chapman and Kirby-Turner, 2002). Two studies, Rocha et al. (2009) and Mathias et al. (2020), used the VAS Faces Pain Scale-Revised (FPS-R) (Hicks et al. 2001) while one study, Pala et al. (2016), used the Face, Legs,

Activity, Cry, Consolability scale (FLACC) for assessing intra-operative pain (Malviya et al., 2006).

Regarding measuring anxiety, Versloot et al. (2008) used the parent's version of the Dental Subscale of the Children's Fear Survey Schedule (CFSS-DS) (Aartman et., 1998), Krekmanova et al. (2009) used a Dental Anxiety Scale (DAS) (Corah, 1969) and Rocha et al. (2009) used the trait anxiety portion of the Spielberger State-Trait Anxiety Inventory for Children (Spielberger et al., 1975).

Included studies	Country	Setting	Design	Sample size	Age	Intervention	Outcome variable	Outcome measure
<b>Krekmanova 2009</b>	Sweden	Three Public Dental Service clinics in the city of Goteborg	Retrospective cohort study	368	8-19 years old	Extraction, drilling, LA, restoration, scaling, probing, x-ray, and polishing	Pain and Anxiety	0-100 The Visual Analogue Scale for pain and Dental Anxiety Scale for anxiety
<b>Rocha 2009</b>	Canada	Six dental practices serving families from both urban and rural settings	Prospective cohort study	36	5-12 years old	Dental procedures (e.g., polishings, check-ups, diagnostic examinations, fillings, and extractions)	Pain and Anxiety	0-10 The VAS "Faces Pain Scale-Revised (FPS-R) and the trait anxiety portion of the Spielberger State- Trait Anxiety Inventory for Children
<b>Ghanei 2018</b>	Sweden	Seven Public Dental Service clinics in RVG and from five in ROC	Prospective cohort study	2363	3-19 years old	LA, extraction, drilling, and x-ray	Pain	0-10 The Visual Analogue Scale
<b>Mathias 2020</b>	Brazil	The Paediatric Dentistry Clinic of the School of Dentistry at the Federal University of Pelotas	Cross-sectional study	192	6-13 years old	Polishing, restoration, and extraction	Pain	0-10 The VAS "Faces Pain Scale-Revised (FPS-R)
<b>Pala 2016</b>	India	Narayana Dental College and Hospital	Cross-sectional study	107	4-13 years old	LA and extraction	Pain	0-10 Face, Legs, Activity, Cry, Consolability scale
<b>Versloot 2008</b>	Netherlands	A special dental care clinic	Cross-sectional study	147	4-11 years old	LA	Pain and Anxiety	0-10 Modified version of the visual analogue scale for pain and the parent's version of the Dental Subscale of the Children's Fear Survey Schedule for anxiety

**Table 1.** The characteristics of included studies.

### 3.3.3 Quality assessment of included studies

The findings regarding the quality assessment for the included studies are summarised in Table 2. All studies were considered as being overall of a good quality level except one study (Rocha et al., 2009) was rated as a fair quality level. The criteria “Participation rate > 50%” and “Loss to follow-up after baseline 20% or less” could not be determined in one study (Rocha et al., 2009). Only two studies (Rocha et al., 2009; Versloot et al., 2008) did not justify their sample size. All studies did not measure exposures prior to outcomes because the exposures and outcomes are measured during the same timeframe. The answer for the criterion “sufficient timeframe” was no for the cross-sectional studies as this study design assesses the exposures and outcomes at the same time (Versloot et al., 2008; Pala et al., 2016; Mathias et al., 2020). Two studies (Mathias et al., 2020; Pala et al., 2016) did not assess exposure more than once over time. Outcome assessors were not blinded in three studies (Versloot et al., 2008; Pala et al., 2016; Ghanei et al., 2018) while it could not be determined that whether outcome assessors were blinded or not in the remaining studies (Krekmanova et al., 2009; Rocha et al., 2009; Mathias et al., 2020).

Included studies	Clear aim	Sample defined	Participation rate > 50%	Inclusion and exclusion criteria	Sample size justification	Exposure measured prior to outcome	Sufficient time frame	Levels of exposure	Exposure measures	Exposure assessed more than once over time	Outcome measures	Assessors blinding	Loss to follow-up after baseline 20% or less	Adjusted for confounders	Total Score*	Quality Rating*
Krekmanova 2009	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	CD*	Yes	Yes	12/14	Good
Rocha 2009	Yes	Yes	CD*	Yes	No	No	Yes	Yes	Yes	Yes	Yes	CD*	CD*	Yes	9/14	Fair
Ghanei 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	12/14	Good
Mathias 2020	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	CD*	Yes	Yes	10/14	Good
Pala 2016	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	No	Yes	Yes	10/14	Good
Versloot 2008	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	10/14	Good

\* CD, Cannot Determine; NA, Not Applicable; NR, Not Reported

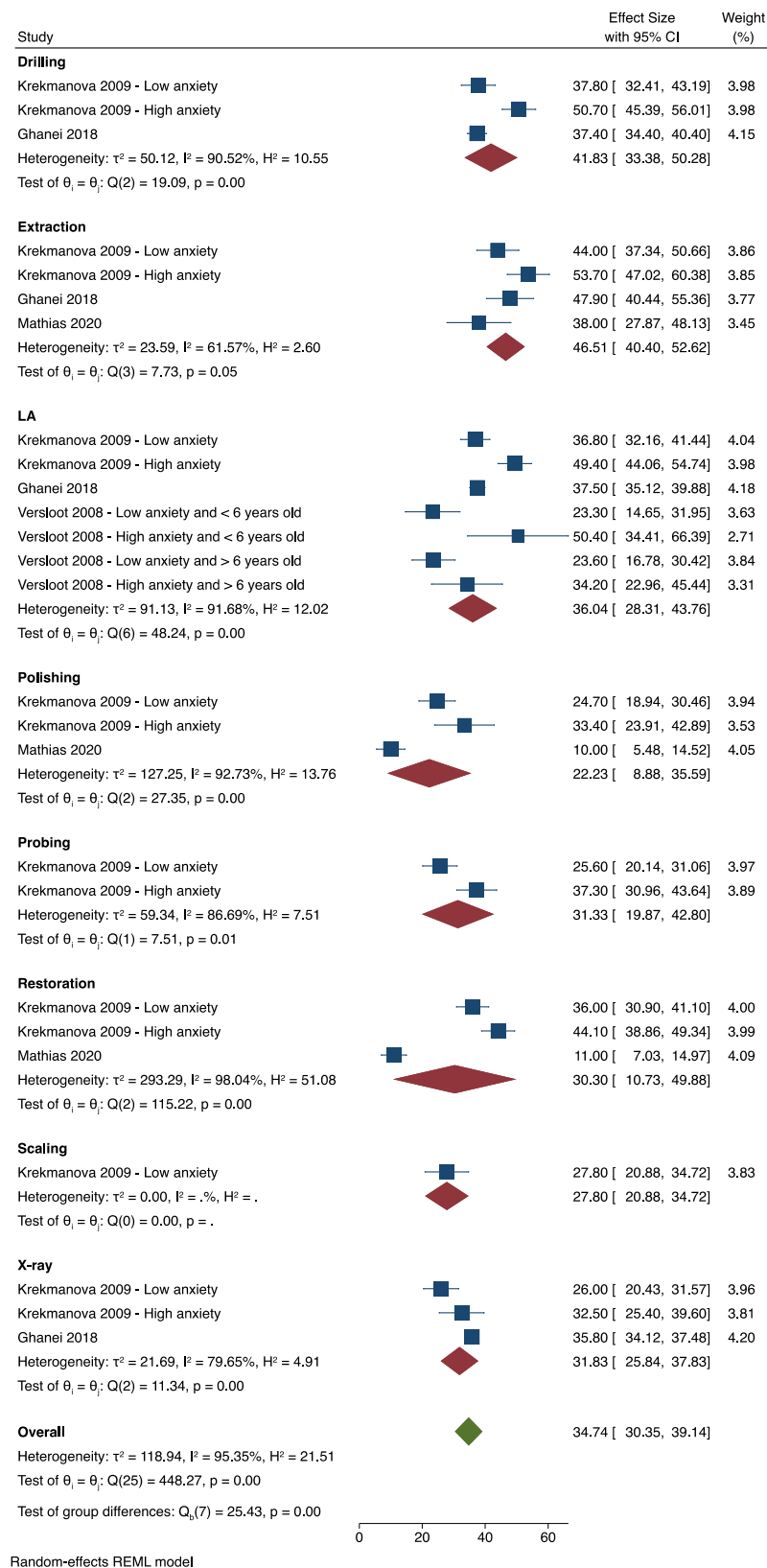
\* Total score: Number of Yes

\* Quality rating: 0-4 (Poor), 5-9 (Fair) and 10-14 (Good)

**Table 2.** Quality assessment summary.



### 3.3.4 Meta-analysis of intra-operative pain outcome



**Figure 2.** Random-effects meta-analysis evaluation of pain associated with dental procedures.

Figure 2 shows the main results of the meta-analysis of intra-operative pain outcome. A total of four studies were included in the meta-analysis. The VAS of 0-10 scores was converted to 0-100 because pain associated with the dental procedures was mostly measured using the VAS of 0-100 scores. The subgroup analysis of dental procedures showed that the most painful procedure was extraction (MD VAS 46.51, 95% CI 40.40 to 52.62) followed by drilling (MD VAS 41.83, 95% CI 33.38 to 50.28), and local anaesthesia (MD VAS 36.04, 95% CI 28.31 to 43.76). The heterogeneity was generally high for each subgroup; thus, the random-effects model was the best approach to pool the data of included studies. The heterogeneity could be explained by different methodologies used in the included studies, population characteristics, components of the predictors and outcome measures.

### **3.3.5 Meta-regression of intra-operative pain outcome**

The results for the meta-regression of dental procedures and anxiety levels are shown in Tables 3 and 4.

#### **3.3.5.1 Dental procedures**

Polishing was considered as a reference score for the meta-regression of dental procedures because it was the least painful procedure; the MD VAS pain score for polishing was 22.28, 95% CI 8.24 to 36.31. The results demonstrated that the MD VAS pain score for dental extraction was higher than polishing by 23.80, 95% CI 5.13 to 42.46 which was statistically and

clinically significant (P-value = 0.012 and the MD VAS score was > 10 mm). The mean pain score for drilling was also found to be higher than polishing by 19.64, 95% CI 0.001 to 39.28 which was statistically and clinically significant (P-value = 0.05 and the MD VAS score were > 10 mm). Although the mean VAS pain score for LA was not statistically significant (P-value = 0.108), it was reported to be more painful than polishing by 13.84, 95% CI -3.03 to 30.72 i.e., a clinically significant finding as the MD VAS score was > 10 mm.

Dental Procedures	Mean Pain Score Difference (95% CI)	P-value
Extraction	23.80 (5.13 - 42.46)	0.012
LA	13.84 (-3.03 - 30.72)	0.108
Drilling	19.64 (.001 - 39.28)	0.05
Probing	9.12 (-12.94 - 31.18)	0.418
Restoration	7.96 (-11.69 - 27.61)	0.427
Scaling	5.52 (-22.57 - 33.62)	0.700
Radiograph	9.22 (-10.47 - 28.91)	0.359
Polishing (the reference score)		

**Table 3.** Random-effects meta-regression evaluation of pain associated with dental procedures.

### 3.3.5.2 Anxiety levels

The meta-regression of anxiety levels used low anxiety levels as a reference score because they were reported with a lower mean pain score of 30.73, 95% CI 25.99 to 35.46. The results showed that children with high anxiety

levels reported significantly higher mean pain scores by 12.31, 95% CI 5.23% to 19.40%, P-value = 0.001 than those with low anxiety levels.

Anxiety Level	Mean Pain Score Difference (95% CI)	P-value
High anxiety	12.31 (5.23 - 19.40)	0.001
Low anxiety (the reference score)		

**Table 4.** Random-effects meta-regression evaluation of pain associated with anxiety level.

### 3.4 Discussion

The aim of this systematic review was to identify predictors of intra-operative and post-operative pain associated with routine dental treatment in children. Data were assembled from six studies comprising 3213 children who had routine dental care. Four studies were included in the meta-analysis. Findings revealed that dental procedures were strong predictors of intra-operative pain, and that the strongest predictor was extraction followed by drilling when the pain was assessed intra-operatively. High anxiety levels were also found to be a predictor of intra-operative pain associated with routine paediatric dental treatment.

The primary outcome of this review was intra-operative and post-operative pain. The included studies measured intra-operative pain using different pain scales. The pain scales consisted of the VAS, the modified version of VAS and the VAS (FPS-R) and the FLACC. The self-report measure of pain has

been considered as the gold standard for assessing pain in children (Abdellatif 2011). The FLACC scale is a pain assessment scale used when a self-report of pain is not applicable, and it assesses pain through observation of five categories including face, legs, activity, cry, and consolability (Crosta, 2014). The measurement of pain may be influenced by the child's anxiety (Versloot et al., 2008). The present review included two large studies, Krekmanova et al. (2009) and Versloot et al. (2008), with sufficient sample size and good quality level, that measured anxiety before dental treatment using the DAS and the parent's version of the CFSS-DS, respectively.

This review found that dental anxiety, extraction, and drilling were the strongest predictors of intra-operative pain associated with routine dental treatment in children. It showed that extraction significantly emerged as the most painful dental procedure followed by drilling. It also revealed that children who had a high level of anxiety significantly reported higher pain scores than those with a low level of anxiety. The review also showed that local anaesthesia was another predictor of intra-operative pain which presented clinically significant importance as it was found to be more painful than polishing, the reference score. Therefore, these predictors are important for general dental practitioners and paediatric dentists to be considered when they provide dental treatment for children. General dental practitioners and paediatric dentists should carefully listen to and be aware of the implications of the responses of their paediatric patients in order to provide acceptable and effective anaesthesia so that procedures can be completed pain-free. They should also assess their young patients pre-

operatively for dental anxiety as a means to use appropriate anxiety management techniques. It is important for general dental practitioners and paediatric dentists to identify children with dental anxiety from an early stage at a new patient appointment. A systematic review carried out by Porritt et al. in 2013 assessing children's dental anxiety recommended using a dental anxiety measure which involves different specific questions related to dental procedures, and it can be completed in the waiting room by a wide range of ages. They also provided different useful dental anxiety measures which have these desirable properties and can be used in primary dental care such as Modified Child Dental Anxiety Scale (MCDAS), Smiley Faces Programme (SFP), Dental Fear Survey (DFS) and Facial Image Scale (FIS).

It is well recorded in the literature that exposing children to a painful dental procedure may have a variety of adverse consequences such as anxiety, fear, lack of cooperation, delay in seeking dental care or the need for sedation or general anaesthesia for dental treatment. Fear of pain has been thought to be a source of anxiety which could make children postpone seeking further dental treatment (Arntz et al., 1990). It has also been shown that patients who have experienced a painful dental treatment may face some difficulties in their treatment and may avoid any future dental care (Carr et al., 1999). Similarly, it has been reported that repeated painful experience during dental treatment is one of the most leading reasons for dental practitioners to consider general anaesthesia for delivering dental care in some children (Savanheimo et al., 2005). Despite some benefits of having dental treatment under general anaesthesia, there are associated

risks and complications with using this way of providing treatment.

Therefore, a good understanding of the predictors of pain associated with routine dental procedures can play an important role in reducing the number of children requiring general anaesthesia for their dental treatment through using appropriate pharmacological and non-pharmacological interventions to target painful predictors to help relieve pain and anxiety.

The main strength of the present systematic review is that it represents the first comprehensive systematic review to investigate the predictors of pain associated with routine paediatric dental procedures, providing the main predictors of intra-operative pain. Additionally, the quality standards according to PRISMA were employed in this review (Liberati et al., 2009; Moher et al., 2009). Moreover, a broad search strategy of several databases without language and date restrictions was considered. This allowed the reviewers to identify and include many potentially eligible studies; therefore, the risk of selection bias was minimised (Higgins et al., 2019). Furthermore, the reviewers independently assessed studies for eligibility, extracted data and evaluated the quality of the included studies to minimise selection and information bias and error and to improve the reliability and validity of this review.

Some limitations are noticed in this review. None of the included studies measured post-operative pain as their main interest was to assess intra-operative pain associated with dental procedures, and the participants were not followed up for any presence or absence of post-operative pain.

Therefore, it is important for future research to consider measuring post-operative pain associated with routine dental treatment in children as this pain may impact future dental care. Although the overall quality assessment was good for the majority of included studies in this review, flaws were identified in the methodology of included studies. Participation rate could not be determined in one study whether it was more or less than 50% of eligible children who participated in the study. If the participation rate is less than 50%, this raises concern that the study population does not adequately represent the target population (National Heart, 2014). Also, the sample size was not justified in two studies. However, the lack of the sample size justification was not considered as a fatal flaw as these studies were exploratory (National Heart, 2014), and the samples of a number of studies were combined in this review to increase the level of statistical power. Moreover, blinding of outcome assessors was not achieved in half of the studies, and it could not be determined in the remaining studies. This could introduce some bias as the assessor may influence the participant and the subsequent results (Petrisor and Bhandari, 2007). However, the outcome of the most included studies in this review was measured using the self-report measure of pain which could reduce the chance of detection bias. Although the literature reported that age may be a predictor of pain associated with routine dental treatment, it was not possible to group children according to their age in the meta-analysis because the included studies did not subgroup their participants in terms of age. Therefore, it would be useful for future research to subgroup their participants into different age groups to help researchers better understand the impact of age on children's pain perception. Other outcomes such as patients and parent acceptability might



have influenced children's pain perception but none of the included studies reported this outcome. Therefore, it would be worthwhile for future research to consider this outcome to determine the impact of patients and parent acceptability on children's pain perception.

Based on the literature review and the results of this systematic review, interventions targeted toward reducing dental anxiety and making dental extractions and other procedures like drilling less painful should be a priority for future research and implementation as they have the potential to reduce pain and anxiety which will keep the child co-operative and therefore prevent the need for GA which is costly, resource intensive, not readily available and has increased morbidity and mortality.

### **3.5 Conclusion**

This systematic review demonstrates that dental extraction and drilling are the most predictors of intra-operative pain associated with routine dental treatment in children. It also shows that children with high anxiety levels reported more intra-operative pain for the similar procedures. A good understanding of the predictors of pain associated with routine dental procedures could play an important role in providing appropriate pharmacological and behavioural support to help children cope better with dental care. This in turn could reduce the number of children requiring general anaesthesia for their dental treatment through using appropriate pharmacological and non-pharmacological interventions to target these

predictors to reduce pain and anxiety associated with dental procedures.

Based on these findings, the next logical step is to explore interventions that have the strongest effect in reducing intra-operative and post-operative pain and which can be recommended for use for paediatric dental procedures.

The next chapter will describe the findings of a systematic review of such interventions.

## **Chapter 4: The Second Systematic Review and Meta-analysis**

### **Interventions for intra-operative and post-operative pain associated with routine dental procedures in children: A systematic review and meta-analysis**

#### **4.1 Aim**

The aim of this review was to evaluate the effectiveness or otherwise of interventions used to relieve intra-operative and post-operative pain associated with routine paediatric dental procedures.

#### **4.2 Methods**

This systematic review and meta-analysis were undertaken following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009; Moher et al., 2009). The protocol was registered and published in the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD42020177771).

The protocol is available at:

[https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42020177771](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020177771)

[71.](#)

## **4.2.1 Criteria for considering studies for this review**

### **4.2.1.1 Types of studies**

As discussed in chapter 2, the best study designs that can assess the efficacy of interventions or treatments in medicine and dentistry are randomised controlled clinical trials (RCTs) because randomisation can prevent selection biases during group allocation and blinding (single, double, or triple) can reduce detection and performance bias (West et al., 2008; Cioffi and Farella, 2011; Hariton and Locascio, 2018). Therefore, single, double, or triple-blinded randomised controlled clinical trials were included.

### **4.2.1.2 Types of participants**

Studies involving children and adolescents who were old enough to be able to answer the pain evaluation (3 years) aged up to 19 years were included. Children aged 19 years were included as World Health Organisation (WHO) considers this age as adolescence. Children and adolescents receiving routine dental treatment with or without local anaesthesia (LA) were included, and those receiving dental treatment under N<sub>2</sub>O/O<sub>2</sub> inhalation sedation were also included. The other forms of sedation such as oral, intranasal and intravenous have been systemically reviewed by Ashley et al. 2018. In addition, those forms of sedation are only available in secondary dental care and this study wanted to look at interventions which when applied early in the treatment pathway can improve co-operation and prevent GA so those that might work in primary dental care. Hence only

nitrous oxide was included as this can be delivered in primary care whereas the others cannot.

Children and adolescents having dental care under GA were excluded according to the aim of this review which focused on interventions that were used to manage pain associated with routine paediatric dental care in the dental chair in order to reduce the number of children requiring GA for dental treatment.

#### **4.2.1.3 Types of interventions**

Classification of interventions used to relieve pain and anxiety associated with dental procedures is quite complex, and interventions are often overlapping. Therefore, a consensus panel consisting of the author, a consultant in paediatric dentistry, an oral surgeon with methodological expertise in systematic reviews and a primary care dentist with a special interest in pain met after the results of the preliminary search and assimilated the information to group the interventions for facilitating the process of meta-analysis as follows:

##### **4.2.1.3.1 Computer Driven LA Versus Conventional LA**

Studies that investigated computer driven devices such as the Wand to deliver LA through infiltration or inferior alveolar nerve block (IANB) and compared this technique to conventional LA were grouped together.

Computer driven devices might be expensive, difficult to access and time-

consuming (Banerjee, 2020). Thus, it is necessary to understand whether there is an effect to justify using these expensive techniques.

#### **4.2.1.3.2 Intra-osseous/Intra-ligamentary LA Versus Conventional LA**

Studies that used a computer driven device such as the Wand to deliver LA through intra-ligamentary injection and compared this technique to conventional LA were grouped together. Likewise, studies that used another device such as QuickSleeper™ to deliver LA through intra-osseous injection and compared this technique to conventional LA were grouped together. In addition to the disadvantages of the Wand that were mentioned in the previous section (4.2.1.3.1), the QuickSleeper™ device has similar drawbacks (Angelo and Polyvios, 2018). Intra-osseous/Intra-ligamentary injections might be painful therefore it is worth reviewing the relevant published literature to justify the use of these devices for these injections regardless of their drawbacks.

#### **4.2.1.3.3 LA Agent (Articaine Versus Lidocaine)**

Studies that used and compared different types of LA agent anaesthesia were grouped together. Inferior alveolar nerve block (IANB) injections using Lidocaine LA might be painful (Mumtaz et al., 2021). Therefore, it is necessary to review the literature to find an alternative LA injection such as using Articaine mandibular infiltration LA that shows more/similar efficacy to the Lidocaine IANB.

#### **4.2.1.3.4 Topical Anaesthesia**

Studies that used and compared different types of topical anaesthesia were grouped together. The literature shows that some types of topical anaesthesia might be more effective in reducing the pain of dental injections in children than others. Thus, reviewing the available evidence about topical anaesthesia may help primary and secondary dental care providers identify which type of topical anaesthesia is more effective than others in relieving dental injection pain in children.

#### **4.2.1.3.5 Mechanoreceptor and thermal receptor stimulation**

Studies assessing different types of mechanoreceptors and thermal receptors stimulation were grouped together. According to the gate control theory of pain, the transmission of pain signals from the spinal cord to the brain can be permitted or impeded by the neurological gate (Dickenson, 2002). The stimulation of large diameter A- $\beta$  nerve fibres through mechano/thermoreceptors re-activates inhibitory neurons which block the gate to stop the transmission of pain signals (Dickenson, 2002).

Mechanoreceptor and thermal receptor stimulation were then grouped together as they both interfere with the nerve pathway. Therefore, reviewing the available evidence about these interventions may determine whether their use is warranted.

#### **4.2.1.3.6 Pharmacological Interventions**

Studies investigating either oral analgesics or inhalation sedation with nitrous oxide/oxygen (N<sub>2</sub>O/O<sub>2</sub>) were grouped together. N<sub>2</sub>O/O<sub>2</sub> inhalation sedation might help relieve pain and anxiety in children having dental treatment (Paterson and Tahmassebi, 2003; SDCEP, 2017). Also, oral analgesics might reduce pain associated with routine paediatric dental procedures (Ashley et al., 2016). Thus, reviewing the available evidence about these interventions may help primary and secondary dental care providers justify their use in children.

#### **4.2.1.3.7 Behavioural Interventions**

Studies that used any type of behaviour management were grouped together. The literature shows that behavioural interventions might help relieve anxiety and pain in children having routine dental treatment. Therefore, reviewing the available evidence about these interventions may help primary and secondary dental care providers identify which behavioural interventions are effective and easy to use with children.

#### **4.2.1.4 Types of outcome measures**

The outcomes that were considered for this review were intra-operative and post-operative pain measured using a validated pain scale. Anxiety outcome was also considered, and it was measured using a validated anxiety scale.



#### **4.2.1.5 Search methods for identification of studies**

This review used electronic searches with detailed search strategies developed for each database searched to identify eligible studies. The search strategies were formulated by the author (Mohammed Alzubaidi) under the supervision of a specialist librarian at the University of Leeds (Appendix 5). A combination of controlled vocabulary and free text terms was considered for the search strategy to identify eligible studies with no restrictions regarding language or date of publication. If there were non-English studies, they would be translated into English. The following electronic databases were searched up to the 11th of March 2022: Cochrane Library (Wiley), MEDLINE via OVID, EMBASE via OVID, PsycINFO via OVID, WHO International Clinical Trials Registry Platform, Clinical Trials.gov, Web of Science and PubMed. These databases were selected to ensure that as many related studies as possible are identified and to minimise the risk of selection bias (Higgins et al., 2019). The included studies' references were also checked to identify more additional eligible studies. Hand searching in the related dental journals was considered when electronic copies were not available.

#### **4.2.2 Data collection and analysis**

##### **4.2.2.1 Selection of studies**

All references were exported into EndNote version X9 then the studies were imported into Covidence systematic review software where duplicated

records were identified and removed. Covidence is a custom-built data system designed for assisting reviewers to use a structured data collection form for online form building, data entry, data sharing, and efficient data management (Veritas Health Innovation, 2014; Li et al., 2015). This software was therefore used to mitigate the effect of Covid-19 as it allowed data extraction and consensus to be done remotely. Titles and abstracts of relevant articles were independently assessed by the two review authors (Mohammed Alzubaidi and Dr Adam Jones). Discussion and consensus were considered to resolve any disagreement; however, a third reviewer was consulted (Dr Vishal Aggarwal) when consensus was not achieved.

#### **4.2.2.2 Data extraction and management**

Any study that met the eligibility criteria regardless of the study quality was included. Study authors were contacted for more details when there was missing data or inconsistent reporting. The required information was extracted in duplicate by the two reviewers (Mohammed Alzubaidi and Dr Adam Jones) using Covidence systematic review software. The following study characteristics were obtained:

- Name of the first author.
- Journal of publication.
- Year of publication.
- Country.
- Setting.
- Study design.
- Population and participants' characteristics.

- Sample size.
- Dental procedure.
- Intervention.
- Type of outcome.
- Methods of measurement.

#### **4.2.3 Quality assessment of the included studies**

The quality assessment of the included studies was undertaken independently by the same reviewers (Mohammed Alzubaidi and Dr Adam Jones) in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2011). The following seven domains were investigated for included studies: “sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and any other bias relevant to the study” (Higgins & Green, 2011). A study was considered as low risk of bias when all seven domains were judged as low risk, as unclear risk of bias when any domain was judged as unclear risk, and as high risk of bias when any domain was judged as high risk. Discussion and consensus were considered to resolve any disagreement; however, a third reviewer was consulted (Dr Vishal Aggarwal) when consensus was not achieved.

#### 4.2.4 Data synthesis and analysis

All extracted data were exported and managed in an Excel file (Microsoft Inc, USA). The data extraction form was then modified to facilitate the process of data analysis (Appendix 6).

Meta-analyses were carried out if there were sufficient studies reporting the same outcomes. The Cohen's d standardised mean differences (SMD) 95% confidence intervals (CIs) were considered for continuous outcomes that were measured with different scales to estimate the efficacy of interventions used to relieve pain and anxiety associated with routine dental treatment in children. Data collection for the meta-analysis included the following information:

- Name of the first author.
- Dental procedures included.
- Intervention used.
- Pain outcome (Mean, Standard of Deviation (SD), Number of Participants (N), and Standard of Error (SE)).
- Anxiety outcome (Mean, SD, N, and SE).

Forest plots were generated using Stata 16 statistical software (StataCorp LLC, Texas, USA) using a random-effects model. The random-effects model was considered because the large heterogeneity that was expected to be found across studies and later was corroborated in the analyses.

Clinical heterogeneity of included studies was accounted for by inclusion criteria for studies, participants, components of the interventions and outcome measures.  $I^2$  statistics were used for statistical heterogeneity;  $I^2$  statistics with values of 50% or greater represented substantial heterogeneity. A p-value  $\leq 0.05$  was considered statistically significant.

#### **4.2.5 Quality of evidence**

Based on the Cochrane Handbook for Systematic Reviews of Interventions, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was considered for assessing the quality and certainty of the body of evidence per outcome using the programme GRADEpro GDT (Higgins & Green, 2011). The quality of the evidence was downgraded from a high-quality level of evidence by one or more levels when there were limitations in the risk of bias, consistency of the results and/or precision of the pooled estimate. Depending on the number of limitations, the quality level of evidence was then graded as either high, moderate, low, or very low.

The GRADE recommendations, strong (I), moderate (IIa), weak (IIb) or recommendation not to do (III), were made based on conclusions of evidence as follows:

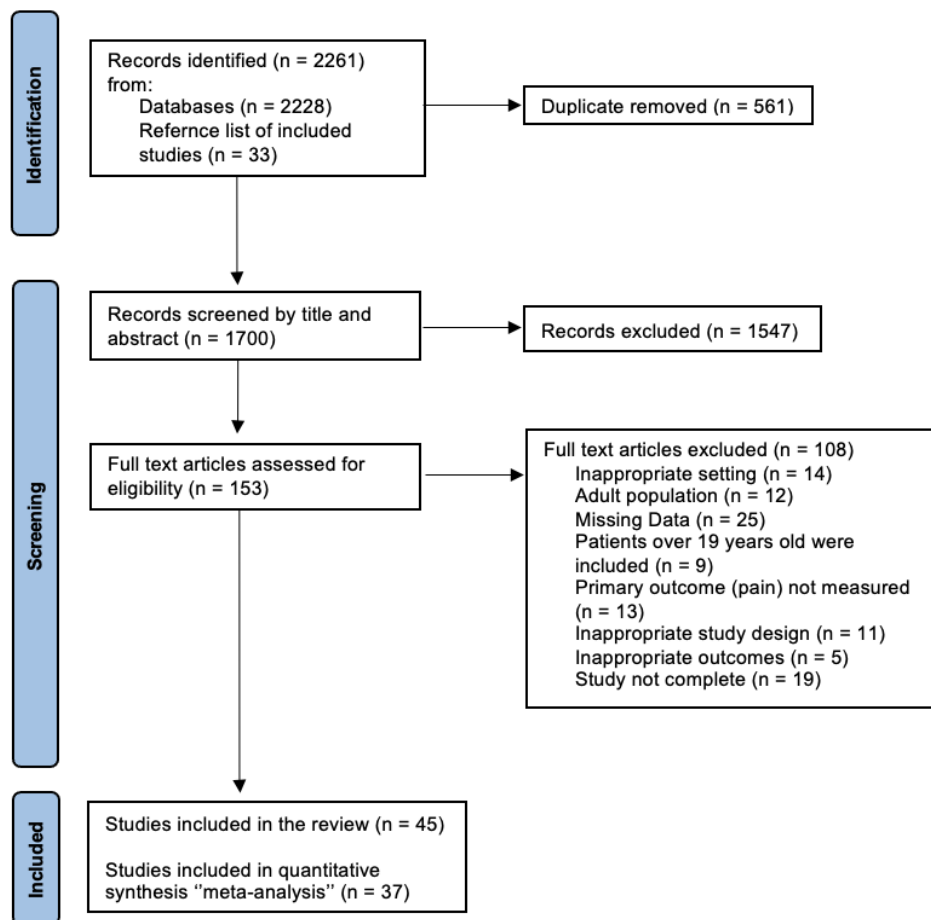
- A: for high level of evidence; consistent evidence.
- B: for moderate/low level of evidence; evidence with few important limitations.

- C: for very low level of evidence; evidence with serious flaws.

## **4.3 Results**

### **4.3.1 Study Selection**

Initially, a total of 2261 studies were identified after the electronic and manual search, while 1700 remained after excluding duplicates. Following the title and abstract screening, 153 articles were selected for full-text review and examined against the eligibility criteria in detail, and 108 studies were excluded (Appendix 7). Twenty-five studies had missing data although the 25 authors were contacted, this data was not provided (response rate: 20%). Fourteen studies had an inappropriate setting. Moreover, twelve studies involved an adult population, and nine studies included patients over 19-years-of-age. Five studies had inappropriate outcomes, and thirteen studies did not measure pain. Additionally, eleven studies had an inappropriate study design. Finally, nineteen studies were excluded because they were not complete. Consequently, forty-five studies were identified and included in the review, and thirty-seven studies were eligible for the meta-analysis (Figure 3).



**Figure 3.** PRISMA flowchart of the study selection process.

### **4.3.2 Study characteristics**

The characteristics of included studies are summarised in Appendix 8 and described as follows:

#### **4.3.2.1 Study design**

Twenty-five included studies adopted parallel group randomised controlled trials (Law et al., 2000; Bernhardt et al., 2001; Versloot et al., 2005; Versloot et al., 2008; Huet et al., 2011; Kamath, 2013; Alamoudi et al., 2015; Baghlaif et al., 2015; Mittal et al., 2015; Abdelmoniem and Mahmoud, 2016; Agarwal et al., 2017; Ramirez-Carrasco et al., 2017; Al-Halabi et al., 2018; Arcari and Moscati, 2018; Tung et al., 2018; Sridhar et al., 2019; Massignan et al., 2020; Obadiah and Subramanian, 2020; Santos et al., 2020; Smolarek et al., 2020; Alshami et al., 2021; Mumtaz et al., 2021; Raslan and Zouzou, 2021; Vidigal et al., 2021; Helmy et al., 2022) whereas nineteen studies were crossover group randomised controlled trials (Baghdadi, 1999; Primosch and Rolland-Asensi, 2001; Oztas et al., 2005; Ram and Amir, 2006; Ghaderi et al., 2013; Atabek et al., 2015; Asvanund et al., 2015; Attar and Baghdadi, 2015; Shilpapiya et al., 2015; Dak-Albab et al., 2016; Alinejhad et al., 2018; Garrocho-Rangel et al., 2018; Wambier et al., 2018; Alanazi et al., 2019; Gumus and Aydinbelge, 2020; Yildirim et al., 2020; AmruthaVarshini et al., 2021; Daneshvar et al., 2021; Jain et al., 2021) and one study used both parallel group and split mouth randomised controlled trials (Smail-Faugeron et al., 2019) (Appendix 8).



#### **4.3.2.2 Sample size**

The sample size ranged from 25 to 160, and each study had a different sample size with a total number of 3093 children who had different interventions to relieve pain and/or anxiety associated with dental procedures (Appendix 8).

#### **4.3.2.3 Settings**

Nine studies were carried out in India, five studies in Brazil, five studies in Saudi Arabia, four studies in the USA, four studies in Syria, four studies in Turkey, three studies in Iran, two studies in Egypt, two studies in the Netherlands, two studies in France, two studies in Mexico, one study in Italy, one study in Israel, and one study in Thailand (Appendix 8).

#### **4.3.2.4 Participants**

Studies included children aged from three to sixteen years-of-age, and a different age range of children was considered for each study (Appendix 8). One study did not report the age range of its sample but only included children with a maximum age of 16 years (Law et al., 2000).

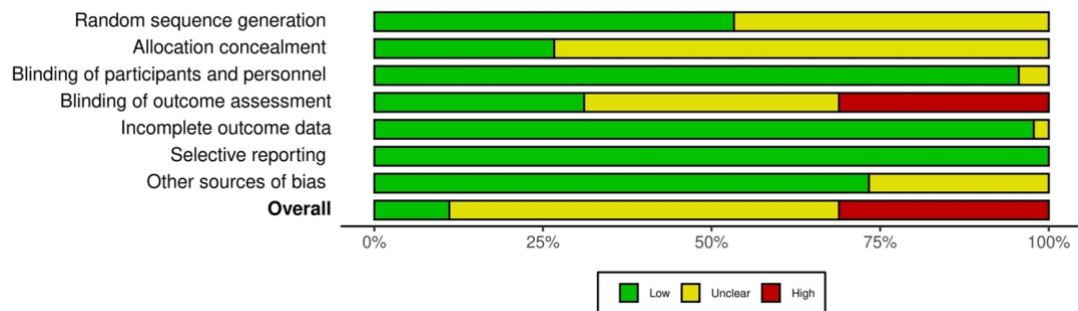
#### **4.3.2.5 Outcomes**

All studies reported on the primary outcomes: intra-operative and/or post-operative pain associated with paediatric dental procedures while only nine studies assessed anxiety levels before and after the dental procedures (Versloot et al., 2005; Versloot et al., 2008; Huet et al., 2011; Attar and

Baghdadi, 2015; Sridhar et al., 2019; Obadiah and Subramanian, 2020; Smolarek et al., 2020; Alshami et al., 2021; Vidigal et al., 2021). Most of the included studies used self-report measures of pain scales which are dependent on the patient's self-report. Also, different anxiety scales were considered to measure anxiety levels. The different methods used by authors to assess pain and anxiety are summarised in Appendix 8 (The characteristics of included studies).

### 4.3.3 Quality assessment of the included studies

Figures 4 and 5 illustrate the overall risk of bias and the individual plots for each study. The details for the quality assessment of the included studies are reported in Appendix 8 (The characteristics of included studies).



**Figure 4.** Overall risk of bias.

Study	Risk of bias							Overall
	D1	D2	D3	D4	D5	D6	D7	
Agarwal 2017	+	-	+	-	+	+	+	-
Santos 2020	+	+	+	+	+	+	+	+
Ramirez-Carrasco 2017	-	-	+	+	+	+	+	-
Versloot 2008	+	-	+	+	-	+	+	+
Obadiah 2020	-	-	+	-	+	+	+	-
Baghdadi 1999	-	-	+	-	+	+	+	-
Smolarek 2020	+	+	+	-	+	+	+	-
Massignan 2020	+	+	+	+	+	+	+	+
Small-Faugeron 2019	+	-	+	+	+	+	+	-
Alanazi 2019	-	-	+	+	+	+	+	+
Versloot 2005	+	-	+	+	+	+	+	+
Arcari 2018	-	-	+	+	+	+	+	+
Baghlaf 2015	-	-	+	+	+	+	+	+
Sridhar 2019	+	+	+	+	+	+	+	+
Attar 2015	-	-	+	-	+	+	+	-
Atabek 2015	-	-	+	+	+	+	+	-
Dak-Albab 2016	-	-	+	+	+	+	+	-
Ram 2006	-	-	-	+	+	+	-	-
Garrocho-Rangel 2018	+	-	+	+	+	+	+	+
Yildirim 2020	+	+	+	-	+	+	+	-
Alinejhad 2018	-	-	+	+	+	+	+	+
Gumus 2020	+	-	+	-	+	+	+	-
Tung 2018	+	+	+	+	+	+	+	+
Shilpapiya 2015	-	-	+	-	+	+	-	-
Alamoudi 2015	+	-	+	+	+	+	-	-
Mumtaz 2021	-	-	+	-	+	+	-	-
Abdelmoniem 2016	-	-	+	-	+	+	+	-
Huet 2011	+	-	+	+	+	+	+	+
Bernhardt 2001	-	-	+	+	+	+	+	-
Law 2000	-	-	+	+	+	+	+	-
Alshami 2021	-	+	+	+	+	+	+	+
Helmy 2022	+	+	+	+	+	+	+	+
Vidigal 2021	+	+	+	+	+	+	+	+
Ghaderi 2013	+	-	+	+	+	+	-	-
Jain 2021	+	-	+	-	+	+	+	-
AmruthaVarshini 2021	+	+	+	-	+	+	-	-
Al-Halabi 2018	+	-	+	+	+	+	-	+
Primosch 2001	-	-	+	+	+	+	-	+
Daneshvar 2021	+	-	-	-	+	+	-	-
Kamath 2013	+	-	+	-	+	+	-	-
Asvanund 2015	-	-	+	+	+	+	+	+
Mittal 2015	+	-	+	-	+	+	-	-
Oztas 2005	-	-	+	-	+	+	-	-
Wambier 2018	+	+	+	-	+	+	+	-
Raslan 2021	+	+	+	+	+	+	+	+

D1: Random sequence generation  
D2: Allocation concealment  
D3: Blinding of participants and personnel  
D4: Blinding of outcome assessment  
D5: Incomplete outcome data  
D6: Selective reporting  
D7: Other sources of bias

Judgement  
High  
Unclear  
Low

Figure 5. Risk of bias for individual studies.

### **4.3.3.1 Allocation (selection bias)**

#### **4.3.3.1.1 Sequence generation**

Twenty-four studies described adequate methods of sequence generation, and these studies were judged to be at low risk of bias (Versloot et al., 2005; Versloot et al., 2008; Huet et al., 2011; Ghaderi et al., 2013; Kamath, 2013; Alamoudi et al., 2015; Mittal et al., 2015; Al-Halabi et al., 2018; Garrocho-Rangel et al., 2018; Tung et al., 2018; Wambier et al., 2018; Smail-Faugeron et al., 2019; Sridhar et al., 2019; Gumus and Aydinbelge, 2020; Massignan et al., 2020; Santos et al., 2020; Smolarek et al., 2020; Yildirim et al., 2020; AmruthaVarshini et al., 2021; Daneshvar et al., 2021; Jain et al., 2021; Raslan and Zouzou, 2021; Vidigal et al., 2021; Helmy et al., 2022). Different methods of sequence generation were described by the authors such as coin toss, lottery, chit method, block randomisation technique, table of random numbers, or computer randomisation. Sequence generation was reported as 'randomised' in twenty-one studies, but the authors did not describe the method of sequence generation, and these studies were therefore judged to be at unclear risk of bias for this domain (Baghdadi, 1999; Law et al., 2000; Bernhardt et al., 2001; Primosch and Rolland-Asensi, 2001; Oztas et al., 2005; Ram and Amir, 2006; Asvanund et al., 2015; Atabek et al., 2015; Attar and Baghdadi, 2015; Baghlaf et al., 2015; Shilpapiya et al., 2015; Abdelmoniem and Mahmoud, 2016; Dak-Albab et al., 2016; Agarwal et al., 2017; Ramirez-Carrasco et al., 2017; Alinejhad et al., 2018; Arcari and Moscati, 2018; Alanazi et al., 2019; Obadiah and Subramanian, 2020; Alshami et al., 2021; Mumtaz et al., 2021).

#### **4.3.3.1.2 Concealment of allocation**

The method of allocation concealment was reported in twelve studies, and these studies were judged to be at low risk of bias (Tung et al., 2018; Wambier et al., 2018; Sridhar et al., 2019; Massignan et al., 2020; Santos et al., 2020; Smolarek et al., 2020; Yildirim et al., 2020; Alshami et al., 2021; AmruthaVarshini et al., 2021; Raslan and Zouzou, 2021; Vidigal et al., 2021; Helmy et al., 2022). Tung et al. (2018) used “a random number sequence was generated using the Stata (Stata Corp, College Station, Texas, USA) command runiform to assign treatment sequence order to subjects at enrolment”. Opaque, consecutively numbered, and sealed envelopes were used in eight studies (Wambier et al., 2018; Massignan et al., 2020; Santos et al., 2020; Smolarek et al., 2020; AmruthaVarshini et al., 2021; Raslan and Zouzou, 2021; Vidigal et al., 2021; Helmy et al., 2022). In Sridhar et al. (2019) study, they entered the generated treatment group codes (A or B) into cards and placed them in opaque envelopes with covering the cards with aluminium foil and then sealed and sequentially numbered. In Yildirim et al. (2020) study, the clinician was asked to select the side to do the first treatment before revealing the pre-anaesthesia method by the researcher. In Alshami et al. (2021) study, participants were assigned with an ID number which placed them in a randomised group. The remaining thirty-three studies provided insufficient information about allocation concealment, and the authors did not discuss this; therefore, these studies were judged to be at unclear risk of bias for this domain.

### **4.3.3.2 Blinding**

#### **4.3.3.2.1 Blinding of participants and personnel (performance bias)**

It is notable that operators and/or participants were not blinded in the majority of included studies due to the nature of the intervention; these studies were therefore decided to be judged at low risk of bias. Two studies were judged to be at unclear risk of bias because of insufficient information to enable a judgement to be made, and the authors did not discuss this (Ram and Amir, 2006; Daneshvar et al., 2021).

#### **4.3.3.2.2 Blinding of outcome assessment (detection bias)**

Fourteen studies blinded outcome assessors to the intervention and these studies were judged to be at low risk of detection bias (Law et al., 2000; Bernhardt et al., 2001; Ram and Amir, 2006; Ghaderi et al., 2013; Alamoudi et al., 2015; Atabek et al., 2015; Dak-Albab et al., 2016; Ramirez-Carrasco et al., 2017; Smail-Faugeron et al., 2019; Massignan et al., 2020; Santos et al., 2020; Raslan and Zouzou, 2021; Vidigal et al., 2021; Helmy et al., 2022). Seventeen studies either could not blind the assessor or did not discuss blinding of outcome assessment were judged to be at unclear risk of detection bias (Baghdadi, 1999; Oztas et al., 2005; Kamath, 2013; Attar and Baghdadi, 2015; Mittal et al., 2015; Shilpapiya et al., 2015; Abdelmoniem and Mahmoud, 2016; Agarwal et al., 2017; Wambier et al., 2018; Obadiah and Subramanian, 2020; Gumus and Aydinbelge, 2020; Smolarek et al., 2020; Yildirim et al., 2020; AmruthaVarshini et al., 2021; Daneshvar et al.,

2021; Jain et al., 2021; Mumtaz et al., 2021). The remaining fourteen studies were judged to be at high risk of bias (Primosch and Rolland-Asensi, 2001; Versloot et al., 2005; Versloot et al., 2008; Huet et al., 2011; Asvanund et al., 2015; Baghlaf et al., 2015; Al-Halabi et al., 2018; Alinejhad et al., 2018; Arcari and Moscati, 2018; Garrocho-Rangel et al., 2018; Tung et al., 2018; Alanazi et al., 2019; Sridhar et al., 2019; Alshami et al., 2021).

#### **4.3.3.3 Incomplete outcome data (attrition bias)**

Majority of the studies either evaluated all included participants or reported on incomplete outcome data and were therefore judged to be at low risk of attrition bias. Only one study was considered to be at unclear risk because of insufficient information to enable a judgement to be made (Versloot et al., 2008).

#### **4.3.3.4 Selective reporting (reporting bias)**

None of the included studies had selective reporting and therefore were judged to be at low risk of bias for selective reporting.

#### **4.3.3.5 Other potential sources of bias**

Twelve studies were judged to be at unclear risk of bias as eleven of these studies did not report on baseline population characteristics (Primosch and Rolland-Asensi, 2001; Oztas et al., 2005; Ghaderi et al., 2013; Kamath, 2013; Alamoudi et al., 2015; Mittal et al., 2015; Shilpapiya et al., 2015; Al-Halabi et al., 2018; AmruthaVarshini et al., 2021; Daneshvar et al., 2021;

Mumtaz et al., 2021), and one study did not report which LA agent was given by infiltration or mandibular block injections (Ram and Amir, 2006). The remaining thirty-three studies were rated as low risk of bias because they did not show other obvious potential sources of bias.

#### **4.3.3.6 Overall risk of bias**

The overall risk of bias for five studies was rated as low risk of bias because all domains of the quality assessment for these studies were considered to be low risk of bias (Massignan et al., 2020; Santos et al., 2020; Raslan and Zouzou, 2021; Vidigal et al., 2021; Helmy et al., 2022). Fourteen studies were judged to be at high risk of bias for at least one domain (Primosch and Rolland-Asensi, 2001; Versloot et al., 2005; Versloot et al., 2008; Huet et al., 2011; Asvanund et al., 2015; Baghlaf et al., 2015; Al-Halabi et al., 2018; Garrocho-Rangel et al., 2018; Alinejhad et al., 2018; Arcari and Moscati, 2018; Tung et al., 2018; Alanazi et al., 2019; Sridhar et al., 2019; Alshami et al., 2021). The remaining twenty-six studies were rated as unclear risk of bias.



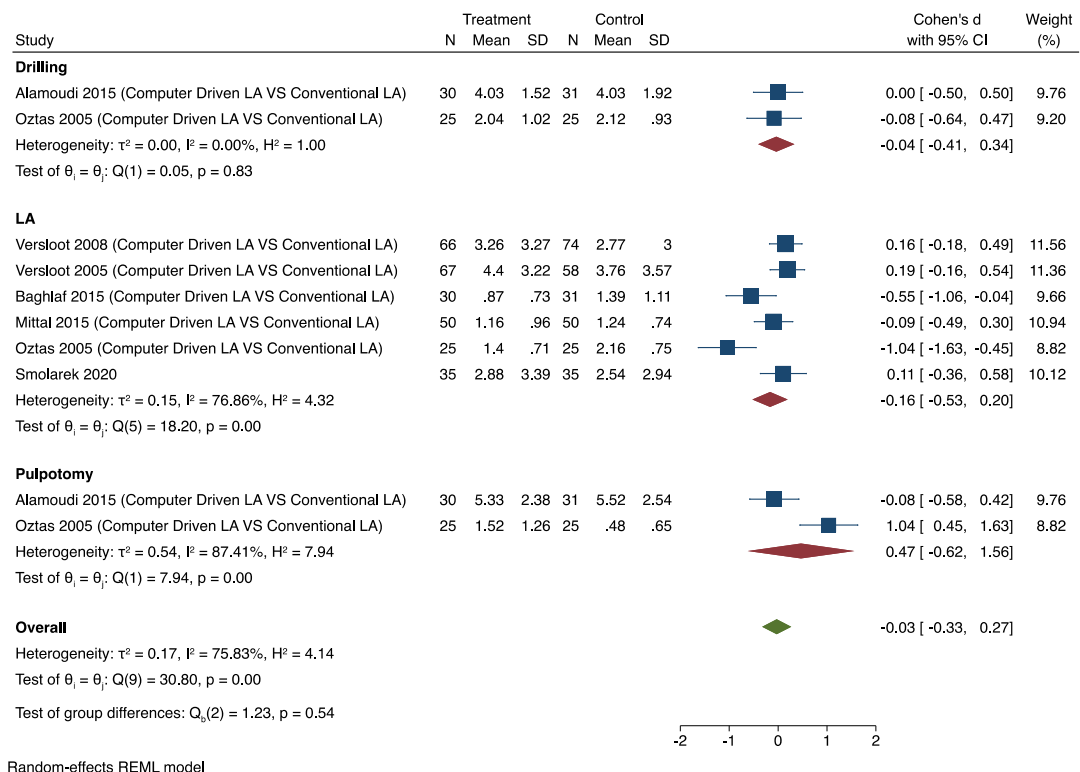
### **4.3.4 Effect of interventions and meta-analyses**

#### **4.3.4.1 Intra-operative pain outcome**

##### **4.3.4.1.1 Computer Driven LA Versus Conventional LA**

Seven studies evaluated pain perception rates in paediatric patients with a computerized system (The Wand) to deliver LA through infiltration or inferior alveolar nerve block (IANB) compared to conventional LA (Oztas et al., 2005; Versloot et al., 2005; Versloot et al., 2008; Alamoudi et al., 2015; Baghlaf et al., 2015; Mittal et al., 2015; Smolarek et al., 2020). Four studies reported that there was no significant difference in pain perception when using computer driven LA or conventional LA (Versloot et al., 2005; Versloot et al., 2008; Alamoudi et al., 2015; Smolarek et al., 2020). One study found that there was no difference in pain experience when using computer driven LA for buccal infiltration (Mittal et al., 2015). However, the authors reported that pain perception at palatal sites was reduced with using computer driven LA. In addition, one study reported that there was significantly lower pain perception in the computer driven LA group (Baghlaf et al., 2015). Likewise, one more study reported that pain perception during LA was significantly lower in the computer driven LA group whereas pain perception during drilling and pulpotomy was significantly lower in the conventional LA group (Oztas et al., 2005).

Seven studies provided comparable data for this outcome (Oztas et al., 2005; Versloot et al., 2005; Versloot et al., 2008; Alamoudi et al., 2015; Baghlaf et al., 2015; Mittal et al., 2015; Smolarek et al., 2020). Figure 6 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that the use of computer driven LA (infiltration/IANB) was not found to significantly relieve intra-operative pain associated with dental procedures (SMD  $-0.03$ , 95% CI  $-0.33$  to  $0.27$ ). The substantial heterogeneity ( $I^2 = 75.83\%$ ) in this estimate is likely due to the different tools used to measure the outcome and the ways of delivering LA via infiltration/IANB in each trial.

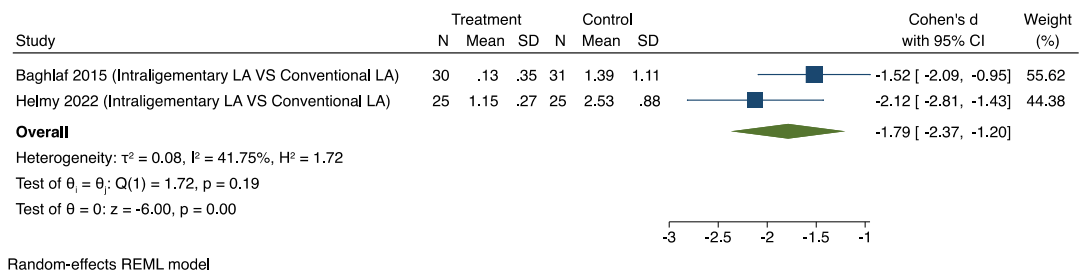


**Figure 6.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 1: computer driven LA versus conventional LA.

#### 4.3.4.1.2 Intraosseous/Intra-ligamentary LA Versus Conventional LA

Three studies assessed pain experience in paediatric patients with intra-ligamentary LA using the Wand device compared to conventional LA (Alamoudi et al., 2015; Baghlaf et al., 2015; Helmy et al., 2022). One study reported that there was no significant difference in pain perception when using intra-ligamentary LA by the Wand or conventional LA (Alamoudi et al., 2015). In contrast, two studies reported that there was significantly lower pain perception with using intra-ligamentary LA by the Wand (Baghlaf et al., 2015; Helmy et al., 2022).

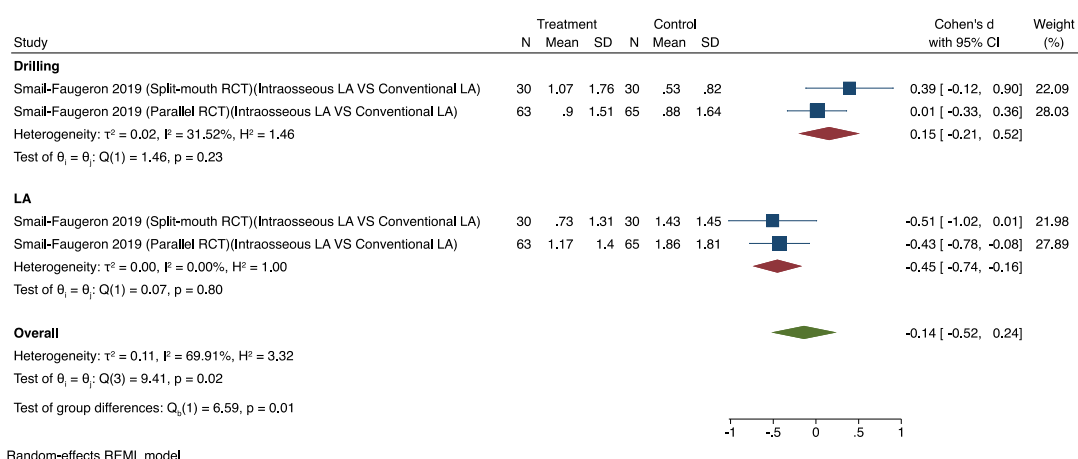
Two studies provided comparable data for this outcome (Baghlaf et al., 2015; Helmy et al., 2022). Figure 7 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that using intra-ligamentary LA by the Wand significantly relieved intra-operative pain associated with LA (SMD  $-1.79$ , 95% CI  $-2.37$  to  $-1.20$ ). The heterogeneity is low ( $I^2 = 41.75\%$ ) in this estimate.



**Figure 7.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 2: intra-ligamentary LA versus conventional LA.

One trial using two study designs (parallel group and split-mouth RCTs) assessed pain experience in paediatric patients with intra-osseous LA using QuickSleeper™ compared to conventional LA (Smail-Faugeron et al., 2019). They found that intra-osseous LA by QuickSleeper™ was associated with significantly less painful experience than conventional LA (Smail-Faugeron et al., 2019).

As there were two study designs in this trial, it was possible to provide comparable data for this outcome. Figure 8 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that the use of intra-osseous LA did not significantly relieve intra-operative pain associated with dental procedures (LA and drilling) (SMD -0.14, 95% CI -0.52 to 0.24). The substantial heterogeneity ( $I^2 = 69.91\%$ ) in this estimate is likely due to the different study designs used in this trial. Considering subgroups of dental procedures, a significant difference was observed in favour of using intra-osseous LA in relieving intra-operative pain associated with LA (SMD -0.45 95% CI -0.74 to -0.16).



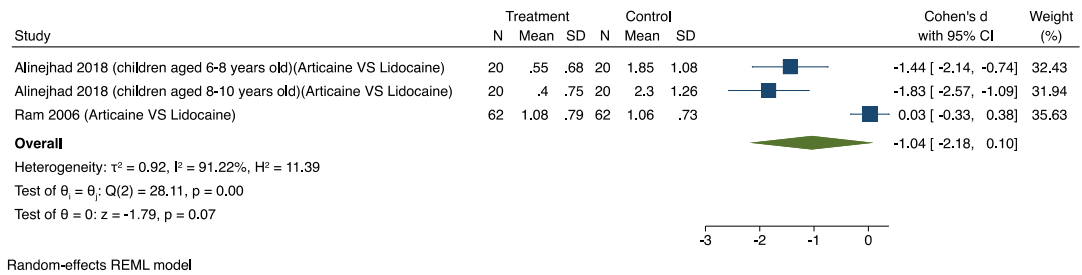
**Figure 8.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 3: intraosseous LA versus conventional LA.

#### 4.3.4.1.3 LA Agent (Articaine Versus Lidocaine)

Four studies evaluated pain perception during dental procedures with 4% Articaine infiltration LA or 2% Lidocaine IANB LA (Ram and Amir, 2006; Alinejhad et al., 2018; Daneshvar et al., 2021; Mumtaz et al., 2021). Two studies reported that 4% Articaine LA was as effective as 2% Lidocaine LA (Ram and Amir, 2006; Mumtaz et al., 2022). One study found that there was significantly lower pain perception with using 4% Articaine LA (Alinejhad et al., 2018). However, one study found that pain perception was significantly lower with using 2% Lidocaine LA (Daneshvar et al., 2021).

Two studies provided comparable data for this outcome (Ram and Amir, 2006; Alinejhad et al., 2018). Figure 9 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that the use of Articaine infiltration LA was not shown to significantly relieve intra-

operative pain associated with LA (SMD  $-1.04$ , 95% CI  $-2.18$  to  $0.10$ ). The considerable heterogeneity ( $I^2 = 91.22\%$ ) in this estimate is likely due to the different tools used to measure the outcome and the ways of delivering LA in each trial.



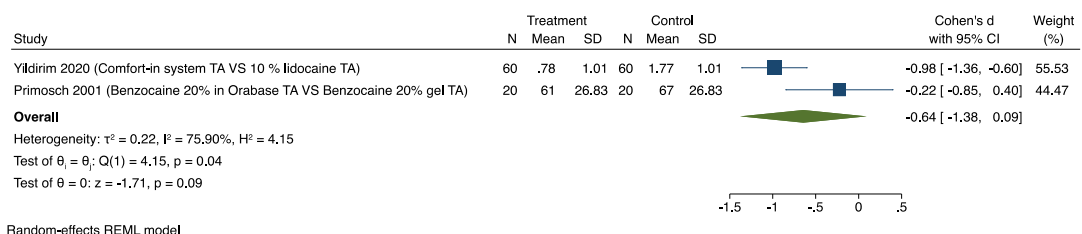
**Figure 9.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 4: LA agent (Articaine versus Lidocaine).

#### 4.3.4.1.4 Topical Anaesthesia

Three studies assessed pain perception during LA injections/clamp placement with using different types of topical anaesthesia. One study compared using the Comfort-in™ injection system topical anaesthesia to using 10 % Lidocaine topical anaesthesia (Yildirim et al., 2020). The authors found that pain perception was significantly lower with using the Comfort-in™ injection system topical anaesthesia before LA injections. One study compared using a topical anaesthetic agent (Benzocaine 20% in Orabase) to using a topical anaesthetic agent (Benzocaine 20% gel) or (EMLA 5% cream: Lidocaine 2.5% and Prilocaine 2.5%) (Primosch and Rolland-Asensi, 2001). The authors reported that all the topical anaesthetic agents were equivalent in injection pain response comparisons. One study compared using a light-cured topical anaesthetic gel (Tetracaine hydrochloride 5%,

inhibitor, monomers, photoinitiator, co-initiator, dye, and inert load) to using a placebo gel (similar to the light-cured topical anaesthetic gel but without tetracaine hydrochloride 5%) (Wambier et al., 2018). The authors concluded that using the light-cured topical anaesthetic gel significantly reduced pain perception during clamp placement without LA.

Two studies provided comparable data for this outcome (Primosch and Rolland-Asensi, 2001; Yildirim et al., 2020). Figure 10 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that the use of different topical anaesthesia did not significantly relieve intra-operative pain associated with LA (SMD  $-0.64$ , 95% CI  $-1.38$  to  $0.09$ ). The substantial heterogeneity ( $I^2 = 75.90\%$ ) in this estimate is likely because the studies considered different tools used to measure the outcome, different types of topical anaesthesia used and the ways of delivering LA via infiltration/IANB in each trial.



**Figure 10.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 5: topical anaesthesia.

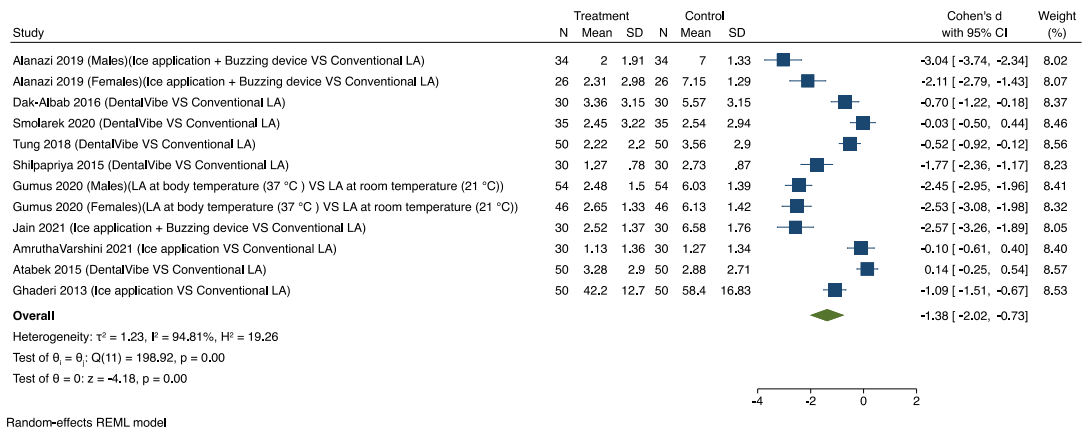
#### 4.3.4.1.5 Mechanoreceptor and thermal receptor stimulation

Several researchers evaluated pain perception during LA while using mechanoreceptor and thermal receptor stimulation. Baghdadi (1999) compared using the Electronic Dental Anaesthesia system (EDA: “a maximum of 60 mA by means of a control knob situated on the front of the control unit, is transmitted to the patient by means of a pair of adhesive pads that adhere to the skin of the patient’s face”) (3M Dental Electronic Anesthesia System 8670) to using conventional LA and found that there was no significant difference in pain perception between the two methods. Alanazi et al. (2019) and Jain et al. (2021) compared using a cold and vibration device (Buzzing device as a distraction, Buzzy®, MMJ labs, Atlanta, GA, USA) to conventional LA and concluded that combining external cold stimulation with a vibrating device might be effective in reducing discomfort in children undergoing LA. Five studies looked at using DentalVibe as an electrical vibration device compared to conventional LA (Atabek et al., 2015; Shilpapiya et al., 2015; Dak-Albab et al., 2016; Tung et al., 2018; Smolarek et al., 2020). Smolarek et al. (2020) and Atabek et al. (2015) reported that using DentalVibe showed no significant difference in reducing pain during LA injections. However, the other studies concluded that DentalVibe might reduce pain for paediatric patients receiving LA injections (Shilpapiya et al., 2015; Dak-Albab et al., 2016; Tung et al., 2018). Gumus and Aydinbelge (2020) compared the use of LA at body temperature (37 °C) to using LA at room temperature (21 °C) and found that pain perception during LA was significantly lower with the application of LA at body temperature. AmruthaVarshini et al. (2021) compared the effect of ice on the injection site and laser biostimulation (LBS) before injecting LA to conventional topical



anaesthetic and LA. They reported that ice and LA gel showed similar efficacy whereas LBS therapy showed less efficacy in reducing pain during LA injections in children compared to the other two techniques. Ghaderi et al. (2013) compared using both a topical anaesthetic agent (Benzocaine) and ice to using Benzocaine alone. They reported that pain perception was reduced by pre-cooling the injection site.

Ten studies provided comparable data for this outcome (Ghaderi et al., 2013; Atabek et al., 2015; Shilpapiya et al., 2015; Dak-Albab et al., 2016; Tung et al., 2018; Alanazi et al., 2019; Gumus and Aydinbelge, 2020; Smolarek et al., 2020; AmruthaVarshini et al., 2021; Jain et al., 2021). Figure 11 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed a significant difference in favour of using mechanoreceptor and thermal receptor stimulation to relieve intra-operative pain associated with LA (SMD  $-1.38$ , 95% CI  $-2.02$  to  $-0.73$ ). The considerable heterogeneity ( $I^2 = 94.81\%$ ) in this estimate is likely due to the studies considered different tools to measure the outcome and different mechanoreceptor and thermal receptor stimulation used in each trial.



**Figure 11.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 6: mechanoreceptor and thermal receptor stimulation.

#### 4.3.4.1.6 Pharmacological Interventions

Two studies evaluated pain experience during dental procedures using different pharmacological interventions. Arcari and Moscati (2018) evaluated pain perception during restoration (no pulp involvement) by comparing nitrous oxide-oxygen relative analgesia alone to using nitrous oxide-oxygen relative analgesia and LA. The authors found that the two methods showed no significant difference in reducing pain perception. Raslan and Zouzou (2021) evaluated pain perception during LA and extraction by comparing the use of pre-emptive oral paracetamol/ibuprofen to using an oral placebo solution. They found that the use of pre-emptive analgesics showed lower pain scores compared to the placebo.

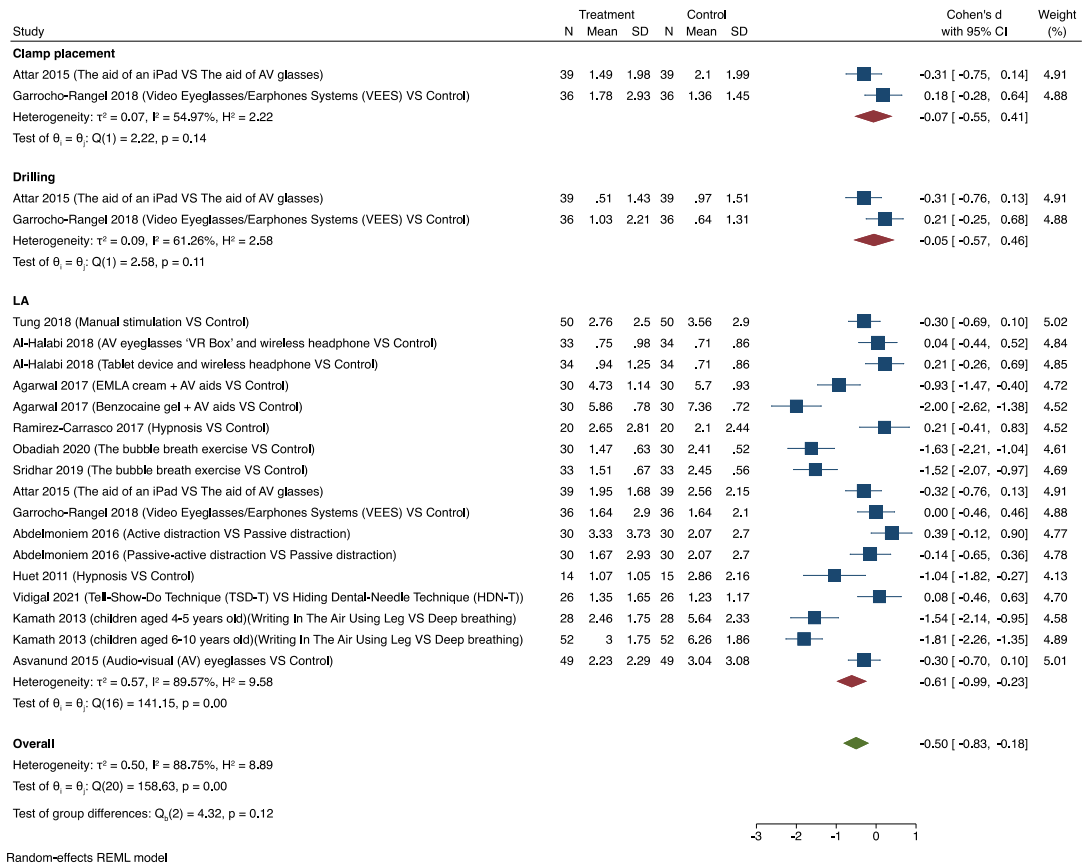
#### 4.3.4.1.7 Behavioural Interventions

Several authors assessed pain perception during dental procedures using different behavioural interventions. Tung et al. (2018) compared applying manual vibration with the operator's finger adjacent to the injection site to conventional LA. They found that the manual stimulation group presented a non-significant reduction in pain scores when compared to the conventional LA. Al-Halabi et al. (2018) compared the use of audio-visual (AV) distraction by a virtual reality (VR) box or a tablet to a control group having no distraction during LA. They reported that the two audio-visual distraction methods showed no differences in reducing pain during LA compared to the control group. Agarwal et al. (2017) compared using AV distraction with EMLA (lidocaine 2.5% and prilocaine 2.5%) cream to using EMLA alone during LA. They concluded that the use of EMLA with AV aids significantly reduced pain during LA. Agarwal et al. (2017) also compared using AV distraction and Benzocaine (20%) gel to using Benzocaine (20%) gel alone during LA. They found that the use of Benzocaine (20%) with AV distraction significantly relieved pain during LA. Two studies investigated the influence of hypnosis on reducing pain perception by comparing children who had hypnosis prior to and during LA to children who had LA without hypnosis (Huet et al., 2011; Ramirez-Carrasco et al., 2017). Huet et al. (2011) suggested that hypnosis may be effective in reducing pain in children receiving LA. However, Ramirez-Carrasco et al. (2017) found that the two groups showed no significant difference in reducing pain in children receiving LA. Two studies compared the effect of breathing exercises (bubble breath exercise: children were asked to blow the bubble blower using the same deep breathing pattern that they had practised before) with

LA to a control group having only LA (Sridhar et al., 2019; Obadiah and Subramanian, 2020). Sridhar et al. (2019) reported that pain perception during LA was significantly lower with the use of bubble breath exercise. However, Obadiah and Subramanian (2020) found that the two groups showed no significant difference in reducing pain perception during LA. Attar and Baghdadi (2015) compared using AV glasses to using an iPad video game. They reported that pain perception during dental procedures (LA, clamp placement and pulpotomy) was significantly lower when using the iPad video game. Garrocho-Rangel et al. (2018) compared using the Video Eyeglasses/Earphones System (VEES) to a control group. They reported that the two groups showed no significant difference in reducing pain perception during dental procedures (LA and restoration). One study compared the influence of passive distraction (children were listening to a song on headphones), active distraction (children were moving legs up and down), and passive-active distraction (children were listening to a song on headphones while moving legs up and down) on reducing pain perception during LA (Abdelmoniem and Mahmoud, 2016). They found that the three groups exhibited no significant differences in pain during LA. Vidigal et al. (2021) compared using the Tell-Show-Do Technique (TSD-T) and the Hiding Dental-Needle Technique (HDN-T). They reported that no significant difference in reducing pain perception during LA was shown between the two groups. Kamath (2013) compared using a distraction technique of Writing In The Air Using Leg (WITAUL) to a deep breathing exercise. She found that pain perception during LA was significantly lower with the use of WITAUL. Asvanund et al. (2015) compared the influence of using AV

glasses to a control group. They reported that the use of AV glasses significantly reduced pain perception during LA.

Thirteen studies provided comparable data for this outcome (Huet et al., 2011; Kamath, 2013; Asvanund et al., 2015; Attar and Baghdadi, 2015; Abdelmoniem and Mahmoud, 2016; Agarwal et al., 2017; Ramirez-Carrasco et al., 2017; Al-Halabi et al., 2018; Garrocho-Rangel et al., 2018; Tung et al., 2018; Sridhar et al., 2019; Obadiah and Subramanian, 2020; Vidigal et al., 2021). Figure 12 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that the use of different behavioural Interventions significantly relieved intra-operative pain associated with dental procedures (clamp placement, LA and drilling) (SMD -0.50, 95% CI -0.83 to -0.18). The considerable heterogeneity ( $I^2 = 88.75\%$ ) in this estimate is likely due to the different tools used to measure the outcome and the different behavioural interventions used in each trial.



**Figure 12.** Random-effects meta-analysis evaluation of intra-operative pain for comparison 7: behavioural interventions.

#### 4.3.4.2 Post-operative pain outcome

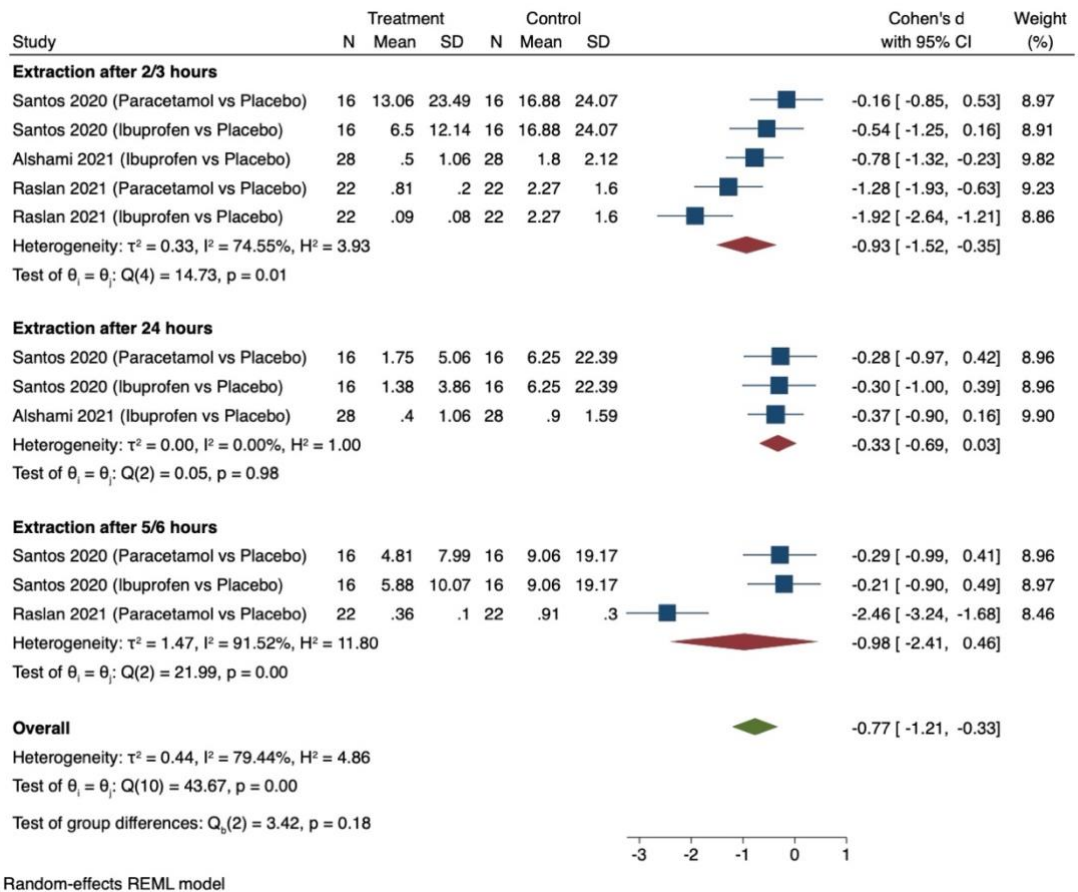
##### 4.3.4.2.1 LA Agent (Articaine Versus Lidocaine)

Two studies evaluated pain perception experience after dental procedures (restorations and extractions) using 4% Articaine infiltration LA compared to 2% Lidocaine IANB LA (Ram and Amir, 2006; Massignan et al., 2020). They reported that 4% Articaine LA was as effective as 2% lidocaine LA.

#### 4.3.4.2.2 Pharmacological Interventions

Five studies evaluated pain experience after dental procedures using pre-emptive oral analgesics (paracetamol/ibuprofen) compared to using an oral placebo solution. Three studies evaluated pain perception after extraction at different times (Santos et al., 2020; Alshami et al., 2021; Raslan and Zouzou, 2021). Santos et al. (2020) concluded that the use of pre-emptive analgesics did not significantly reduce post-operative pain in children after primary molar extraction. However, Alshami et al. (2021) and Raslan and Zouzou (2021) found that the use of pre-emptive analgesics showed lower post-extraction pain scores compared to a placebo solution. Two orthodontic studies evaluated pain perception after separator placement (Law et al., 2000; Bernhardt et al., 2001). Both studies concluded that the patients who had taken ibuprofen one hour before separator placement had significantly lower pain perception after two hours.

Three studies provided comparable data for this outcome (Santos et al., 2020; Alshami et al., 2021; Raslan and Zouzou, 2021). Figure 13 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed that the use of pre-emptive analgesics significantly relieved post-operative pain associated with extraction between intervention and control groups (SMD  $-0.77$ , 95% CI  $-1.21$  to  $-0.33$ ). The considerable heterogeneity ( $I^2 = 79.44\%$ ) in this estimate is likely due to the studies considered different tools to measure the outcome and different pre-emptive analgesics used at different times in each trial.



**Figure 13.** Random-effects meta-analysis evaluation of post-operative pain for comparison 8: pharmacological interventions (oral analgesics versus placebo).

#### 4.3.4.2.3 Behavioural Interventions

One study assessed pain perception five minutes after pulpotomy while using AV glasses compared to using an iPad video game (Attar and Baghdadi, 2015). They found that there was no significant difference in reducing pain perception five minutes after the pulpotomy between the two methods of distraction.



#### **4.3.4.3 Anxiety outcome**

##### **4.3.4.3.1 Computer Driven LA Versus Conventional LA**

Three studies evaluated anxiety during LA while using computer driven LA (infiltration or IANB) compared to conventional LA (Versloot et al., 2005; Versloot et al., 2008; Smolarek et al., 2020). Versloot et al. (2005) concluded that children with low anxiety levels seemed to benefit from the use of computer driven LA. However, Versloot et al. (2008) and Smolarek et al. (2020) reported that the two groups did not show significant differences in reducing anxiety between the two groups in their studies.

##### **4.3.4.3.2 Mechanoreceptor and thermal receptor stimulation**

One study evaluated anxiety before and during LA while using DentalVibe as an electrical vibration device with conventional LA compared to conventional LA alone (Smolarek et al., 2020). They reported that anxiety was not significantly reduced during LA between the two groups.

##### **4.3.4.3.3 Pharmacological Interventions**

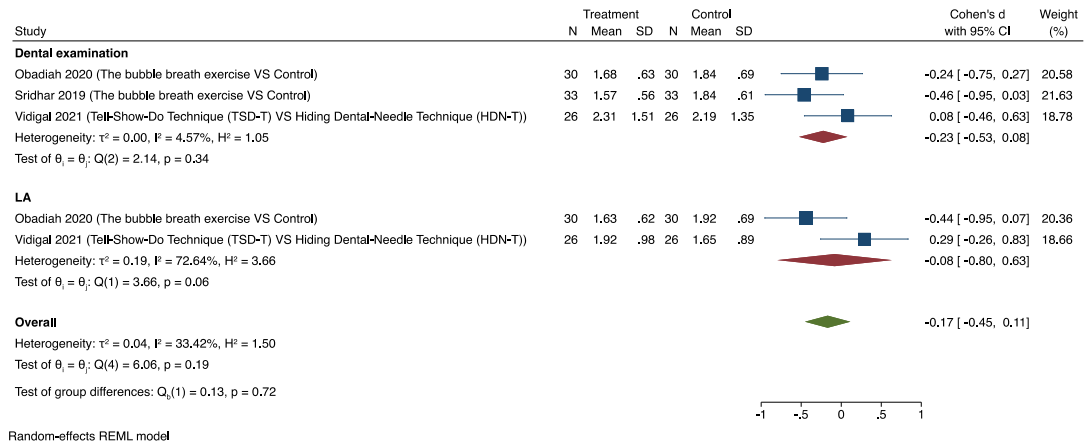
One study evaluated anxiety before and/or after extraction when using pre-emptive oral analgesics (paracetamol/ibuprofen) compared to using an oral placebo solution (Alshami et al., 2021). They found that the pre-emptive analgesics group showed lower post-extraction anxiety scores compared to the group who had the placebo solution.

#### 4.3.4.3.4 Behavioural Interventions

Five studies evaluated anxiety during dental procedures using different behavioural interventions. Two studies compared the effect of breathing exercises (bubble breath exercise: children were asked to blow the bubble blower using the same deep breathing pattern that they had practised before) with LA to a control group having only LA (Sridhar et al., 2019; Obadiah and Subramanian, 2020). Sridhar et al. (2019) found no significant difference in reducing anxiety with LA between the two groups. However, Obadiah and Subramanian (2020) found that the bubble breath exercise was effective in reducing anxiety during giving LA. Vidigal et al. (2021) compared using the Tell-Show-Do Technique (TSD-T) and the Hiding Dental-Needle Technique (HDN-T). They reported that anxiety was not significantly reduced during LA between the two groups. Huet et al. (2011) investigated the effect of hypnosis on anxiety reduction by comparing children having hypnosis prior to and during LA to children having LA without hypnosis. They suggested that hypnosis may be effective in reducing anxiety in children receiving LA. Attar and Baghdadi (2015) compared using AV glasses to using an iPad video game. They reported that no significant difference in anxiety reduction during pulpotomy between the two groups.

Three studies provided comparable data for this outcome (Sridhar et al., 2019; Obadiah and Subramanian, 2020; Vidigal et al., 2021). Figure 14 shows the results of the meta-analysis. Pooling the results of these studies using a random-effects model and the Cohen's d standardised mean difference (SMD) showed no significant difference in reducing anxiety

associated with dental procedures between intervention and control groups (SMD  $-0.17$ , 95% CI  $-0.45$  to  $0.11$ ). The heterogeneity is low ( $I^2 = 33.42\%$ ) in this estimate.



**Figure 14.** Random-effects meta-analysis evaluation of anxiety for comparison 9: behavioural interventions.

#### 4.3.5 Quality of evidence

The certainty of the evidence was assessed using the GRADE criteria and considered to be moderate for all interventions measuring intra-operative and post-operative pain and anxiety outcomes (Appendix 9). The main drivers for downgrading the certainty of evidence to moderate evidence were the high risk of bias detected in some studies due to the lack of blinding of outcome assessors and the presence of imprecision. The GRADE recommendations were strong (IB) based on the moderate level of evidence for the effectiveness of mechanoreceptor and thermal receptor stimulation, behavioural interventions, and pre-emptive oral analgesics in reducing pain associated with routine dental care in children (Table 5).

Intervention	Effect size and conclusions	GRADE recommendation
Mechanoreceptor and thermal receptor stimulation (Intra-operative pain outcome)	SMD 1.38 SD lower (2.02 lower to 0.73 lower) Moderate level of evidence	IB, strong recommendation based on the moderate level of evidence
Behavioural Interventions (Intra-operative pain outcome)	SMD 0.5 SD lower (0.83 lower to 0.18 lower) Moderate level of evidence	IB, strong recommendation based on the moderate level of evidence
Pharmacological Interventions 'oral analgesics' (Post-operative pain outcome)	SMD 0.77 SD lower (1.21 lower to 0.33 lower) Moderate level of evidence	IB, strong recommendation based on the moderate level of evidence

**Table 5.** The GRADE recommendations.

#### 4.4 Discussion

The aim of this systematic review was to assess the effectiveness of interventions used to relieve intra-operative and post-operative pain with routine paediatric dental procedures. Data were assembled from forty-five studies comprising 3093 children who had routine dental care. The risk of bias of individual studies was low in only five trials, with all other trials being rated as having either a high or unclear risk of bias. Thirty-seven studies were included in the meta-analysis and provided nine comparisons, of which seven were on the outcome of intra-operative pain, one was on post-operative pain outcome, and one was on an anxiety outcome. There were significant effects shown for improvement in intra-operative pain associated with local anaesthesia when mechanoreceptor and thermal receptor stimulation was used, and with local anaesthesia and drilling when behavioural interventions were considered. Also, there was a significant effect in relieving post-operative pain associated with extraction when pre-

emptive analgesics were used. The certainty of the evidence for all interventions measuring main outcomes was assessed by the GRADE to be moderate.

This review found that there are many interventions used in contemporary paediatric dentistry that may produce a positive effect on pain perception and anxiety in children undergoing routine dental care. This review also presents to general dental practitioners and paediatric dentists some of the interventions that may be used in primary and secondary dental care in order to hopefully reduce the number of children requiring GA for their dental care. It has been found that children in some areas of the UK and other countries may have to wait more than 12 months to have dental treatment under GA (Paterson and Tahmassebi, 2003). Therefore, using some of these interventions reviewed in this present study may improve children's pain perception and anxiety associated with routine dental procedures and allow more treatment in the chair which could reduce dental general anaesthesia waiting times.

A newer concept of delivering local anaesthesia through Computer Controlled Anaesthetic Devices (the Wand System and QuickSleeper™) were designed to minimise pain perception during the injection of local anaesthesia. The present review found no beneficial effects of the Wand System when used as infiltration/IANB over conventional delivery of LA for different dental procedures. In contrast to this finding, the review also showed that the Wand System might significantly relieve intra-operative pain

associated with LA when intra-ligamentary anaesthesia was considered, but it was difficult to reach a firm conclusion as only two studies were included in the meta-analysis. Regarding intra-osseous anaesthesia, this review only included one trial that compared the QuickSleeper™ for intra-osseous anaesthesia to conventional anaesthesia using two study designs and found a significant difference in relieving intra-operative pain associated with LA, but it was also found to be difficult to reach a firm conclusion on the benefit of using this device for relieving pain associated with LA. These findings were in agreement with one other similar systematic review and meta-analysis conducted by Smolarek et al. (2020) who analysed whether pain and disruptive behaviour were decreased by the use of computerised local dental anaesthesia in children compared to the use of conventional anaesthesia. The authors combined the Wand System and QuickSleeper™ regardless the injection site into a single meta-analysis and concluded that there was no difference in the pain perception and disruptive behaviour between the computerised and conventional dental local anaesthesia, but the quality of evidence was low.

Based on these results and the GRADE strength of recommendation, the present systematic review and meta-analysis do not consider that investing in Computer Controlled Anaesthetic Devices with the objective of relieving pain associated with paediatric dental procedures is a wise choice. Because conventional anaesthesia may have similar results when performed correctly, and the use of these devices will add no advantage to primary and secondary dental care with regard to pain during local anaesthesia. In

addition, these devices are expensive, need training on their use and are time-consuming (Angelo and Polyvios, 2018; Banerjee, 2020). Therefore, within the context of this study and the results of meta-analysis it is not recommended to use Computer Controlled Anaesthetic Devices for minimising the child's pain perception during the injection of local anaesthesia.

Lidocaine, a popular LA agent, used in dentistry since 1948, has been proven to be efficacious with minor risk of toxicity and low reports of allergic reactions (Malamed, 2013; Tong et al., 2018). Articaine was introduced to clinical practice in 1976 and has been given a superior reputation by numerous reviews and studies (Ram and Amir, 2006; Katyal, 2010). However, a systematic review and meta-analysis conducted by Tong et al. (2018) who assessed the efficacy of 2% Lidocaine and 4% Articaine in clinical paediatric dentistry suggested that both 4% Articaine as infiltration and 2% lidocaine IANB presented the same efficacy when used for routine dental treatments, but the quality of evidence was low. Regarding the findings of this present review, only two studies were included in the meta-analysis comparing the use of 4% Articaine LA as infiltration to 2% Lidocaine LA as IANB. One study showed a significant difference whereas the other study did not show any difference between the LA agents. Therefore, it was difficult to reach a firm conclusion on the benefit of using the 4% Articaine LA agent for relieving intra-operative pain associated with LA.

Different types of topical anaesthesia have been investigated in the literature to reduce intra-oral LA injections (Atabek et al., 2015; Yildirim et al., 2020). There have been mixed results regarding the efficacy of topical anaesthetics in reducing injection pain reported by several authors (Gill and Orr, 1979; Martin et al., 1994; Hutchins et al., 1997; Roghani et al., 1999; Fukayama et al., 2002; Paschos et al., 2006). Regarding the findings of this review, two studies were only included in the meta-analysis comparing two types of topical anaesthesia. One study reported that there was a significant difference whereas the other study did not find any difference between the two groups. Therefore, it was difficult to reach a firm conclusion if one type of topical anaesthesia can give a more positive effect on relieving intra-operative pain associated with LA injections. There are no published reviews that investigated this topic.

Several studies have investigated the efficacy of mechanoreceptor and thermal receptor stimulation on pain perception during LA injections. The working principle of these interventions can be explained by the gate control theory of pain (Melzac and Wall, 1965). An important component of this theory is that stimulation of large diameter A- $\beta$  nerve fibres through mechano/thermoreceptors (pressure, vibration, or temperature) re-activates inhibitory neurons which block the neurological gate to stop the transmission of pain signals (Dickenson, 2002; Nanitsos et al., 2009). The included studies demonstrated different mechanoreceptor and thermal receptor stimulation interventions such as vibrating devices including Buzzy device, DentalVibe, different LA temperatures and ice application. The results of this



review revealed that pain perception was significantly relieved during LA injections when different types of mechanoreceptor and thermal receptor stimulation were applied. There are no published reviews on the influence of mechanoreceptor and thermal receptor stimulation on pain perception during LA injections.

According to these results and the GRADE strength of recommendation, this systematic review and meta-analysis strongly recommend that the use of different types of mechanoreceptor and thermal receptor stimulation can significantly reduce pain in children receiving local anaesthesia for dental treatment in the chair. These interventions are simple, non-invasive, and less costly which can be used in primary and secondary dental care. Furthermore, children might positively accept receiving local anaesthesia and subsequent dental treatment when general dental practitioners and paediatric dentists consider the use of these interventions. Therefore, the number of children requiring dental general anaesthesia, the waiting time for DGA, episodes of pain and infection and the need for repeated antibiotic prescriptions might be decreased.

Several authors have assessed the use of pre-emptive oral analgesics (paracetamol/ibuprofen) for relieving pain in children undergoing routine dental treatment. A systematic review was conducted by Ashley et al. (2016) who assessed the effects of pre-operative analgesics for intra-operative and/or post-operative pain relief in children and adolescents undergoing routine dental treatment. The authors could not determine whether pre-

operative analgesics were of benefit in paediatric dentistry for procedures under local anaesthetic, but the quality of evidence was low. They also suggested that there is probably a benefit in using pre-operative analgesics before orthodontic separator placement. However, the present review found that the use of pre-emptive analgesics can significantly reduce pain two/three hours after extraction of primary molars. The findings of this present review provide a justification for using pre-emptive oral analgesics in children having invasive dental procedures such as extractions under local anaesthesia in order to relieve intra-operative and post-operative pain. Also, this review suggests that taking oral analgesics before placing orthodontic separators and stain steel crowns using the Hall technique may reduce post-operative pain associated with separators and crowns placement.

A considerable amount of literature has been published on the effectiveness of non-pharmacological (behavioural) interventions in reducing pain and anxiety in children receiving dental care. The current review looked at different behavioural interventions such as TSD, hypnosis, bubble breath exercise and distraction. The findings of this review strongly recommend that the use of behavioural interventions can significantly help reduce pain perception during LA injections. This finding seems to be consistent with another similar systematic review conducted by Goettems et al. (2017) who investigated the effectiveness of non-pharmacologic interventions on behaviour, anxiety, and pain perception in children undergoing dental treatment. The authors found that child's behaviour, anxiety, and pain perception were improved by using these non-pharmacologic techniques.

These interventions are simple approaches which can be used in primary and secondary dental settings and have a positive effect on pain perception in children receiving routine dental treatment. However, although pain and anxiety are related, the findings of this present review showed that behavioural interventions were not found to be effective in relieving anxiety associated with the dental examination and LA.

The main strength of the present systematic review is that it represents the first comprehensive systematic review to assess both pharmacological, non-pharmacological and other interventions used to relieve intra-operative and post-operative pain with routine paediatric dental procedures, providing moderate evidence with strong recommendations for the effectiveness of behavioural interventions, mechanoreceptor and thermal receptor stimulation, and pre-emptive oral analgesics that can have a positive effect in reducing pain in children having routine dental care. Additionally, the quality standards according to PRISMA were employed in this review (Liberati et al., 2009; Moher et al., 2009). Moreover, a broad search strategy of several databases without language and date restrictions was considered. This allowed the reviewers to identify and include many potentially eligible studies; therefore, the risk of selection bias was minimised (Higgins et al., 2019). Furthermore, the reviewers independently assessed studies for eligibility, extracted data and evaluated the quality of the included studies to minimise selection and information bias and error and to improve the reliability and validity of this review.

Some limitations are noticed in this review. More than 50% of studies were assessed as being at unclear risk of bias mostly arising from issues related to sequence generation and concealment of allocation which might increase the risk of selection bias. The remaining studies were rated at high risk of bias due to unblinding of outcome assessors which might increase the risk of detection bias, with the exception of five studies which were judged to be at low risk of bias. Due to the nature of the intervention, blinding of operators and/or participants was not possible in the majority of studies. It was therefore decided to judge this domain to be at low risk of bias however the risk of performance bias could be increased. Furthermore, a large number of studies were excluded because they had missing data although the authors were contacted and some of them replied that they no longer have the data. These studies could have influenced the results of this review if there were included. Several ongoing studies were also identified more recently which may be included in an update of this review. Although the interventions were grouped together based on their mechanism of action, pooling of different interventions into a single meta-analysis may have influenced the results of meta-analysis and increased the heterogeneity across the studies that could have an impact of the recommendations. Additionally, this review did not find eligible studies including children or adolescents with special healthcare needs. Therefore, no reliable evidence about interventions used for improvement in pain associated with routine dental procedures in children and adolescents with special healthcare needs. It can be noticed that there is limited evidence in this area and ideally there should be a well-designed RCT in order to explore the best available approach for relieving pain

associated with routine dental care for this group. However, given the diversity and complexity of healthcare needs, this is a difficult prospect.

## **4.5 Conclusion**

This systematic review provides moderate evidence with strong recommendations for the effectiveness of behavioural interventions, mechanoreceptor and thermal receptor stimulation, and pre-emptive oral analgesics in reducing pain associated with routine dental care in children. These interventions can be used in primary and secondary care settings in order to improve the number of children accepting treatment in the dental chair and reduce the number of children requiring general anaesthesia for their dental treatment.

## **Chapter 5: Summary of Findings and Recommendations**

### **5.1 Summary of main findings**

Exposing children to a painful dental procedure may have a variety of adverse consequences such as anxiety, fear, behavioural management difficulties, and delay in seeking dental care which may require GA for dental treatment. Although there are some benefits of having dental treatment under GA, dental treatment under GA is expensive, resource intensive and associated with risks and complications. Furthermore, long waiting lists for dental treatment under GA is another significant issue as the literature reports that children may be waiting over a year to be treated under GA (Knapp et al., 2017; Fox et al., 2022). These children may then experience multiple episodes of pain, distress, and infection during this period which may need multiple visits to primary dental care for placing several temporary dressings or prescribing courses of antibiotics to relieve pain and infection (North et al., 2007; Fox et al., 2022).

Therefore, the aims of this thesis were to identify predictors of intra-operative and post-operative pain associated with routine dental procedures in children and to assess interventions used to reduce this pain in children. The next aim was to develop evidence-based recommendations for managing intra-operative and post-operative pain associated with routine paediatric dental procedures in order to improve the number of children accepting treatment in the dental chair and reduce the number of children requiring

general anaesthesia for their dental treatment. These aims were carried out by undertaking two systematic reviews; the first review appraised the evidence for predictors of intra-operative and post-operative pain associated with routine dental procedures in children whereas the second review appraised the evidence for interventions used to relieve this pain. Then the findings were used to develop evidence-based recommendations.

The first systematic review included six observational studies involving 3213 children having routine dental treatment with four of these studies pooled using meta-analysis and meta-regression. The results of the first review showed evidence that the strongest predictors for intra-operative pain were dental anxiety, extraction, and drilling. The second systematic review included forty-five RCTs comprising 3093 children having routine dental procedures with thirty-seven of these trials pooled using meta-analysis. The results of the second review provided moderate evidence with strong recommendations for the effectiveness of (1) behavioural interventions, (2) mechanoreceptor and thermal receptor stimulation, and (3) pre-emptive oral analgesics in reducing pain in children having routine dental care.

## **5.2 Implications and recommendations for dental care for children**

The findings of this study can assist general dental practitioners and paediatric dentists in terms of decision-making and treatment planning. Having a good understanding of the predictors of pain associated with

routine dental treatment in children can help dentists choose and provide appropriate pharmacological and/or non-pharmacological interventions to help relieve pain and anxiety and allow children to cope better with dental care. This in turn may improve the number of children accepting treatment in the dental chair and reduce the number of children requiring general anaesthesia for their dental treatment.

The findings of the first systematic review showed that predictors of the intra-operative pain were dental procedures and anxiety with dental extractions, as the most predicted painful dental procedure, followed by drilling. Local anaesthesia was also a predictor and although not statistically significant, the mean pain score was clinically significant (mean VAS difference of 13.84 mm). Moreover, the review found that high anxiety levels were another predictor of intra-operative pain associated with routine paediatric dental treatment with clinically and statistically significant differences observed in pain scores between those with high anxiety having a dental procedure when compared to those with low anxiety. The findings of the second systematic review specifically identified behavioural interventions, mechanoreceptor and thermal receptor stimulation, and pre-emptive oral analgesics as having moderate evidence of successfully reducing pain during and/or after various dental procedures. Both reviews provide strong evidence to support the use of behavioural interventions to manage anxiety and pain associated with extractions, drilling and local anaesthesia, the use of mechanoreceptor and thermal receptor stimulation to relieve pain



associated with local anaesthesia, and the use of pre-emptive oral analgesics to reduce pain associated with invasive dental procedures.

Behavioural interventions are simple approaches which can be used early in primary dental care and have a positive effect on pain perception in children receiving routine dental treatment. Examples of these behavioural interventions are Tell-Show-Do (TSD), distraction such as manual stimulation, audio-visual distraction, the Hiding Dental-Needle Technique (HDN-T) and breathing exercises such as bubble breath exercise. Other intervention like hypnosis is more difficult to apply but should also be explored for children in whom the simple techniques do not work and may be more applicable to secondary care. Mechanoreceptor and thermal receptor stimulation during dental treatment is also simple, non-invasive, and less costly and which can be used early in primary dental care. They include vibrating devices (Buzzing device or DentalVibe), using different LA temperatures, and ice application. The findings of the current reviews can also assist primary care and paediatric dental professionals to justify using pre-emptive oral analgesics in children having invasive dental procedures such as extractions under local anaesthesia in order to relieve the intra-operative and post-operative pain. Additionally, the findings of the review suggest that children receiving stain steel crowns using the Hall technique might benefit from taking oral analgesics before the placement of orthodontic separators and crowns to help reduce post-operative pain associated with these procedures.

It is recommended that dentists should consider these predictors when they provide dental treatment for children. They should carefully listen to and be aware of the implications of the responses of their paediatric patients in order to provide acceptable and effective anaesthesia so that procedures can be completed with as little pain as possible. They should also consider what other support may be needed for the particular procedures. It is also recommended that dentists should assess their young patients pre-operatively for dental anxiety using a validated dental anxiety measure to allow them to choose appropriate anxiety management techniques. The anxiety could also be assessed by a dental nurse, receptionist, or parents/carers.

There is enough evidence provided from the reviews to report the information to practising primary care and paediatric dentists and to consider including the information in dental curricula. It can also be recommended that general dental practitioners and paediatric dentists should actively seek information and continuing education on interventions that can be beneficial in relieving pain associated with routine paediatric dental procedures.

### **5.3 Implications for further research**

Based on the literature review and the results of these systematic reviews, the following research investigations to continue to increase knowledge in this area are suggested:

- Investigation of other possible predictors of pain with paediatric dental procedures such as age, gender, infection, previous dental and medical experience and dentists' knowledge and attitudes to pain should be considered in future research to help understand all the factors that contribute to pain and anxiety in children.
- Integrating the components of the interventions identified into an intervention package might be a way forward. For example, the CALM trial (Marshman et al., 2022) is using behavioural interventions like cognitive behaviour therapy to enable nervous children to accept dental treatment. Interventions identified in the reviews may help further alleviate pain and anxiety once the child begins treatment e.g., mechanoreceptor stimulation and pre-emptive analgesics.
- It will be important to develop larger multi-centre trials in primary care such as the CALM trial (Marshman et al., 2022) to allow the interventions identified to be tested in settings where children make their first dental contact. It would also allow us to study different age groups.
- Future research would be useful to explore implementation of the findings of the reviews particularly in primary care. Early application of such interventions can reduce the need for GA or specialist referral. Implementation research needs to explore whether these interventions are acceptable to primary care dentists and would dentists measure anxiety in all their patients? It could also explore what the barriers might be for dentists including time, cost, and training needs.

## 5.4 Conclusion

From the results of these systematic reviews on predictors and interventions for intra-operative and post-operative pain associated with routine paediatric dental procedures, it can be concluded that:

- Dental extraction was the strongest predictor of intra-operative pain associated with paediatric dental procedures followed by drilling. Children with high anxiety levels were more likely to report pain during the dental procedures. Therefore, GDPs and paediatric dentists should carefully consider these predictors to use appropriate pharmacological and non-pharmacological interventions to reduce pain associated with routine dental procedures in children.
- The use of behavioural interventions, mechanoreceptor and thermal receptor stimulation, or pre-emptive oral analgesics are strongly recommended for reducing pain associated with routine dental care in children. These interventions can be used early in primary and secondary care settings in order to improve the number of children accepting treatment in the dental chair and reduce the number of children who require GA for their dental treatment.

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## Appendix 1: Search strategy for the first systematic review

MEDLINE via OVID

1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.
5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatric\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.
13. Pain, Postoperative/
14. (postoperative adj4 pain\*).ti,ab,kw.
15. (post-operative adj4 pain\*).ti,ab,kw.
16. post-operative-pain\*.ti,ab,kw.
17. (post\* adj4 pain\*).ti,ab,kw.
18. (postoperative adj4 analgesi\*).ti,ab,kw.
19. (post-operative adj4 analgesi\*).ti,ab,kw.
20. post-operative analgesi\*.ti,ab,kw.
21. (post-surgical adj4 pain\*).ti,ab,kw.
22. (post surgical adj4 pain\*).ti,ab,kw.
23. (pain\* adj4 after surg\*).ti,ab,kw.



24. (pain\* adj4 after operat\*).ti,ab,kw.
25. (pain\* adj4 follow\* operat\*).ti,ab,kw.
26. (pain\* adj4 follow\* surg\*).ti,ab,kw.
27. (pain adj1 operati\*).ti,ab,kw.
28. (intra adj procedur\* adj pain).ti,ab,kw.
29. (intraoperative adj4 pain\*).ti,ab,kw.
30. (intra-operative adj4 pain\*).ti,ab,kw.
31. intra-operative-pain\*.ti,ab,kw.
32. (intraoperative adj4 analgesi\*).ti,ab,kw.
33. (intra-operative adj4 analgesi\*).ti,ab,kw.
34. intra-operative analgesi\*.ti,ab,kw.
35. (intra-surgical adj4 pain\*).ti,ab,kw.
36. (intrasurgical adj4 pain\*).ti,ab,kw.
37. (pain\* adj4 after surg\*).ti,ab,kw.
38. (pain\* adj4 after operat\*).ti,ab,kw.
39. (pain\* adj4 follow\* operat\*).ti,ab,kw.
40. (pain\* adj4 follow\* surg\*).ti,ab,kw.
41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
46. predictor\*.tw,kw.
47. Protective factors/
48. risk assessment/
49. risk factors/

50. (Risk adj factor\*).tw,kw.
51. (risk adj assessment\*).tw,kw.
52. (protective adj factor\*).tw,kw.
53. Prevalence/
54. Prevalence.tw,kw.
55. Incidence/
56. Incidence.tw,kw.
57. Prognosis/
58. Prognos\*.tw,kw.
59. correlati\*.tw,kw.
60. An?esthetics, Local/
61. An?esthesia, Local/
62. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.
63. Lidocaine/
64. (lidocaine or lignocaine or xylocaine).mp.
65. Carticaine/
66. (carticain\* or articain\*).mp.
67. Prilocaine/
68. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
69. Bupivacaine/
70. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.
71. 1 or 2 or 3 or 4 or 5 or 6
72. 7 or 8 or 9 or 10 or 11 or 12
73. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
74. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
75. 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70

76. 71 and 72 and 73 and 74 and 75

EMBASE via OVID

1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.
5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatric\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.
13. Pain, Postoperative/
14. (postoperative adj4 pain\*).ti,ab,kw.
15. (post-operative adj4 pain\*).ti,ab,kw.
16. post-operative-pain\*.ti,ab,kw.
17. (post\* adj4 pain\*).ti,ab,kw.
18. (postoperative adj4 analgesi\*).ti,ab,kw.
19. (post-operative adj4 analgesi\*).ti,ab,kw.
20. post-operative analgesi\*.ti,ab,kw.
21. (post-surgical adj4 pain\*).ti,ab,kw.
22. (post surgical adj4 pain\*).ti,ab,kw.
23. (pain\* adj4 after surg\*).ti,ab,kw.

24. (pain\* adj4 after operat\*).ti,ab,kw.
25. (pain\* adj4 follow\* operat\*).ti,ab,kw.
26. (pain\* adj4 follow\* surg\*).ti,ab,kw.
27. (pain adj1 operati\*).ti,ab,kw.
28. (intra adj procedur\* adj pain).ti,ab,kw.
29. (intraoperative adj4 pain\*).ti,ab,kw.
30. (intra-operative adj4 pain\*).ti,ab,kw.
31. intra-operative-pain\*.ti,ab,kw.
32. (intraoperative adj4 analgesi\*).ti,ab,kw.
33. (intra-operative adj4 analgesi\*).ti,ab,kw.
34. intra-operative analgesi\*.ti,ab,kw.
35. (intra-surgical adj4 pain\*).ti,ab,kw.
36. (intrasurgical adj4 pain\*).ti,ab,kw.
37. (pain\* adj4 after surg\*).ti,ab,kw.
38. (pain\* adj4 after operat\*).ti,ab,kw.
39. (pain\* adj4 follow\* operat\*).ti,ab,kw.
40. (pain\* adj4 follow\* surg\*).ti,ab,kw.
41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfot\* or tender\* or throb\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
46. predictor\*.tw,kw.
47. Protective factors/
48. risk assessment/
49. risk factors/
50. (Risk adj factor\*).tw,kw.

51. (risk adj assessment\*).tw,kw.
52. (protective adj factor\*).tw,kw.
53. Prevalence/
54. Prevalence.tw,kw.
55. Incidence/
56. Incidence.tw,kw.
57. Prognosis/
58. Prognos\*.tw,kw.
59. correlati\*.tw,kw.
60. An?esthetics, Local/
61. An?esthesia, Local/
62. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.
63. Lidocaine/
64. (lidocaine or lignocaine or xylocaine).mp.
65. Carticaine/
66. (carticain\* or articain\*).mp.
67. Prilocaine/
68. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
69. Bupivacaine/
70. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.
71. 1 or 2 or 3 or 4 or 5 or 6
72. 7 or 8 or 9 or 10 or 11 or 12
73. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
74. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
75. 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70
76. 71 and 72 and 73 and 74 and 75

## PsycINFO via OVID

1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.
5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatric\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.
13. Pain, Postoperative/
14. (postoperative adj4 pain\*).ti,ab,kw.
15. (post-operative adj4 pain\*).ti,ab,kw.
16. post-operative-pain\*.ti,ab,kw.
17. (post\* adj4 pain\*).ti,ab,kw.
18. (postoperative adj4 analgesi\*).ti,ab,kw.
19. (post-operative adj4 analgesi\*).ti,ab,kw.
20. post-operative analgesi\*.ti,ab,kw.
21. (post-surgical adj4 pain\*).ti,ab,kw.
22. (post surgical adj4 pain\*).ti,ab,kw.
23. (pain\* adj4 after surg\*).ti,ab,kw.
24. (pain\* adj4 after operat\*).ti,ab,kw.

25. (pain\* adj4 follow\* operat\*).ti,ab,kw.
26. (pain\* adj4 follow\* surg\*).ti,ab,kw.
27. (pain adj1 operati\*).ti,ab,kw.
28. (intra adj procedur\* adj pain).ti,ab,kw.
29. (intraoperative adj4 pain\*).ti,ab,kw.
30. (intra-operative adj4 pain\*).ti,ab,kw.
31. intra-operative-pain\*.ti,ab,kw.
32. (intraoperative adj4 analgesi\*).ti,ab,kw.
33. (intra-operative adj4 analgesi\*).ti,ab,kw.
34. intra-operative analgesi\*.ti,ab,kw.
35. (intra-surgical adj4 pain\*).ti,ab,kw.
36. (intrasurgical adj4 pain\*).ti,ab,kw.
37. (pain\* adj4 after surg\*).ti,ab,kw.
38. (pain\* adj4 after operat\*).ti,ab,kw.
39. (pain\* adj4 follow\* operat\*).ti,ab,kw.
40. (pain\* adj4 follow\* surg\*).ti,ab,kw.
41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh]
46. predictor\*.tw,kw.
47. Protective factors/
48. risk assessment/
49. risk factors/
50. (Risk adj factor\*).tw,kw.
51. (risk adj assessment\*).tw,kw.
52. (protective adj factor\*).tw,kw.

53. Prevalence/
54. Prevalence.tw,kw.
55. Incidence/
56. Incidence.tw,kw.
57. Prognosis/
58. Prognos\*.tw,kw.
59. correlati\*.tw,kw.
60. An?esthetics, Local/
61. An?esthesia, Local/
62. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.
63. Lidocaine/
64. (lidocaine or lignocaine or xylocaine).mp.
65. Carticaine/
66. (carticain\* or articain\*).mp.
67. Prilocaine/
68. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
69. Bupivacaine/
70. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.
71. 1 or 2 or 3 or 4 or 5 or 6
72. 7 or 8 or 9 or 10 or 11 or 12
73. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
74. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
75. 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70
76. 71 and 72 and 73 and 74 and 75



1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.
5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatic\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.
13. Pain, Postoperative/
14. (postoperative adj4 pain\*).ti,ab,kw.
15. (post-operative adj4 pain\*).ti,ab,kw.
16. post-operative-pain\*.ti,ab,kw.
17. (post\* adj4 pain\*).ti,ab,kw.
18. (postoperative adj4 analgesi\*).ti,ab,kw.
19. (post-operative adj4 analgesi\*).ti,ab,kw.
20. post-operative analgesi\*.ti,ab,kw.
21. (post-surgical adj4 pain\*).ti,ab,kw.
22. (post surgical adj4 pain\*).ti,ab,kw.
23. (pain\* adj4 after surg\*).ti,ab,kw.
24. (pain\* adj4 after operat\*).ti,ab,kw.
25. (pain\* adj4 follow\* operat\*).ti,ab,kw.
26. (pain\* adj4 follow\* surg\*).ti,ab,kw.

27. (pain adj1 operati\*).ti,ab,kw.
28. (intra adj procedur\* adj pain).ti,ab,kw.
29. (intraoperative adj4 pain\*).ti,ab,kw.
30. (intra-operative adj4 pain\*).ti,ab,kw.
31. intra-operative-pain\*.ti,ab,kw.
32. (intraoperative adj4 analgesi\*).ti,ab,kw.
33. (intra-operative adj4 analgesi\*).ti,ab,kw.
34. intra-operative analgesi\*.ti,ab,kw.
35. (intra-surgical adj4 pain\*).ti,ab,kw.
36. (intrasurgical adj4 pain\*).ti,ab,kw.
37. (pain\* adj4 after surg\*).ti,ab,kw.
38. (pain\* adj4 after operat\*).ti,ab,kw.
39. (pain\* adj4 follow\* operat\*).ti,ab,kw.
40. (pain\* adj4 follow\* surg\*).ti,ab,kw.
41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
46. predictor\*.tw,kw.
47. Protective factors/
48. risk assessment/
49. risk factors/
50. (Risk adj factor\*).tw,kw.
51. (risk adj assessment\*).tw,kw.
52. (protective adj factor\*).tw,kw.
53. Prevalence/
54. Prevalence.tw,kw.

55. Incidence/
56. Incidence.tw,kw.
57. Prognosis/
58. Prognos\*.tw,kw.
59. correlati\*.tw,kw.
60. An?esthetics, Local/
61. An?esthesia, Local/
62. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.
63. Lidocaine/
64. (lidocaine or lignocaine or xylocaine).mp.
65. Carticaine/
66. (carticain\* or articain\*).mp.
67. Prilocaine/
68. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
69. Bupivacaine/
70. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.
71. 1 or 2 or 3 or 4 or 5 or 6
72. 7 or 8 or 9 or 10 or 11 or 12
73. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
74. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
75. 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70
76. 71 and 72 and 73 and 74 and 75

#### PubMed

((((((((((DENTISTRY) OR ((dental\* OR dentist\*))) OR oral surg\*) OR ((orthodontic\* OR pulpotom\* OR pulpect\* OR endodont\* OR "pulp cap\*"))))

OR ((fill\* OR restor\* OR extract\* OR remov\* OR "cavity prep\*" OR caries OR carious OR decay\*)) OR ((root canal AND (therap\* OR treat\*))) AND ((((((child) OR Infant) OR adolescent) OR ((Pediatric\* OR paediatric\*))) OR Dental care for children) OR (((child\* OR adolescent\* OR kid OR kids OR youth\* OR youngster\* OR minor OR minors OR teen\* OR preteen\* OR pre-teen\* OR juvenile\* OR "young adult\*" OR "young person" OR "young people" OR p?ediatric\* OR student\* OR pupil OR pupils OR boy OR boys OR girl OR girls OR under 18\* OR under eighteen\* OR underage)))) AND (((((((((Pain, Postoperative) OR ((postoperative pain\* OR post-operative pain\* OR post\* AND pain\*)) OR ((postoperative analgesi\* OR post-operative analgesi\* OR post\* AND analgesi\*)) OR ((postsurgical pain\* OR post-surgical pain\*)) OR ((pain\* AND after surg\* OR pain\* AND after operat\* OR pain\* AND follow\* AND operat\* OR pain\* AND follow\* AND surg\*)) OR Pain, intraoperative) OR ((intraoperative pain\* OR intra-operative pain\* OR intra\* AND pain\*)) OR ((intraoperative analgesi\* OR intra-operative analgesi\* OR intra\* AND analgesi\*)) OR ((intrasurgical pain\* OR intra-surgical pain\*)) OR ((sore\* OR hurt\* OR ache\* OR aching OR discomfort\* OR uncomfot\* OR tender\* OR throb\*))) AND (((((((predictor\*) OR Protective factors) OR risk assessment) OR risk factors) OR Prevalence) OR Incidence) OR Prognos\*) OR correlati\*)) AND (((local anesthetic\* OR local anaesthetic\* OR local anesthesia OR local anaesthesia))) OR ((lidocain\* OR lignocain\* OR xylocain\* OR carticain\* OR articain\* OR prilocain\* OR citanest\* OR propitocain\* OR xylonest OR bupivacain\* OR buvacaina OR carbostesin OR dolanaest OR marcain\* OR sensorcain\* OR svedocain\*))

### Scopus

( TITLE-ABS-KEY ( "dental treatment" OR "dentistry" OR "dental care" OR "dental therapy\*" ) AND TITLE-ABS-KEY ( child\* OR adolescent\* OR kid\* OR youth\* OR youngster\* OR minors OR teen\* OR preteen\* OR pre-teen\* OR juvenile\* OR "young adult\*" OR "young person" OR "young people" OR p?ediatric\* OR student\* OR pupil\* OR boy\* OR girl\* ) AND TITLE-ABS-KEY ( pain OR sore\* OR hurt\* OR ache\* OR aching OR discomfort\* OR uncomfot\* OR tender\* OR throb\* ) AND TITLE-ABS-KEY ( predictor\* OR "Protective factor\*" OR "risk assessment\*" OR "risk factor\*" OR prevalence OR incidence OR prognos\* OR correlati\* ) AND TITLE-ABS-KEY ( "Local An?esthetics" OR "Local An?esthesia" OR lidocaine OR lignocaine OR xylocaine OR

articain\* OR articain\* OR prilocain\* OR citanest\* OR propitocain\* OR xylenes OR bupivacain\* OR bupivacaina OR carbostesin OR solanales OR marcain\* OR sensorcain\* ) )

SciELO (Web of Science)

# 26 #24 AND #23 AND #18 AND #7 AND #6

Refined by: [excluding] WEB OF SCIENCE CATEGORIES: ( ANESTHESIOLOGY OR CRITICAL CARE MEDICINE OR PERIPHERAL VASCULAR DISEASE OR MEDICINE GENERAL INTERNAL OR MEDICINE RESEARCH EXPERIMENTAL OR PHARMACOLOGY PHARMACY OR OBSTETRICS GYNECOLOGY OR PUBLIC ENVIRONMENTAL OCCUPATIONAL HEALTH OR PEDIATRICS OR OTORHINOLARYNGOLOGY OR TOXICOLOGY )

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 25 #24 AND #23 AND #18 AND #7 AND #6

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 24 ALL=(local an?esthetic\* or local an?esthesia)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 23 #22 OR #21 OR #20 OR #19

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 22 ALL FIELDS: (Incidence)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 21 ALL FIELDS: (Prevalence)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 20 ALL FIELDS: (risk factors)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI  
Timespan=All years

# 19 ALL FIELDS: (predictor\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 18 #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9  
OR #8

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 17 ALL FIELDS: (sore\* or hurt\* or ache\* or aching or discomfort\* or  
uncomfort\* or tender\* or throb\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 16 ALL FIELDS: (intrasurgical pain\* or intra-surgical pain\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 15 ALL FIELDS: (intraoperative analgesi\* or intra-operative analgesi\* or  
intra\* analgesi\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 14 ALL FIELDS: (intraoperative pain\* or intra-operative pain\* or intra\*  
pain\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 12 ALL FIELDS: (pain\* after surg\* or pain\* after operat\* or pain\* follow\*  
operat\* or pain\* follow\* surg\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 11 ALL FIELDS: (postsurgical pain\* or post-surgical pain\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 10 ALL FIELDS: (postoperative analgesi\* or post-operative analgesi\* or  
post\* analgesi\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 9 ALL FIELDS: (postoperative pain\* or post-operative pain\* or post\* pain\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 8 ALL FIELDS: (Pain, Postoperative)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 7 ALL=(child\* or adolescent\* or kid or kids or youth\* or young\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or p?ediatric\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 6 #5 OR #4 OR #3 OR #2 OR #1

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 5 ALL FIELDS: (root canal and (therap\* or treat\* )

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 4 ALL FIELDS: (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 3 ALL FIELDS: (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*")

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 2 ALL FIELDS: (oral surg\*)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years

# 1 ALL FIELDS: (DENTISTRY)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

Timespan=All years





### Appendix 3: Meta-regression of the first systematic review

. meta regress i.proc

Effect-size label: Effect Size  
Effect size: Mean  
Std. Err.: SE

Random-effects meta-regression  
Method: REML

Number of obs = 26  
Residual heterogeneity:  
tau2 = 141.7  
I2 (%) = 95.03  
H2 = 20.14  
R-squared (%) = 0.00  
Wald chi2(7) = 8.51  
Prob > chi2 = 0.2902

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
proc					
Extraction	23.79652	9.521589	2.50	0.012	5.134551 42.45849
LA	13.84303	8.610892	1.61	0.108	-3.034003 30.72007
Drilling	19.64087	10.0207	1.96	0.050	.0006587 39.28109
Probing	9.122292	11.25526	0.81	0.418	-12.93761 31.1822
Restoration	7.962066	10.02544	0.79	0.427	-11.68743 27.61156
Scaling	5.52457	14.33336	0.39	0.700	-22.5683 33.61744
X-ray	9.221008	10.0443	0.92	0.359	-10.46545 28.90747
_cons	22.27543	7.160098	3.11	0.002	8.241895 36.30896

Test of residual homogeneity: Q\_res = chi2(18) = 369.81 Prob > Q\_res = 0.0000

.

. meta regress i.group

Effect-size label: Effect Size  
Effect size: Mean  
Std. Err.: SE

Random-effects meta-regression  
Method: REML

Number of obs = 26  
Residual heterogeneity:  
tau2 = 106.3  
I2 (%) = 94.68  
H2 = 18.81  
R-squared (%) = 10.62  
Wald chi2(2) = 5.84  
Prob > chi2 = 0.0539

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
group					
Drilling	8.034699	5.619838	1.43	0.153	-2.979982 19.04938
Extraction	11.73835	4.910152	2.39	0.017	2.114624 21.36207
_cons	28.02123	3.590326	7.80	0.000	20.98432 35.05813

Test of residual homogeneity: Q\_res = chi2(23) = 402.99 Prob > Q\_res = 0.0000

.

. meta regress i.anx

Effect-size label: Effect Size  
Effect size: Mean  
Std. Err.: SE

Random-effects meta-regression  
Method: REML

Number of obs = 19  
Residual heterogeneity:  
tau2 = 48.55  
I2 (%) = 82.52  
H2 = 5.72  
R-squared (%) = 42.90  
Wald chi2(1) = 11.61  
Prob > chi2 = 0.0007

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
anx					
High anxiety	12.31461	3.613774	3.41	0.001	5.231744 19.39748
_cons	30.72615	2.414827	12.72	0.000	25.99317 35.45912

Test of residual homogeneity: Q\_res = chi2(17) = 90.80 Prob > Q\_res = 0.0000

.

.

**Appendix 4: List of studies excluded from the first systematic review following full text article assessment showing exclusion reasons and references**

Study authors	Reasons for exclusion
(Wilson et al., 1990; Lipp et al., 1991; Wright et al., 1991; Oulis et al., 1996; Munshi et al., 2001; Touyz et al., 2004; Chomyszyn-Gajewska et al., 2006; Van Dinter et al., 2006; De Menezes Abreu et al., 2011; Naoumova et al., 2012; Peltz, 2012; Elbay et al., 2015; Sermet Elbay et al., 2016; Alzahrani et al., 2018; Hassanein et al., 2020; Monteiro et al., 2020)	Inappropriate study design
(Venham and Quatrocelli, 1977; Acs et al., 1986; Huq et al., 1992; Jalevik and Klingberg, 2002; Khatri and Kalra, 2012; Novaes et al., 2012; Ching et al., 2014; Vallakatla et al., 2020)	Inappropriate outcomes
(Jones et al., 1995; Versloot et al., 2004; De Andrade Risso et al., 2009; Mustafa et al., 2013, Ortiz et al., 2014; Almeida et al., 2016; Lamarca et al., 2018)	Missing data
(Fagade and Oginni, 2005; Vika et al., 2006; Segura-Egea et al., 2009; Tickle et al., 2012; Aggarwal et al. 2015)	Adult population
(Nakai et al., 2000; Ashkenazi et al., 2005; Ashkenazi et al., 2007; Staman et al., 2013)	Patients receiving nitrous oxide were included
(Meechan and Ledvinka, 2002; Nusstein et al., 2004; Bortoluzzi et al., 2012)	Patients over 19 years old were included
(Rantavuori et al., 2004; Rantavuori et al., 2005; Bajric et al., 2015)	Primary outcomes (pain) not measured
(Laakshmi, 2015)	Opinion paper

**Excluded studies' References**

Acs, G., Moore, P.A., Needleman, H.L. and Shusterman, S. 1986. The incidence of post-extraction pain and analgesic usage in children. *Anesthesia progress*. **33**(3), pp.147-151.

Aggarwal, V., Singla, M., Subbiya, A., Vivekanandhan, P., Sharma, V., Sharma, R., Prakash, V. and Geethapriya, N. 2015. Effect of preoperative pain on inferior alveolar nerve block. *Anesthesia Progress*. **62**(4), pp.135-139.

Almeida, G.F., Longo, D.L., Trevizan, M., de Carvalho, F.K., Nelson-Filho, P., K uchler, E.C. and Queiroz, A.M. 2016. Sex differences in pediatric dental pain perception. *Journal of Dentistry for Children*. **83**(3), pp.120-124.

Alzahrani, F., Duggal, M.S., Munyombwe, T. and Tahmassebi, J.F. 2018. Anaesthetic efficacy of 4% articaine and 2% lidocaine for extraction and pulpotomy of mandibular primary molars: an equivalence parallel prospective randomized controlled trial. *International Journal of Paediatric Dentistry*. **28**(3), pp.335-344.

Ashkenazi, M., Blumer, S. and Eli, I. 2005. Effectiveness of computerized delivery of intrasulcular anesthetic in primary molars. *The Journal of the American Dental Association*. **136**(10), pp.1418-1425.

Ashkenazi, M., Blumer, S. and Eli, I. 2007. Post-operative pain and use of analgesic agents in children following intrasulcular anaesthesia and various operative procedures. *British dental journal*. **202**(5), pp.13-16.

Bajric, E., Kobašljija, S. and Juric, H. 2015. Patients' reactions to local anaesthetic application devices in paediatric dentistry. *Collegium antropologicum*. **39**(3), pp.685-690.

Bortoluzzi, M.C., Manfro, A.R., Nodari Jr, R.J. and Presta, A.A. 2012. Predictive variables for postoperative pain after 520 consecutive dental extraction surgeries. *Gen Dent*. **60**(1), pp.58-63.

Ching, D., Finkelman, M. and Loo, C.Y. 2014. Effect of the DentalVibe injection system on pain during local anesthesia injections in adolescent patients. *Pediatric Dentistry*. **36**(1), pp.51-55.

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## Appendix 5: Search strategy for the second systematic review

MEDLINE via OVID

1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.
5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatric\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.
13. Pain, Postoperative/
14. (postoperative adj4 pain\*).ti,ab,kw.
15. (post-operative adj4 pain\*).ti,ab,kw.
16. post-operative-pain\*.ti,ab,kw.
17. (post\* adj4 pain\*).ti,ab,kw.
18. (postoperative adj4 analgesi\*).ti,ab,kw.
19. (post-operative adj4 analgesi\*).ti,ab,kw.
20. post-operative analgesi\*.ti,ab,kw.
21. (post-surgical adj4 pain\*).ti,ab,kw.
22. (post surgical adj4 pain\*).ti,ab,kw.
23. (pain\* adj4 after surg\*).ti,ab,kw.

24. (pain\* adj4 after operat\*).ti,ab,kw.
25. (pain\* adj4 follow\* operat\*).ti,ab,kw.
26. (pain\* adj4 follow\* surg\*).ti,ab,kw.
27. (pain adj1 operati\*).ti,ab,kw.
28. (intra adj procedur\* adj pain).ti,ab,kw.
29. (intraoperative adj4 pain\*).ti,ab,kw.
30. (intra-operative adj4 pain\*).ti,ab,kw.
31. intra-operative-pain\*.ti,ab,kw.
32. (intraoperative adj4 analgesi\*).ti,ab,kw.
33. (intra-operative adj4 analgesi\*).ti,ab,kw.
34. intra-operative analgesi\*.ti,ab,kw.
35. (intra-surgical adj4 pain\*).ti,ab,kw.
36. (intrasurgical adj4 pain\*).ti,ab,kw.
37. (pain\* adj4 after surg\*).ti,ab,kw.
38. (pain\* adj4 after operat\*).ti,ab,kw.
39. (pain\* adj4 follow\* operat\*).ti,ab,kw.
40. (pain\* adj4 follow\* surg\*).ti,ab,kw.
41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
46. An?esthetics, Local/
47. An?esthesia, Local/
48. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.

49. Lidocaine/
50. (lidocaine or lignocaine or xylocaine).mp.
51. Carticaine/
52. (carticain\* or articaid\*).mp.
53. Prilocaine/
54. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
55. Bupivacaine/
56. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.
57. Analgesi\*.ti,ab,kw.
58. (anti-inflammatory or nitrous oxide sedation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
59. (nonsteroidal anti-inflammatory agent\* or anti inflammatory agent\* or nonsteroidal antiinflammatory agent\* or non steroidal antiinflammatory agent\* or Nonsteroidal analgesic\* or anti-inflammator\* or aspirin-like agent\* or NSAID\*).ti,ab,kw.
60. (ibuprofen or brufen).ti,ab,kw.
61. (acetaminophen or paracetamol).ti,ab,kw.
62. pain management/
63. (pain adj3 management).tw.
64. psychotherapy/
65. psychotherap\*.tw.
66. behavior therapy/
67. (behavi?r adj3 therap\*).tw.
68. cognitive therapy/
69. (cognitive adj3 therap\*).tw.
70. (relax\* adj3 (technique\* or therap\*)).tw.
71. exp mind body therapies/

72. guided imagery.tw.
73. "imagery (Psychotherapy)"/
74. mindfulness.tw.
75. (distraction adj3 therap\*).tw.
76. self regulation training.tw.
77. 1 or 2 or 3 or 4 or 5 or 6
78. 7 or 8 or 9 or 10 or 11 or 12
79. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25  
or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38  
or 39 or 40 or 41 or 42 or 43 or 44 or 45
80. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56
81. 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69  
or 70 or 71 or 72 or 73 or 74 or 75 or 76
82. 77 and 78 and 79 and 80 and 81

#### EMBASE via OVID

1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.
5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or  
"cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or  
minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or  
"young person" or "young people" or p?ediatric\* or student\* or pupil or pupils

or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.

13. Pain, Postoperative/

14. (postoperative adj4 pain\*).ti,ab,kw.

15. (post-operative adj4 pain\*).ti,ab,kw.

16. post-operative-pain\*.ti,ab,kw.

17. (post\* adj4 pain\*).ti,ab,kw.

18. (postoperative adj4 analgesi\*).ti,ab,kw.

19. (post-operative adj4 analgesi\*).ti,ab,kw.

20. post-operative analgesi\*.ti,ab,kw.

21. (post-surgical adj4 pain\*).ti,ab,kw.

22. (post surgical adj4 pain\*).ti,ab,kw.

23. (pain\* adj4 after surg\*).ti,ab,kw.

24. (pain\* adj4 after operat\*).ti,ab,kw.

25. (pain\* adj4 follow\* operat\*).ti,ab,kw.

26. (pain\* adj4 follow\* surg\*).ti,ab,kw.

27. (pain adj1 operati\*).ti,ab,kw.

28. (intra adj procedur\* adj pain).ti,ab,kw.

29. (intraoperative adj4 pain\*).ti,ab,kw.

30. (intra-operative adj4 pain\*).ti,ab,kw.

31. intra-operative-pain\*.ti,ab,kw.

32. (intraoperative adj4 analgesi\*).ti,ab,kw.

33. (intra-operative adj4 analgesi\*).ti,ab,kw.

34. intra-operative analgesi\*.ti,ab,kw.

35. (intra-surgical adj4 pain\*).ti,ab,kw.

36. (intrasurgical adj4 pain\*).ti,ab,kw.

37. (pain\* adj4 after surg\*).ti,ab,kw.

38. (pain\* adj4 after operat\*).ti,ab,kw.

39. (pain\* adj4 follow\* operat\*).ti,ab,kw.

40. (pain\* adj4 follow\* surg\*).ti,ab,kw.

41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
46. An?esthetics, Local/
47. An?esthesia, Local/
48. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.
49. Lidocaine/
50. (lidocaine or lignocaine or xylocaine).mp.
51. Carticaine/
52. (carticain\* or articain\*).mp.
53. Prilocaine/
54. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
55. Bupivacaine/
56. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.
57. Analgesi\*.ti,ab,kw.
58. (anti-inflammatory or nitrous oxide sedation).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
59. (nonsteroidal anti-inflammatory agent\* or anti inflammatory agent\* or nonsteroidal antiinflammatory agent\* or non steroidal antiinflammatory agent\* or Nonsteroidal analgesic\* or anti-inflammator\* or aspirin-like agent\* or NSAID\*).ti,ab,kw.
60. (ibuprofen or brufen).ti,ab,kw.
61. (acetaminophen or paracetamol).ti,ab,kw.



62. pain management/
63. (pain adj3 management).tw.
64. psychotherapy/
65. psychotherap\*.tw.
66. behavior therapy/
67. (behavi?r adj3 therap\*).tw.
68. cognitive therapy/
69. (cognitive adj3 therap\*).tw.
70. (relax\* adj3 (technique\* or therap\*)).tw.
71. exp mind body therapies/
72. guided imagery.tw.
73. "imagery (Psychotherapy)"/
74. mindfulness.tw.
75. (distraction adj3 therap\*).tw.
76. self regulation training.tw.
77. 1 or 2 or 3 or 4 or 5 or 6
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or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38  
or 39 or 40 or 41 or 42 or 43 or 44 or 45
80. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56
81. 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69  
or 70 or 71 or 72 or 73 or 74 or 75 or 76
82. 77 and 78 and 79 and 80 and 81

#### PsycINFO via OVID

1. exp Dentistry/
2. (dental\* or dentist\*).ti,ab.
3. (oral adj5 surg\*).ti,ab.
4. (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*").mp.

5. ((dental or tooth or teeth) adj5 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)).mp.
6. (root canal and (therap\* or treat\*)).mp.
7. child/
8. Infant/
9. adolescent/
10. Pediatrics/
11. Dental care for children/
12. (child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatric\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage).ti,ab,kw.
13. Pain, Postoperative/
14. (postoperative adj4 pain\*).ti,ab,kw.
15. (post-operative adj4 pain\*).ti,ab,kw.
16. post-operative-pain\*.ti,ab,kw.
17. (post\* adj4 pain\*).ti,ab,kw.
18. (postoperative adj4 analgesi\*).ti,ab,kw.
19. (post-operative adj4 analgesi\*).ti,ab,kw.
20. post-operative analgesi\*.ti,ab,kw.
21. (post-surgical adj4 pain\*).ti,ab,kw.
22. (post surgical adj4 pain\*).ti,ab,kw.
23. (pain\* adj4 after surg\*).ti,ab,kw.
24. (pain\* adj4 after operat\*).ti,ab,kw.
25. (pain\* adj4 follow\* operat\*).ti,ab,kw.
26. (pain\* adj4 follow\* surg\*).ti,ab,kw.
27. (pain adj1 operati\*).ti,ab,kw.
28. (intra adj procedur\* adj pain).ti,ab,kw.
29. (intraoperative adj4 pain\*).ti,ab,kw.
30. (intra-operative adj4 pain\*).ti,ab,kw.

31. intra-operative-pain\*.ti,ab,kw.
32. (intraoperative adj4 analgesi\*).ti,ab,kw.
33. (intra-operative adj4 analgesi\*).ti,ab,kw.
34. intra-operative analgesi\*.ti,ab,kw.
35. (intra-surgical adj4 pain\*).ti,ab,kw.
36. (intrasurgical adj4 pain\*).ti,ab,kw.
37. (pain\* adj4 after surg\*).ti,ab,kw.
38. (pain\* adj4 after operat\*).ti,ab,kw.
39. (pain\* adj4 follow\* operat\*).ti,ab,kw.
40. (pain\* adj4 follow\* surg\*).ti,ab,kw.
41. (surg\* adj1 pain).ti,ab,kw.
42. (("post surg\*" or post-surg\*) and (pain\* or discomfort)).ti,ab,kw.
43. (analgesi\* adj4 surg\*).ti,ab,kw.
44. (analgesi\* adj4 operat\*).ti,ab,kw.
45. (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfot\* or tender\* or throb\*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh]
46. An?esthetics, Local/
47. An?esthesia, Local/
48. (local adj5 (anesthetic\* or anaesthetic\* or anesthesia or anaesthesia)).mp.
49. Lidocaine/
50. (lidocaine or lignocaine or xylocaine).mp.
51. Carticaine/
52. (carticain\* or articain\*).mp.
53. Prilocaine/
54. (prilocain\* or citanest\* or propitocain\* or xylonest).mp.
55. Bupivacaine/
56. (bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*).mp.

57. Analgesi\*.ti,ab,kw.
58. (anti-inflammatory or nitrous oxide sedation).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh]
59. (nonsteroidal anti-inflammatory agent\* or anti inflammatory agent\* or nonsteroidal antiinflammatory agent\* or non steroidal antiinflammatory agent\* or Nonsteroidal analgesic\* or anti-inflammator\* or aspirin-like agent\* or NSAID\*).ti,ab,kw.
60. (ibuprofen or brufen).ti,ab,kw.
61. (acetaminophen or paracetamol).ti,ab,kw.
62. pain management/
63. (pain adj3 management).tw.
64. psychotherapy/
65. psychotherap\*.tw.
66. behavior therapy/
67. (behavi?r adj3 therap\*).tw.
68. cognitive therapy/
69. (cognitive adj3 therap\*).tw.
70. (relax\* adj3 (technique\* or therap\*)).tw.
71. exp mind body therapies/
72. guided imagery.tw.
73. "imagery (Psychotherapy)"/
74. mindfulness.tw.
75. (distraction adj3 therap\*).tw.
76. self regulation training.tw.
77. 1 or 2 or 3 or 4 or 5 or 6
78. 7 or 8 or 9 or 10 or 11 or 12
79. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
80. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56

81. 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76

82. 77 and 78 and 79 and 80 and 81

Cochrane Library (Wiley)

#1 DENTISTRY

#2 dental\* or dentist\*

#3 oral surg\*

#4 orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*"

#5 fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*

#6 root canal and (therap\* or treat\*)

#7 #1 or #2 or #3 or #4 or #5 or #6

#8 child

#9 Infant

#10 adolescent

#11 Pediatric\* or paediatric\*

#12 Dental care for children

#13 child\* or adolescent\* or kid or kids or youth\* or youngster\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or "young adult\*" or "young person" or "young people" or p?ediatric\* or student\* or pupil or pupils or boy or boys or girl or girls or under 18\* or under eighteen\* or underage

#14 #8 or #9 or #10 or #11 or #12 or #13

#15 Pain, Postoperative

#16 postoperative pain\* or post-operative pain\* or post\* pain\*

#17 postoperative analgesi\* or post-operative analgesi\* or post\* analgesi\*

#18 postsurgical pain\* or post-surgical pain\*

#19 pain\* after surg\* or pain\* after operat\* or pain\* follow\* operat\* or pain\* follow\* surg\*

#20 Pain, intraoperative

#21 intraoperative pain\* or intra-operative pain\* or intra\* pain\*

- #22 intraoperative analgesi\* or intra-operative analgesi\* or intra\* analgesi\*
- #23 intrasurgical pain\* or intra-surgical pain\*
- #24 sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*
- #25 #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
- #26 Analgesi\* or anti-inflammatory or nitrous oxide sedation
- #27 nonsteroidal anti-inflammatory agent\* or anti inflammatory agent\* or nonsteroidal antiinflammatory agent\* or non steroidal antiinflammatory agent\* or Nonsteroidal analgesic\* or anti-inflammator\* or aspirin-like agent\* or NSAID\*
- #28 ibuprofen or brufen or acetaminophen or paracetamol
- #29 pain management
- #30 psychotherap\*
- #31 behavior therap\* or cognitive therap\* or mind body therap\*
- #32 #26 or #27 or #28 or #29 or #30 or #31
- #33 local anesthetic\* or local anaesthetic\* or local anesthesia or local anaesthesia
- #34 lidocain\* or lignocain\* or xylocain\* or carticain\* or articain\* or prilocain\* or citanest\* or propitocain\* or xylonest or bupivacain\* or buvacaina or carbostesin or dolanaest or marcain\* or sensorcain\* or svedocain\*
- #35 #33 or #34
- #36 #7 and #14 and #25 and #32 and #35

WHO International Clinical Trials Registry Platform

sed\* or analgesi\* or behavio?r management or behavio?r therapy and child\* and dental

Clinical Trials.gov

Keywords: child and dental

Interventions: analgesics

Keywords: child and dental

Interventions: sedation

Keywords: child and dental

Interventions: behaviour management

Pubmed (Randomized Controlled Trial)

(((((Dentistry or oral surg\* or orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*" or fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\* or root canal and (therap\* or treat\*)) AND (child\* or adolescent\* or kid or kids or youth\* or young\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or p?ediatric\*)) AND (postoperative pain\* or post-operative pain\* or post\* pain\* or postoperative analgesi\* or post-operative analgesi\* or post\* analgesi\* or postsurgical pain\* or post-surgical pain\* or pain\* after surg\* or pain\* after operat\* or pain\* follow\* operat\* or pain\* follow\* surg\* or intraoperative pain\* or intra-operative pain\* or intra\* pain\* or intraoperative analgesi\* or intra-operative analgesi\* or intra\* analgesi\* or intrasurgical pain\* or intra-surgical pain\* or sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfot\* or tender\* or throb\*)) AND (Analgesi\* or anti-inflammatory or nitrous oxide sedation or nonsteroidal anti-inflammatory agent\* or anti inflammatory agent\* or nonsteroidal antiinflammatory agent\* or non steroidal antiinflammatory agent\* or Nonsteroidal analgesic\* or anti-inflammator\* or aspirin-like agent\* or NSAID\* or ibuprofen or brufen or acetaminophen or paracetamol or pain management or psychotherap\* or behavior therap\* or cognitive therap\* or mind body therap\*)) AND (Local anesthetic\* OR local anaesthetic\* OR local anesthesia OR local anaesthesia OR lidocain\* OR lignocain\* OR xylocain\* OR carticain\* OR articain\* OR prilocain\* OR citanest\* OR propitocain\* OR xylonest OR bupivacain\* OR buvacaina OR carbostesin OR dolanaest OR marcain\* OR sensorcain\* OR svedocain\*))

Web of Science

#1 (DENTISTRY)

#2 (oral surg\*

#3 (orthodontic\* or pulpotom\* or pulpect\* or endodont\* or "pulp cap\*")

#4 (fill\* or restor\* or extract\* or remov\* or "cavity prep\*" or caries or carious or decay\*)

#5 (root canal and (therap\* or treat\* )

#6 #5 OR #4 OR #3 OR #2 OR #1

#7(child\* or adolescent\* or kid or kids or youth\* or young\* or minor or minors or teen\* or preteen\* or pre-teen\* or juvenile\* or p?ediatric\*

#8 (Pain, Postoperative)

#9 (postoperative pain\* or post-operative pain\* or post\* pain\*)

#10 (postoperative analgesi\* or post-operative analgesi\* or post\* analgesi\*)

#11 (postsurgical pain\* or post-surgical pain\*)

#12 (pain\* after surg\* or pain\* after operat\* or pain\* follow\* operat\* or pain\* follow\* surg\*)

#13 (Pain, intraoperative)

#14 (intraoperative pain\* or intra-operative pain\* or intra\* pain\*)

#15 (intraoperative analgesi\* or intra-operative analgesi\* or intra\* analgesi\*)

#16 (intrasurgical pain\* or intra-surgical pain\*)

#17 (sore\* or hurt\* or ache\* or aching or discomfort\* or uncomfort\* or tender\* or throb\*)

#18 #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8

#19 (Analgesi\* or anti-inflammatory or nitrous oxide sedation)

#20 (nonsteroidal anti -inflammatory agent\* or anti-inflammatory agent\* or nonsteroidal antiinflammatory agent\* or non steroidal antiinflammatory agent\* or Nonsteroidal analgesic\* or anti-inflammator\* or aspirin-like agent\* or NSAID\*)

#21 (ibuprofen or brufen or acetaminophen or paracetamol)

#22(pain management or psychotherap\* or behavior therap\* or cognitive therap\* or mind body therap\*)

#23 #22 OR #21 OR #20 OR #19

#24 (local an?esthetic\* or local an?esthesia)

#25 #24 AND #23 AND #18 AND #7 AND #6









AutoSave OFF Intra-op pain (Behavioural Interventions)

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B36

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	Study ID	Procedure	Intervention Group	Mean of Intervention	SD of Intervention	N of Intervention	SE	Control Group	Mean of Control	SD of Control	N of Control	SE	Pain Scale
2	Tung 2018	IA	Manual stimulation	2.76	2.5	50	0.353553391	No stimulation	3.56	2.9	50	0.4101219	Wong-Baker FACES 0-10
4	Al-Halabi 2018	IA	IANB with AV eyeglasses 'VR Box' and wireless headphon	0.75	0.98	33	0.170596103	IANB with basic behaviour guidance techniques and without distraction aids	0.71	0.86	34	0.1474888	Wong-Baker PRS 0-5
5	Al-Halabi 2018	IA	IANB with tablet device and wireless headphon	0.94	1.25	34	0.214373231	IANB with basic behaviour guidance techniques and without distraction aids	0.71	0.86	34	0.1474888	Wong-Baker PRS 0-5
7	Agarwal 2017 (EMLA cream)	IA	EMLA cream group with AV aids	4.73	1.14	30	0.208134572	EMLA cream group without AV aids	5.7	0.93	30	0.169794	VAS 0-10
8	Agarwal 2017 (Benzocaine gel)	IA	Benzocaine gel with AV aids	5.86	0.78	30	0.142407865	Benzocaine gel without AV aids	7.36	0.72	30	0.1314534	VAS 0-10
10	Ramirez-Carrasco 2017	IA	Hypnosis intervention	2.65	2.81	20	0.628335102	Without hypnosis	2.1	2.44	20	0.5456006	FLACC 0-10
12	Obadiah 2020	IA	Bubble toy	1.47	0.63	30	0.115021737	Without bubble toy	2.41	0.52	30	0.0949386	Wong-Baker FACES 0-10
14	Sridhar 2019	IA	The bubble breath exercise	1.51	0.67	33	0.116632029	Without the bubble breath exercise	2.45	0.56	33	0.0974835	Wong-Baker FACES 0-10
16	Attar 2015	IA	Treatment with the aid of an iPad	1.95	1.68	39	0.269015298	Treatment with the aid of AV glasses	2.56	2.15	39	0.3442755	Wong-Baker faces 0-3
17	Attar 2015	Clamp place	Treatment with the aid of an iPad	1.49	1.98	39	0.317053745	Treatment with the aid of AV glasses	2.1	1.99	39	0.318655	Wong-Baker faces 0-3
18	Attar 2015	Drilling	Treatment with the aid of an iPad	0.51	1.43	39	0.22898326	Treatment with the aid of AV glasses	0.97	1.51	39	0.2417935	Wong-Baker faces 0-3
20	Garrocho-Rangel 2018	IA	With video Eyeglasses/Earphones Systems (VEES)	1.64	2.9	36	0.483333333	Without video Eyeglasses/Earphones Systems (VEES)	1.64	2.1	36	0.35	FLACC 0-10
21	Garrocho-Rangel 2018	Clamp place	With video Eyeglasses/Earphones Systems (VEES)	1.78	2.93	36	0.488333333	Without video Eyeglasses/Earphones Systems (VEES)	1.36	1.45	36	0.2416667	FLACC 0-10
22	Garrocho-Rangel 2018	Drilling	With video Eyeglasses/Earphones Systems (VEES)	1.03	2.21	36	0.368333333	Without video Eyeglasses/Earphones Systems (VEES)	0.64	1.31	36	0.2183333	FLACC 0-10
24	Abdelmoniem 2016	IA	Active distraction	3.33	3.73	30	0.681001713	Passive distraction	2.07	2.7	30	0.4929503	Wong-Baker FACES 0-10
25	Abdelmoniem 2016	IA	Passive-active distractio	1.67	2.93	30	0.534942364	Passive distraction	2.07	2.7	30	0.4929503	Wong-Baker FACES 0-10
27	Huet 2011	IA	Hypnosis	1.07	1.05	14	0.280624304	Without hypnosis	2.86	2.16	15	0.5577096	Modified objective pain score (mOPS) 0-10
29	Vidigal 2021	IA	Tell-Show-Do Technique (TSD-T)	1.35	1.65	26	0.323591623	Hiding Dental-Needle Technique (HDN-T)	1.23	1.17	26	0.2294559	Wong-Baker FACES 1-5
31	Kamath 2013 (children aged 4-5 years old)	IA	Writing In The Air Using Leg	2.46	1.75	28	0.330718914	Deep breathing	5.64	2.33	28	0.4403286	TPPPS 0-10
32	Kamath 2013 (children aged 6-10 years old)	IA	Writing In The Air Using Leg	3	1.75	52	0.242681336	Deep breathing	6.26	1.86	52	0.2579356	FPS- R 0-10
34	Avanund 2015	IA	Audio-visual (AV) eyeglasses	2.23	2.29	49	0.327142857	without audio-visual (AV) eyeglasses	3.04	3.08	49	0.44	FPS- R 0-10





**Appendix 7: List of studies excluded from the second systematic review following full text article assessment showing exclusion reasons and references**

Study authors	Reasons for exclusion
(Primosch et al., 1993; Primosch et al., 1995; Gibson et al., 2000; Allen et al., 2002; Aminabadi et al., 2008; Aminabadi et al., 2009; Koyuturk et al., 2009; Tahmassebi et al., 2009; Yassen, 2010; Baygin et al., 2011; Arrow, 2012; Kandiah and Tahmassebi, 2012; Lee and Lee, 2013; Elbay et al., 2015; Takkar et al., 2015; Mony et al., 2016; Usichenko et al., 2016; Alzahrani et al., 2018; Kurien et al., 2018; Chompu-Inwai et al., 2018; Abou El Fadl et al., 2019; Kharouba et al., 2019; Altan et al., 2021; Muzumdar et al., 2021; Shekarchi et al., 2022)	Missing data
(Wilson et al., 1986; Lokken et al., 1994; Roelofse et al., 1996; Wilson et al., 2002; Ran and Peretz, 2003; Van Bochove, and Amerongen, 2006; Wilson et al., 2006; Bhananker et al., 2008; Ram et al., 2010; Chan et al 2012; Calis et al., 2014; Jalevik and Klingberg, 2014; Priya et al., 2014; Sheta et al., 2014)	Inappropriate sitting
(Clark et al., 1987; Penniston and Hargreaves, 1996; Meechan et al., 1998; Lindemann et al., 2008; Parirokh et al., 2010; Prasanna et al., 2011; Singh and Garg, 2013; Kammerer et al., 2015; Yadav et al., 2015; Wolf et al., 2016; Shadmehr et al., 2017; Kumar et al., 2020)	Adult population
(Roelofse et al., 1998; Lozano-Chourio et al., 2006; Hjertton and Bagesund, 2013; Moreira et al., 2013; Ujaoney et al., 2013; Al-Namankany et al., 2014; Paryab and Arab 2014; Al-Khotani et al., 2016; Oberoi et al., 2016; Shahnavaz et al., 2016; Perugia et al., 2017; Zeitoun et al., 2020; Padminiee et al., 2022)	Primary outcomes (pain) not measured
(Nadanovsky et al., 2001; Al-Kahtani, 2014; Bultema et al., 2016; Gazal and Al-Samadani, 2017; Al-Shayyab, 2017; Bansal et al., 2018; Singh et al., 2018; Suzuki et al., 2018)	Patients over 19 years old were included
(Joris, 1996; Burke, 1997; Asarch et al., 1999; Tate and Acs, 2002; Thakare et al., 2014; Muthu Laakshmi, 2015; Mohiuddin et al., 2015; Baillargeau et al., 2020; Iyengar et al., 2021; Prathyusha et al., 2021; Alshatrat et al., 2022)	Inappropriate study design
(Peric et al., 2009; Yilmaz et al., 2011; Ram et al., 2012; Nieuwenhuizen et al., 2013; Shavit et al., 2017)	Inappropriate outcomes
(NCT04226651; NCT03445182; TCTR20200609003; RBR-93djd9; Irct20191015045116N; Irct2017101036699N; RBR-3t597f; NCT04629924; CTRI/2018/05/014298; ISRCTN98093105; TCTR20201002008; CTRI/2011/091/000169; IRCT2015022221177N1; NCT02591797; NCT03902158; NCT03885271; NCT03908489; NCT04886141; PACTR202105602764595)	Study not complete

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## Appendix 8: Characteristics of included studies of the second systematic review

Agarwal 2017

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: India  Setting: Department of Paedodontics and Preventive Dentistry, Institute of Dental Studies and Technologies	
<b>Participants</b>	Children requiring local anaesthesia for the dental treatment  Sample size: 120  Age: 3-14 years old  Mean age: 8.8 years old	
<b>Interventions</b>	Group A: EMLA (lidocaine 2.5% and prilocaine 2.5%) cream group without Audio Visual (AV) aids (n=30)  Group B: EMLA cream group with AV aids (n=30)  Group C: Benzocaine (20%) gel without AV aids (n=30)  Group D: Benzocaine gel with AV aids (n=30)  Sony Vaio laptop with earphones used as AV aids and DVD used were nursery rhymes and cartoon movies	
<b>Outcomes</b>	Pain during LA: 0-10 Visual Analogue Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind

<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Santos 2020

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Brazil  Setting: The Pediatric Postgraduate Clinic of Federal University of Santa Catarina	
<b>Participants</b>	Children requiring extraction of primary molars  Sample size: 48  Age: 5-10 years old  Mean age: 7.17 years old	
<b>Interventions</b>	Group A (Control): received placebo solution 1 hour before LA (n=16) Group B: received paracetamol 200 mg/mL 1 hour before LA (n=16) Group C: received ibuprofen 100 mg/mL 1 hour before LA (n=16) All analgesics were taken orally	
<b>Outcomes</b>	Pain after extraction at 2, 6, 24 hours: 0-100 Visual Analogue Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A randomised block design with permuted blocks of 4 and 6 patients each was used
<b>Allocation concealment</b>	Low risk	"Allocation was concealed with a pre-specified computer-generated randomization list, placed in numbered opaque sealed envelopes by a person not involved on the research"
<b>Blinding of participants and personnel for</b>	Low risk	Participants and operator were blind

<b>all outcomes</b>		
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The trial authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Ramirez-Carrasco 2017

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Mexico  Setting: The Pediatric Dentistry Clinic at the Autonomous University of San Luis Potos	
<b>Participants</b>	Children requiring local anaesthesia for the dental treatment for the first time  Sample size: 40  Age: 5-9 years old  Mean age: 7.5 years old	
<b>Interventions</b>	Group A (Control): children were told to use headphones to block out the dental drill's noise. No sound was transmitted (n=20).  Group B (Case): children were listed to a classic directive hypnosis intervention (n=20).	
<b>Outcomes</b>	Pain during LA: 0-10 Face, Legs, Activity, Cry, Consolability scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly assigned
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Versloot 2008

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Netherlands  Setting: Secondary dental care practice specialised in treating children	
<b>Participants</b>	Children requiring local anaesthesia for two subsequent treatment sessions  Sample size: 147  Age: 4-11 years old  Mean age: 6.4 years old	
<b>Interventions</b>	Group A (Control): received traditional syringe injection via infiltration for maxillary teeth and IANB for mandibular teeth (N=76)  Group B (Case): received Wand injection via infiltration for maxillary teeth and periodontal ligament for mandibular teeth (N=71)	
<b>Outcomes</b>	Pain during LA: 0-10 Modified version of the visual analogue scale  Anxiety during dental treatment: 1-5 the Dental Subscale of the Children's Fear Survey Schedule CFSS-DS	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	Randomisation list generated by SPSS (SPSS Inc, 12.0, Chicago, USA)
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported

<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	All treatments were videotaped and analysed by two independent observers
<b>Incomplete outcome data for all outcomes</b>	Unclear risk	"For 20 children only their first treatment session could be included due to rescheduling of the second appointment"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Obadiah 2020

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: India  Setting: Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical sciences, Saveetha University	
<b>Participants</b>	Children requiring local anaesthesia for extraction or pulpotomy  Sample size: 60  Age: 4-13 years old  Mean age: 8.43 years old	
<b>Interventions</b>	Group A (Case): Children were provided with the Bubble toy and deep breathing exercise was taught to the children (n=30)  Group B (Control): children were not taught about this breathing exercise and were not provided with any soap solutions (n=30)	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale  Anxiety at dental examination and during LA: 1-5 the Facial Index Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>



<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Method of allocation concealment was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Baghdadi 1999

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Crossover</p> <p>Location: Syria</p> <p>Setting: Department of Pediatric Dentistry, Damascus University</p>
<b>Participants</b>	<p>Children requiring local anaesthesia for restoring of two primary/permanent antimere molars with lesions of similar size</p> <p>Sample size: 28</p> <p>Age: 6-12 years old</p> <p>Mean age: 10.21 years old</p>
<b>Interventions</b>	<p>Group A (Control): received conventional LA (2% lidocaine with 1:80,000 epinephrine and restoration</p> <p>Group B (Experimental): received Electronic dental anaesthesia (EDA) and restoration</p> <p>EDA is a device that provides anaesthesia but with no needles and injections and it works on the gate control theory of pain</p>
<b>Outcomes</b>	Pain during stages of restoration: 0-3 the Sound, Eye, and Motor (SEM) scale and 0-3 Color Scale

<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly divided
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Smolarek 2020

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Parallel groups</p> <p>Location: Brazil</p> <p>Setting: The dental practice office at an elementary school called Integral Care Centre for Child and Adolescent and paediatric dental clinics from the Department of Dentistry at Ponta Grossa State University (UEPG), Ponta Grossa, Parana</p>
<b>Participants</b>	<p>Children requiring local anaesthesia for restoring of the upper posterior teeth</p> <p>Sample size: 105</p> <p>Age: 5-8 years old Mean age: 6.56 years old</p>
<b>Interventions</b>	<p>Group A: received conventional anaesthesia (CA) (n=35)</p> <p>Group B: received vibrational anaesthesia (VBA) using DentalVibe (n=35)</p> <p>Group C: received computer-controlled local anaesthesia delivery (CCLAD) (n=35)</p>
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES, 0-10 Visual Analogue Scales for pain

	Anxiety before treatment, at dental office and immediately after LA: 0-8 The Venham Picture Test modified (VPTm) Scale	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation	Low risk	Computer-generated tables with blocked randomisation were used
Allocation concealment	Low risk	"accomplished by distributing the obtained codes in numbered black opaque envelopes"
Blinding of participants and personnel for all outcomes	Low risk	It was not possible to blind the operators/participants to the intervention
Blinding of outcome assessors for all outcomes	Unclear risk	It is unclear whether assessors were blind
Incomplete outcome data for all outcomes	Low risk	The authors evaluated all included participants
Selective outcome reporting	Low risk	The authors reported all expected outcomes
Other sources of bias	Low risk	No other bias

Massignan 2020

Characteristics of included studies	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Brazil  Setting: Pediatric Postgraduate Clinic of Federal University of Santa Catarina
<b>Participants</b>	Children requiring local anaesthesia for extraction of primary molars  Sample size: 43  Age: 6-10 years old  Mean age: 7.42 years old
<b>Interventions</b>	Group A (Control): received lidocaine 2% by infiltration (n=22)  Group B (Intervention): received articaine 4% by infiltration (n=21)

<b>Outcomes</b>	Pain after extraction at 2 and 6 hours: 0-10 the Faces Pain Scale-Revised (FPS-R)	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	"The randomisation sequence was generated using WebSite Randomization.com ( <a href="http://www.randomization.com">http://www.randomization.com</a> )"
<b>Allocation concealment</b>	Low risk	sequentially numbered, opaque, sealed envelopes were considered
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	Participant and the clinician were blind
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Smail-Faugeron 2019

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups and Split mouth  Location: France  Setting: Paediatric dentistry departments of three French universities (Nice, Paris and Rennes)
<b>Participants</b>	Children requiring local anaesthesia for restoring of 1st permanent molars  Sample size: 158  Age: 7-15 years old  Mean age: 9 years old for split mouth and 10.4 years old for parallel groups
<b>Interventions</b>	Split mouth RCT: one permanent first molar was randomly allocated to the intraosseous anaesthesia (IOA) and the other permanent first molar belonging to the

	same dental arch in the same child was allocated to the conventional infiltration anaesthesia (CIA) (n=30).	
	Parallel-arm RCT: one patient with one permanent molar first was randomly allocated to one of the techniques (IOA or CIA) (n=128).	
<b>Outcomes</b>	Pain during LA and restoration: 0-10 Visual Analogue Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A computer-generated, permuted-block randomisation sequence, with two block sizes randomly varied were used
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	Participants were blind but it was not possible to blind clinicians to the intervention.
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Alanazi 2019

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover  Location: Saudi Arabia  Setting: Department of Paediatric Dentistry, Riyadh Elm University
<b>Participants</b>	Children requiring bilateral maxillary buccal infiltration analgesia for the dental treatment in the posterior teeth  Sample size: 60  Age: 6-7 years old  Mean age: 6.57 years old

<b>Interventions</b>	Group A (Control): received traditional LA via maxillary buccal infiltration	
	Group B (Test): received traditional LA via maxillary buccal infiltration and the cold and vibration device (Buzzing device as distraction)	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly divided
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessor was not blind to the treatment
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Versloot 2005

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Netherlands  Setting: A specialist clinic
<b>Participants</b>	Children requiring local anaesthesia for the dental treatment  Sample size: 125  Age: 4-11 years old  Mean age: 6.2 years old
<b>Interventions</b>	Group A: received traditional LA via infiltration for maxillary teeth and IANB for mandibular teeth (n=58)

	Group B: received Wand LA via infiltration for maxillary teeth and periodontal ligament for mandibular teeth (n=67)	
<b>Outcomes</b>	Pain during LA: 0-10 Modified version of the visual analogue scale  Anxiety during dental treatment: 1-5 the Dental Subscale of the Children's Fear Survey Schedule CFSS-DS	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A randomisation list generated by SPSS (SPSS, 11.0; Chicago, IL, USA) was used
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	"All treatments were videotaped and analysed by two independent observers"
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Arcari 2018

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Italy  Setting: Two private practice dental offices
<b>Participants</b>	Children requiring local anaesthesia for restoring of primary molars (class I/ II)  Sample size: 90  Age: 3-10 years old  Mean age: 6.2 years old
<b>Interventions</b>	Group A (Control): received nitrous oxide-oxygen (40% N <sub>2</sub> O and 60% O <sub>2</sub> ) relative analgesia and LA (n=42)

	Group B (Study): received nitrous oxide-oxygen (40% N <sub>2</sub> O and 60% O <sub>2</sub> ) relative analgesia (n=48)	
<b>Outcomes</b>	Pain during restoration: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly assigned
<b>Allocation concealment</b>	Unclear risk	Method of allocation concealment not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessors were not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Baghlaf 2015

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Saudi Arabia  Setting: The pediatric dentistry specialty clinics, King Abdulaziz University
<b>Participants</b>	Children requiring local anaesthesia for pulpotomy of primary mandibular 2nd molars  Sample size: 91  Age: 5-9 years old  Mean age: Not reported
<b>Interventions</b>	Group A: received traditional IANB (Inferior alveolar nerve block) (n=31)  Group B: received IANB with a CCLAD (Inferior alveolar nerve block with computer-controlled local anaesthetic delivery (CCLAD IANB)) (n=30)



	Group C: received ILA with a CCLAD STA system (Intraligamental anaesthesia with computer-controlled local anesthetic delivery (CCLAD interligamental)) (n=30)	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly assigned using a block randomisation technique
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessors were not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "nine participants were excluded due to failure of the anaesthesia technique, or uncontrolled bleeding of the pulp, extraction or they refused to apply the rubber dam"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Sridhar 2019

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: India  Setting: The Department of Paedodontics and Preventive Dentistry
<b>Participants</b>	Children requiring maxillary buccal infiltration anaesthesia for dental treatment  Sample size: 66  Age: 7-11 years old  Mean age: 8.75 years old
<b>Interventions</b>	Group A (control): not used the bubble breath exercise (n=33)

	Group B: used the bubble breath exercise (n=33)	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale  Anxiety at the 1st appointment before dental examination and the 2nd appointment before local anaesthesia: 1-5 the Facial Image Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	"Block randomization method with a block size of four was used"
<b>Allocation concealment</b>	Low risk	"The treatment group codes so generated (A or B) were entered into cards and placed in envelopes that were sequentially numbered. The envelopes were rendered opaque by covering the cards with aluminium foil and then sealed"
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessors were not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Attar 2015

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Split mouth  Location: Saudi Arabia  Setting: The paediatric clinic in the Department of Preventive Dentistry Riyadh Colleges of Dentistry and Pharmacy
<b>Participants</b>	Children requiring local anaesthesia for pulpotomy of two primary antimere molars  Sample size: 39  Age: 4-8 years old

	Mean age: 6.27 years old	
<b>Interventions</b>	Group A (Control): received treatment with the aid of audio-visual (AV) glasses	
	Group B (Exposure): received treatment with the aid of an iPad video game	
<b>Outcomes</b>	Pain at 5 mins before LA, during LA and stages of pulpotomy and 5 mins post-operatively: 0-3 Wong-Baker FACES scale	
	Anxiety before dental treatment: 1-5 The Modified Dental Anxiety Scale (MDAS)	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Atabek 2015

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover
	Location: Turkey
	Setting: The Department of Pedodontics, Faculty of Dentistry, Gazi University
<b>Participants</b>	Children requiring bilateral maxillary infiltration anaesthesia for restoring maxillary primary molars
	Sample size: 50
	Age: 8-12 years old

	Mean age: 9 years old	
<b>Interventions</b>	Group A (Control): received topical anaesthetic solution of 10 % lidocaine pump spray  Group B (Case): received three-in-one injection comfort system (ICS) which provides tissue retraction, illumination of the area, and pain blockage	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Randomisation method was not reported
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Dak-Albab 2016

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover  Location: Syria  Setting: Pediatric Dentistry department in the Dental College, Damascus University
<b>Participants</b>	Children requiring two mandibular nerve block analgesia for symmetric dental treatment  Sample size: 30  Age: 8-12 years old  Mean age: Not reported

<b>Interventions</b>	Technique A: received benzocaine 20% topical gel and LA	
	Technique B: received vibration using DentalVibe and LA	
<b>Outcomes</b>	Pain during LA: 0-10 Face, Legs, Activity, Cry, Consolability scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Ram 2006

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover
	Location: Israel
	Setting: Two established paediatric dental clinics in Jerusalem and Tel Aviv
<b>Participants</b>	Children requiring two local analgesia for similar operative procedures in the same arch
	Sample size: 62
	Age: 5-13 years old
	Mean age: 8.4 years old
<b>Interventions</b>	Group A: received lidocaine HCl 2% with 1: 100 000 epinephrine
	Group B: received articaine HCl 4% with 1: 200 000 epinephrine

<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Unclear risk	It is unclear whether participants and clinicians were blind
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	The authors did not report which LA agent was given by infiltration or mandibular block injections

## Garrocho-Rangel 2018

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover  Location: Mexico  Setting: The paediatric dentistry clinic, San Luis Potosi University
<b>Participants</b>	Children requiring two local analgesia for restoring two upper or lower primary molars  Sample size: 36  Age: 5-8 years old  Mean age: 6.2 years old
<b>Interventions</b>	Group A (Control): received treatment without using the Video Eyeglasses/Earphones System (VEES)  Group B (Experimental): received treatment with using the VEES
<b>Outcomes</b>	Pain during LA and restoration: 0-10 Face, Legs, Activity, Cry, Consolability scale
<b>Risk of bias</b>	

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A randomisation block scheme was used
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessor was not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Yildirim 2020

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Crossover</p> <p>Location: Turkey</p> <p>Setting: Faculty of Dentistry, Istanbul Okan University</p>
<b>Participants</b>	<p>Children requiring two mandibular nerve block analgesia for dental treatment their bilateral mandibular primary or permanent molars</p> <p>Sample size: 60</p> <p>Age: 6-12 years old</p> <p>Mean age: 8.37 years old</p>
<b>Interventions</b>	<p>Group A (Control): received topical anaesthesia (TA) spray containing 10% lidocaine with a cotton pellet for 60s</p> <p>Group B (Case): received Comfort-in™ injection system (CIS) which uses the “liquid jet” system to inject the anaesthetic solution rapidly (one-third of a second) from a 0.15-mm hole with high pressure</p>
<b>Outcomes</b>	Pain during LA: 0-5 Wong-Baker FACES scale and 0-10 Face, Legs, Activity, Cry, Consolability scale
<b>Risk of bias</b>	

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A computer-assisted program was used
<b>Allocation concealment</b>	Low risk	"The operator was asked to select the side to do the first treatment before the researcher revealed the pre-anaesthesia method to be applied, to avoid possible operator bias"
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Alinejhad 2018

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover  Location: Iran  Setting: The Department of Pediatrics of the Faculty of Dentistry at Shahid Sadoughi University of Medical Sciences
<b>Participants</b>	Children requiring local anaesthesia for pulpotomy of primary mandibular 2 <sup>nd</sup> molars  Sample size: 40  Age: 6-10 years old  Mean age: Not reported
<b>Interventions</b>	Group A: received 2% lidocaine with epinephrine 1:100,000 by IANB  Group B: received 4% articaine with epinephrine 1:100,000 by buccal infiltration
<b>Outcomes</b>	Pain during LA: 0-4 Visual Analogue Scale



<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessors were not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Gumus 2020

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Split mouth</p> <p>Location: Turkey</p> <p>Setting: The Pediatric Dentistry Clinic of the Erciyes University, Faculty of Dentistry</p>
<b>Participants</b>	<p>Children requiring two local analgesia for dental treatment of bilateral maxillary primary molars</p> <p>Sample size: 100</p> <p>Age: 5-8 years old</p> <p>Mean age: 6.5 years old for girls and 6.42 years old for boys</p>
<b>Interventions</b>	<p>Group A: received a cartridge containing 2 mL of LA solution was placed in the CALSET composite heater and warmed to body temperature (37 °C)</p> <p>Group B: received a cartridge containing a LA solution was immersed in a 21 °C water bath, half an hour prior to the procedure</p>
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale
<b>Risk of bias</b>	

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	"MS Excel 2013 (Microsoft Corporation, Redmond, WA, USA) software was used to randomly determine which side(right/left) of the maxilla was to be infiltrated with the anaesthetic solution and at which temperature (21 °C or 37 °C) in the first session"
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Tung 2018

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Parallel groups</p> <p>Location: USA</p> <p>Setting: Herman Ostrow school of dentistry, university of Southern California</p>
<b>Participants</b>	<p>Children requiring a maxillary infiltration injection or mandibular inferior alveolar block and long buccal anaesthesia for operative dental treatment</p> <p>Sample size: 150</p> <p>Age: 7-14 years old</p> <p>Mean age: 11.1 years old for groups A and C and 10.7 years old for group B</p>
<b>Interventions</b>	Group A: received an injection without stimulation (n=50)

	Group B: received an injection with manual stimulation (n=50)	
	Group C: received an injection with Dental Vibe (n=50)	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	"Using a table of randomly generated numbers, the subjects were assigned to one of three groups"
<b>Allocation concealment</b>	Low risk	Participants were randomised prior to attendance
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessors were not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Shilpapiya 2015

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Crossover  Location: India  Setting: The Department of Pedodontics and Preventive Dentistry of Ragas Dental College and Hospital
<b>Participants</b>	Children requiring bilateral local anaesthesia for dental treatment  Sample size: 30  Age: 6-12 years old  Mean age: 7.5 years old
<b>Interventions</b>	Group A: received an injection without DentalVibe  Group B: received an injection with DentalVibe

<b>Outcomes</b>	Pain during LA: 0-10 Universal Pain Assessment Tool	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Method of randomisation was not reported
<b>Allocation concealment</b>	Unclear risk	Method of allocation concealment not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No population characteristics other than age

Alamoudi 2015

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Parallel groups</p> <p>Location: Saudi Arabia</p> <p>Setting: Faculty of Dentistry, King Abdulaziz University</p>
<b>Participants</b>	<p>Children requiring local anaesthesia for pulpotomy of primary mandibular 2<sup>nd</sup> molars</p> <p>Sample size: 91</p> <p>Age: 5-9 years old</p> <p>Mean age: Not reported</p>
<b>Interventions</b>	<p>Group A: received traditional IANB (Inferior alveolar nerve block) (n=31)</p> <p>Group B: received IANB with a CCLAD (Inferior alveolar nerve block with computer-controlled local anaesthetic delivery (CCLAD IANB) (n=30)</p> <p>Group C: received ILA with a CCLAD STA system (Intraligamental anaesthesia with computer-controlled local anaesthetic delivery) (n=30)</p>

<b>Outcomes</b>	Pain during stages of pulpotomy: 1-4 the Sounds, Eyes, and Motor (SEM) scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	"Block randomisation technique was applied to assign participants to one of the three study groups"
<b>Allocation concealment</b>	Unclear risk	The authors referred to allocation concealment but did not explain the method
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessors was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Mumtaz 2021

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: India  Setting: The Department of Pedodontics and Preventive Dentistry
<b>Participants</b>	Children requiring local anaesthesia for extraction of mandibular primary molars  Sample size: 70  Age: 8-10 years old  Mean age: Not reported
<b>Interventions</b>	Group A: received 1.5ml of 2 % lignocaine with 1:100000 epinephrine via inferior alveolar nerve block (n=35)  Group B: received 1.5 ml of 4 % articaine with 1:10000 epinephrine via buccal and lingual infiltration (n=35)
<b>Outcomes</b>	Pain during extraction: 0-10 Visual Analogue Scale

<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Abdelmoniem 2016

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Parallel groups</p> <p>Location: Egypt</p> <p>Setting: Pediatric Dentistry and Dental Public Health Department, Faculty of Oral and Dental Medicine, Cairo University</p>
<b>Participants</b>	<p>Children requiring inferior alveolar nerve block for extraction of mandibular primary molar</p> <p>Sample size: 90</p> <p>Age: 4-9 years old</p> <p>Mean age: 7.18 years old for group A and 7.02 years old for group B and 7.65 years old for group C</p>
<b>Interventions</b>	<p>Group A: received passive distraction by listening to the same song on headphones (n=30)</p> <p>Group B: received active distraction by moving legs up and down alternatively as a game (n=30)</p> <p>Group C: received passive-active distraction group (n=30)</p>

<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operators/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It was not reported
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Huet 2011

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: France  Setting: Department of Pediatric Dentistry at Rennes University Hospital
<b>Participants</b>	Children requiring local anaesthesia for dental treatment  Sample size: 29  Age: 7-12 years old  Mean age: Not reported
<b>Interventions</b>	Group A: received LA with hypnosis (n=14)  Group B: received LA without hypnosis (n=15)
<b>Outcomes</b>	Pain during LA: 0-10 Modified Objective Pain Score (mOPS) Scale

	Anxiety at during the initial interview, on arrival in the waiting room, in the dentist's chair and at the time of the dental anaesthesia: 0-100 The Modified Yale Preoperative Anxiety Scale (mYPAS)	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation	Low risk	Participants were randomly allocated by lottery
Allocation concealment	Unclear risk	Allocation concealment method was not reported
Blinding of participants and personnel for all outcomes	Low risk	It was not possible to blind operator/participants to the intervention
Blinding of outcome assessors for all outcomes	High risk	Assessor was not blind
Incomplete outcome data for all outcomes	Low risk	The authors reported on incomplete data "One child excluded because of un-usable data" from the intervention group
Selective outcome reporting	Low risk	The authors reported all expected outcomes
Other sources of bias	Low risk	No other bias

Bernhardt 2001

Characteristics of included studies	
<b>Methods</b>	Study design: RCT, Parallel groups  Location: USA  Setting: Department of Orthodontics, College of Dentistry
<b>Participants</b>	Children requiring separator placement for orthodontic treatment  Sample size: 41  Age: 9-16 years old  Mean age: 12.1 years old for group A and 13.5 years old for group B and 12.8 years old for group C
<b>Interventions</b>	Group A: received 400 mg ibuprofen 1 hour preoperatively and 400 mg ibuprofen 6 hours after the initial dose (n=13)



	<p>Group B: received 400 mg ibuprofen 1 hour preoperatively and placebo 6 hours after the initial dose (n=14)</p> <p>Group C: received placebo 1 hour preoperatively and 400 mg ibuprofen 6 hours after the initial dose (n=14)</p> <p>All analgesics were taken orally</p>	
<b>Outcomes</b>	Pain after separator placement: 0-100 Visual Analogue scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	Operator and participants were blind to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "22 of whom took additional medication and were excluded from the study. These 22 patients were evenly distributed among the 3 groups"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

## Law 2000

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Parallel groups</p> <p>Location: USA</p> <p>Setting: Department of Orthodontics, College of Dentistry</p>
<b>Participants</b>	<p>Children requiring separator placement for orthodontic treatment</p> <p>Sample size: 63</p> <p>Age: a maximum age of 16 years old</p>

	Mean age: 13 years old	
<b>Interventions</b>	<p>Group A: received 400 mg ibuprofen 1 hour preoperatively and placebo immediately after the appointment (n=22)</p> <p>Group B: received placebo 1 hour preoperatively and 400 mg ibuprofen immediately after the appointment (n=19)</p> <p>Group C: received placebo 1 hour preoperatively and placebo immediately after the appointment (n=22)</p> <p>All analgesics were taken orally</p>	
<b>Outcomes</b>	Pain after separator placement: 0-100 Visual Analogue scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	Operator and participants were blind to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "28 subjects did not receive separators at their next appointment and 17 subjects forgot to take the pretreatment dose before their appointment"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Alshami 2021

<b>Characteristics of included studies</b>	
<b>Methods</b>	<p>Study design: RCT, Parallel groups</p> <p>Location: Saudi Arabia</p> <p>Setting: Princess Nourah bint Abdulrahman University's dental clinic</p>
<b>Participants</b>	Children requiring local anaesthesia for extraction of symptomatic primary molars

	Sample size: 56 Age: 5-13 years old Mean age: 9.4 years old
<b>Interventions</b>	Group A: received 7.5–15 ml/kg ibuprofen preoperatively (n=28) Group B: received placebo preoperatively (n=28) All analgesics were taken orally
<b>Outcomes</b>	Pain at baseline and after extraction at 3 and 24 hours: 0-10 Wong-Baker FACES scale Anxiety at baseline and after extraction at 3 and 24 hours: 1-5 the Modified Child Dental Anxiety scale
<b>Risk of bias</b>	
<b>Bias</b>	<b>Authors' judgement</b> <b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk      Participants were randomly allocated
<b>Allocation concealment</b>	Low risk      "Once participants underwent consent, they were assigned an ID number which placed them in a randomised group"
<b>Blinding of participants and personnel for all outcomes</b>	Low risk      Operator and participants were blind to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk      Assessor was not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk      The authors reported on incomplete data "One participant was removed from the analysis because they had three extractions, while the other participants had only one or two"
<b>Selective outcome reporting</b>	Low risk      The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk      No other bias

Helmy 2022

<b>Characteristics of included studies</b>	
<b>Methods</b>	Study design: RCT, Parallel groups Location: Egypt

	Setting: The Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Alexandria University	
<b>Participants</b>	Children requiring local anaesthesia for extraction of mandibular primary molars  Sample size: 50  Age: 5-7 years old  Mean age: 6.10 years old	
<b>Interventions</b>	Group A: received Computer-controlled Intraligamentary anaesthesia (CC-ILA) (n=25)  Group B: received Inferior alveolar nerve block (IANB) (n=25)	
<b>Outcomes</b>	Pain during LA and extraction: 1-4 the Sounds, Eyes, and Motor (SEM) scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A computer-generated list of random numbers was used
<b>Allocation concealment</b>	Low risk	"Each child was given a serial number written in identical sheets of paper with the group to which each child is allocated and placed inside opaque envelopes carrying their respective names"
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "One participant was removed from the analysis because they had three extractions, while the other participants had only one or two"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Vidigal 2021

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Brazil  Setting: The Dental School, University of Sao Paulo	
<b>Participants</b>	Children requiring local anaesthesia for extraction or pulpotomy of mandibular primary molars  Sample size: 52  Age: 3-5 years old  Mean age: Not reported	
<b>Interventions</b>	Group A: received Tell-Show-Do Technique (TSD-T) (n=26)  Group B: received Hiding Dental-Needle Technique (HDN-T) (n=26)  LA was given by IANB with 1.8 ml of Lidocaine 2% with 1:100.000 epinephrine.	
<b>Outcomes</b>	Pain during LA: 1-5 Wong-Baker FACES scale  Anxiety before and during LA: 1-5 the Facial Image scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A statistical program MedCalc Software, version 12.4.0.0 was used
<b>Allocation concealment</b>	Low risk	"The sequence of numbers generated was distributed in opaque envelopes by an external researcher. The envelopes were opened only by the operator at the time of the block mandibular anesthesia."
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessors were blind

<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Ghaderi 2013

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Crossover  Location: Iran  Setting: Department of Pediatric Dentistry, Shiraz University of Medical Sciences	
<b>Participants</b>	Children requiring bilateral buccal infiltration of local anaesthesia for extraction of maxillary primary canine on both sides  Sample size: 50  Age: 8-10 years old  Mean age: 8.94 years old	
<b>Interventions</b>	Group A: received a topical anaesthetic agent (Benzocaine) on one side for 1 min and plus ice  Group B: received a topical anaesthetic agent (Benzocaine) on the other side for 1 min	
<b>Outcomes</b>	Pain during LA: 0-100 Visual Analogue Scale and 0-3 the Sounds, Eyes, and Motor (SEM) scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	"Random number table have been used for block randomization. The number was chosen by tracing a line starting from random number till reaching to a block which was chosen as designated number."
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Jain 2021

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Split mouth  Location: India  Setting: Department of Paediatric and Preventive Dentistry, Sri Aurobindo College of Dentistry	
<b>Participants</b>	Children requiring bilateral buccal infiltration of local anaesthesia for dental treatment of posterior maxillary teeth  Sample size: 30  Age: 5-10 years old  Mean age: Not reported	
<b>Interventions</b>	Group A: received infiltration of 1.8 mL of 2% lignocaine in addition to 1:100,000 adrenaline and external cold and a vibrating device (Buzzing device as distraction)  Group B: received infiltration of 1.8 mL of 2% lignocaine in addition to 1:100,000 adrenaline	
<b>Outcomes</b>	Pain during LA: 1-5 RMS Pictorial Scale and 0-10 the revised Face, Legs, Activity, Cry, Consolability scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	The usage of flip coin method was considered
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "This study was successfully completed by thirty children with a total of four dropouts"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

AmruthaVarshini 2021

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Crossover  Location: India  Setting: The Outpatient Department of Paediatric Dentistry	
<b>Participants</b>	Children requiring local anaesthesia for extraction of maxillary primary molars  Sample size: 30  Age: 9-12 years old  Mean age: Not reported	
<b>Interventions</b>	Group A: received LA gel application  Group B: received Ice application  Group C: received Laser biostimulation with 0.3 W power at a wavelength of 810 nm and probe tip kept 2 mm away from the surface in pulsed mode for 1 minute	
<b>Outcomes</b>	Pain during LA: 0-10 Wong-Baker FACES scale and 1-4 the Sounds, Eyes, and Motor (SEM) scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	The lottery method was used
<b>Allocation concealment</b>	Low risk	Sequentially numbered, opaque, and sealed envelopes were used
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention



<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Al-Halabi 2018

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Syria  Setting: Department of Pediatric Dentistry, Faculty of Dentistry, Damascus University	
<b>Participants</b>	Children requiring inferior alveolar nerve block  Sample size: 101  Age: 6-10 years old  Mean age: 7.4 years old	
<b>Interventions</b>	Group A: received IANB with basic behaviour guidance techniques and without distraction aids (n=34)  Group B: received IANB with audio-visual (AV) eyeglasses 'virtual reality (VR) Box' and wireless headphone (n=33)  Group C: received IANB with tablet device and wireless headphone (n=34)	
<b>Outcomes</b>	Pain during LA: 0-5 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A randomization website 'Random.org' was used
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessor was not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "one patient was excluded due to behavioral problems"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Primosch 2001

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Crossover  Location: USA  Setting: Department of Pediatric Dentistry, Faculty of Dentistry, University of Florida	
<b>Participants</b>	Children requiring bilateral palatal anaesthesia for restoring maxillary molars  Sample size: 40  Age: 7-15 years old  Mean age: 10.75 years old	
<b>Interventions</b>	Phase 1: received topical anaesthesia benzocaine 20% gel versus Orabase-B (sodium carboxymethylcellulose oral adhesive with benzocaine 20%)  Phase 2: received topical anaesthesia Orabase-B versus EMLA 5% cream (lidocaine 2.5% and prilocaine 2.5% manually mixed in Orabase Plain "(sodium carboxymethylcellulose oral adhesive)	
<b>Outcomes</b>	Pain during LA: 0-100 Visual Analogue scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessor was not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Daneshvar 2021

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Crossover  Location: Iran  Setting: Department of Pediatric Dentistry, School of Dentistry, Guilan University of Medical Sciences	
<b>Participants</b>	Children requiring local anaesthesia for pulpotomy of bilateral primary mandibular 2 <sup>nd</sup> molars  Sample size: 40  Age: 5-8 years old  Mean age: 6.72 years old	
<b>Interventions</b>	Group A: received 4% articaine with epinephrine 1:100,000 by infiltration  Group B: received 2% lidocaine with epinephrine 1:80,000 by IANB	
<b>Outcomes</b>	Pain during Pulpotomy: 1-5 the Facial Image Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	Random number table in Excel was used
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Unclear risk	Insufficient information to make the judgement
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	Insufficient information to make the judgement

<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Kamath 2013

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: India  Setting: The Narayana Hrudayalaya Dental Clinics	
<b>Participants</b>	Children requiring local anaesthesia for the dental treatment  Sample size: 160  Age: 4-10 years old  Mean age: 7.6 years old for males and 7.2 years old for females in group A and 7.8 years old for males and 7.6 years old for females in group B	
<b>Interventions</b>	Group A (Control): used deep breathing (n=80)  Group B (Intervention): used distraction technique Writing In The Air Using Leg (WITAIL) (n=80)  LA was given by IANB with Lignocaine 2%	
<b>Outcomes</b>	Pain during LA: 0-10 the Modified Toddler- Preschooler Post-operative Pain Scale (TPPPS) for children aged 4-5 years old and 0-10 the FACES Pain Scale–Revised (FPS-R) for children aged 6-10 years old	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	The usage of flip coin method was considered
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Asvanund 2015

<b>Characteristics of included studies</b>		
<b>Methods</b>	<p>Study design: RCT, Crossover</p> <p>Location: Thailand</p> <p>Setting: The pediatric dental clinic at the Golden Jubilee Medical Center, Salaya campus, Nakornpathom and dental clinic at Nong Don Community Hospital, Saraburibprovince</p>	
<b>Participants</b>	<p>Children requiring local anaesthesia for dental treatment of bilateral carious molars</p> <p>Sample size: 49</p> <p>Age: 5-8 years old</p> <p>Mean age: 7 years old</p>	
<b>Interventions</b>	<p>Group A: received an injection without wearing audio-visual (AV) eyeglasses</p> <p>Group B: received an injection with wearing AV eyeglasses</p> <p>LA was given by IANB for mandibular teeth and by infiltration for maxillary teeth with 1.5 ml of mepivacaine with 1:100,000 epinephrine</p>	
<b>Outcomes</b>	Pain during LA: 0-10 the Faces Pain Scale-Revised (FPS-R)	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Participants were randomly allocated
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported

<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	High risk	Assessors were not blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors reported on incomplete data "two who failed to return for a second visit and one refused to wear AV eyeglasses for the second visit"
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Mittal 2015

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: India  Setting: Department of Pedodontics and Preventive Dentistry	
<b>Participants</b>	Children requiring local anaesthesia for extraction of primary molars  Sample size: 100  Age: 8-13 years old  Mean age: 9.14 years old	
<b>Interventions</b>	Group A (Control): received buccal and palatal infiltration using traditional syringe (n=50)  Group B (Intervention): received buccal and palatal infiltration using Wand (n=50)	
<b>Outcomes</b>	Pain during LA: 0-100 Visual Analogue scale and 1-4 the Sounds, Eyes, and Motor (SEM) scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	Random sampling using chit method was considered
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported

<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Oztas 2005

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Crossover Location: Turkey Setting: Not reported	
<b>Participants</b>	Children requiring local anaesthesia for pulpotomy of contralateral primary mandibular 2 <sup>nd</sup> molars Sample size: 25 Age: 6-10 years old Mean age: Not reported	
<b>Interventions</b>	Group A (Control): received traditional IANB (Inferior alveolar nerve block) Group B (Study): received periodontal ligament injection by Wand	
<b>Outcomes</b>	Pain during preparation, LA and pulpotomy: 0-3 the Eland Color Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Unclear risk	Method of randomisation was not reported
<b>Allocation concealment</b>	Unclear risk	Allocation concealment method was not reported
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	It was not possible to blind the operator/participants to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Unclear risk	No baseline characteristics reported

Wambier 2018

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Crossover  Location: Brazil  Setting: The School of Dentistry	
<b>Participants</b>	Children requiring topical anaesthesia for sealant placement on the contralateral permanent mandibular 1st molars under rubber dam  Sample size: 82  Age: 8-12 years old  Mean age: 10.4 years old	
<b>Interventions</b>	Group A (Control): received placebo gel  Group B (Study): received the light-cured anaesthetic gel	
<b>Outcomes</b>	Pain during clamp placement: 0-5 Facial Expression Wong-Baker Scale, 0-10 Numeric Rating Scale (NRS) and 0-10 Face, Legs, Activity, Cry, Consolability (FLACC) Scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A software ( <a href="http://www.sealedenvelop.com">www.sealedenvelop.com</a> ) was used
<b>Allocation concealment</b>	Low risk	Opaque, consecutively numbered and sealed envelopes were used
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	The operator and participants were blind to the intervention
<b>Blinding of outcome assessors for all outcomes</b>	Unclear risk	It is unclear whether assessors were blind



<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

Raslan 2021

<b>Characteristics of included studies</b>		
<b>Methods</b>	Study design: RCT, Parallel groups  Location: Syria  Setting: Department of Paediatric Dentistry, Tishreen University	
<b>Participants</b>	Children requiring local anaesthesia for extraction of primary molars  Sample size: 66  Age: 6-8 years old  Mean age: 7.37 years old	
<b>Interventions</b>	Group A: received Paracetamol 160 mg/5 ml 30 mins preoperatively (n=22)  Group B: received placebo 30 mins preoperatively (n=22)  Group C: received 100 mg/5 ml ibuprofen 30 mins preoperatively (n=22)  All analgesics were taken orally	
<b>Outcomes</b>	Pain after extraction at 3, 4 and 5 hours: 0-10 Wong-Baker FACES scale	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
<b>Random sequence generation</b>	Low risk	A randomized table was used
<b>Allocation concealment</b>	Low risk	"Group identifiers were included in dark and sealed envelopes with session numbers identical to those assigned to patients by the randomization table"
<b>Blinding of participants and personnel for all outcomes</b>	Low risk	The operator and participants were blind to the intervention

<b>Blinding of outcome assessors for all outcomes</b>	Low risk	Assessor was blind
<b>Incomplete outcome data for all outcomes</b>	Low risk	The authors evaluated all included participants
<b>Selective outcome reporting</b>	Low risk	The authors reported all expected outcomes
<b>Other sources of bias</b>	Low risk	No other bias

## Appendix 9: GRADE assessment for the certainty of evidence of the second systematic review

### Summary of findings:

#### Computer Driven LA compared to Conventional LA for children and adolescents having routine dental treatment

**Patient or population:** children and adolescents having routine dental treatment

**Setting:** Dental clinic

**Intervention:** Computer Driven LA

**Comparison:** Conventional LA

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N <sub>e</sub> of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Conventional LA	Risk with Computer Driven LA				
Intra-operative Pain	-	SMD 0.03 SD lower (0.33 lower to 0.27 higher)	-	607 (7 RCTs)	⊕⊕⊕○ Moderate	See footnotes

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

#### GRADE Working Group grades of evidence

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

### Explanations

a. Certainty of the evidence downgraded by 1 level for three studies rated at high risk of bias due to lack of blinding of outcome assessors.

### Summary of findings:

#### Intra-ligament LA compared to Conventional LA for relieving pain in children and adolescents having routine dental treatment

**Patient or population:** relieving pain in children and adolescents having routine dental treatment

**Setting:** Dental clinic

**Intervention:** Intra-ligament LA

**Comparison:** Conventional LA

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N <sub>e</sub> of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Conventional LA	Risk with Intra-ligament LA				
Intra-Operative Pain	-	SMD 1.79 SD lower (2.37 lower to 1.2 lower)	-	111 (2 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

#### GRADE Working Group grades of evidence

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

### Explanations

a. Certainty of the evidence downgraded by 1 level for one study rated at high risk of bias due to lack of blinding of outcome assessors.

## Summary of findings:

**Intra-osseous LA compared to Conventional LA for relieving pain in children and adolescents having routine dental treatment**

**Patient or population:** relieving pain in children and adolescents having routine dental treatment

**Setting:** Dental clinic

**Intervention:** Intra-osseous LA

**Comparison:** Conventional LA

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Conventional LA	Risk with Intra-osseous LA				
Intra-Operative Pain	-	SMD 0.14 SD lower (0.52 lower to 0.24 higher)	-	188 (1 RCT)	⊕⊕⊕○ Moderate <sup>a</sup>	

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

**GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

**Explanations**

a. Certainty of the evidence downgraded by 1 level for imprecision.

## Summary of findings:

**4% Articaine compared to 2% Lidocaine for LA for relieving pain in children and adolescents having routine dental treatment**

**Patient or population:** LA for relieving pain in children and adolescents having routine dental treatment

**Setting:** Dental clinic

**Intervention:** 4% Articaine

**Comparison:** 2% Lidocaine

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 2% Lidocaine	Risk with 4% Articaine				
Intra-Operative Pain	-	SMD 1.04 SD lower (2.18 lower to 0.1 higher)	-	204 (2 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

**GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

**Explanations**

a. Certainty of the evidence downgraded by 1 level for one study rated at high risk of bias due to lack of blinding of outcome assessors.

## Summary of findings:

### Different methods of topical anaesthesia compared to Conventional topical anaesthesia for LA for relieving pain in children and adolescents having routine dental treatment

**Patient or population:** LA for relieving pain in children and adolescents having routine dental treatment

**Setting:** Dental clinic

**Intervention:** Different methods of topical anaesthesia

**Comparison:** Conventional topical anaesthesia

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Conventional topical anaesthesia	Risk with Different methods of topical anaesthesia				
Intra-Operative Pain	-	SMD 0.64 SD lower (1.38 lower to 0.09 higher)	-	160 (2 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	See footnotes

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

#### GRADE Working Group grades of evidence

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

### Explanations

a. Certainty of the evidence downgraded by 1 level for one study rated at high risk of bias due to lack of blinding of outcome assessors.

## Summary of findings:

### Mechanoreceptor and thermal receptor stimulation compared to for for relieving pain in children and adolescents having routine dental treatment

**Patient or population:** for relieving pain in children and adolescents having routine dental treatment

**Setting:** Dental clinic

**Intervention:** mechanoreceptor and thermal receptor stimulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with	Risk with mechanoreceptor and thermal receptor stimulation				
Intra-Operative Pain	-	SMD 1.38 SD lower (2.02 lower to 0.73 lower)	-	930 (10 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	See footnotes

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

#### GRADE Working Group grades of evidence

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

### Explanations

a. Certainty of the evidence downgraded by 1 level for two studies rated at high risk of bias due to lack of blinding of outcome assessors.

## Summary of findings:

**Behavioural Interventions compared to for relieving pain and anxiety in children and adolescents having routine dental treatment**

Patient or population: relieving pain and anxiety in children and adolescents having routine dental treatment

Setting: Dental clinic

Intervention: Behavioural Interventions

Comparison:

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with	Risk with Behavioural Interventions				
Intra-Operative pain	-	SMD 0.5 SD lower (0.83 lower to 0.18 lower)	-	1130 (13 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	See footnotes
Anxiety	-	SMD 0.17 SD lower (0.45 lower to 0.11 higher)	-	178 (3 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	See footnotes

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

**GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

**Explanations**

- a. Certainty of the evidence downgraded by 1 level for six studies rated at high risk of bias due to lack of blinding of outcome assessors.  
b. Certainty of the evidence downgraded by 1 level for one study rated at high risk of bias due to lack of blinding of outcome assessors.

## Summary of findings:

**Pre-emptive oral analgesics compared to Oral placebo solution for relieving pain in children and adolescents having routine dental treatment**

Patient or population: relieving pain in children and adolescents having routine dental treatment

Setting: Dental clinic

Intervention: Pre-emptive oral analgesics

Comparison: Oral placebo solution

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Oral placebo solution	Risk with Pre-emptive oral analgesics				
Post-Operative Pain	-	SMD 0.77 SD lower (1.21 lower to 0.33 lower)	-	208 (3 RCTs)	⊕⊕⊕○ Moderate <sup>a</sup>	

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; SMD: standardised mean difference

**GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

**Explanations**

- a. Certainty of the evidence downgraded by 1 level for one study rated at high risk of bias due to lack of blinding of outcome assessors.