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TITLE PAGE

Title:

Outcomes to evaluate care for adults with acute dental pain and infection: a systematic narrative review.

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Competing interests statement

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ABSTRACT

Objective: To identify outcomes reported in peer-reviewed literature for evaluating the care of adults with acute dental pain or infection.

Design: Systematic narrative review.

Setting/Participants: Primary research studies published in peer-reviewed literature and reporting care provided for adults with acute dental pain or infection across healthcare settings were included. Reports not in English language were excluded.

Study selection: Seven databases were searched from inception to December 2020. Risk of bias was assessed using the Critical Appraisal Skills Programme checklist for randomised controlled trials and Quality Assessment Tool for Studies of Diverse Design for other study types.

Outcomes: Narrative synthesis included all outcomes of care for adults with acute dental pain or infection. Excluded were outcomes about pain management to facilitate treatment, prophylaxis of post-surgical pain/infection or traumatic injuries.

Results: Searches identified 19,437 records and 27 studies (dating from 1993 to 2020) were included. Across dental, pharmacy, hospital emergency and rural clinic settings, 20 studies were undertaken in high-income countries and 7 in low- & middle-income countries. Two clinical outcome categories were identified: signs and symptoms of pain or infection, and complications following treatment (including adverse drug reactions and unplanned visits for the same problem). Patient-reported outcomes included satisfaction with the outcome of care. Data collection methods included patient diaries, interviews and in-person reviews.

Discussion: A heterogenous range of study types and qualities were included: one study, published in 1947, was excluded only due to lack of outcome details. Studies from dental settings reported just clinical outcomes; across wider healthcare more outcomes were included.

Conclusions: A combination of clinical and patient-reported outcomes are recommended to evaluate care for adults with acute dental pain or infection. Further research is recommended to align these outcomes with the international consensus on oral health outcomes.

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Strengths and limitations of this study

- The first systematic review to examine outcome measures of care for adults with acute dental pain or infection across healthcare settings.
- The outcomes will be important for evaluating new dental antibiotic and opioid stewardship interventions, as these drugs are frequently overprescribed for adults with acute dental pain and infection, exacerbated by the COVID-19 pandemic.
- Studies about paediatric patients, studies about the post-operative management of pain, studies about local anaesthesia to facilitate dental treatment, studies about traumatic injuries and papers not in English language were excluded due to key differences in clinical management.
- Two independent reviewers extracted data and two different reviewers assessed the quality using either the Critical Appraisal Skills Programme (for the randomised controlled trials) or the Quality Assessment Tool for Studies with Diverse Designs.
- Reporting based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 guidelines, with searches of seven major electronic databases from their inception to December 2020.

MAIN TEXT

Introduction:

Acute dental pain has a significant impact on quality of life.[1 2] Timely intervention for the relief of dental pain and infection is essential to prevent worsening of ill health and reduce the risk of potentially life-threatening complications, such as sepsis, airway occlusion or analgesic overdose.[3 4] Failure of initial treatment to relieve dental pain and infection can result in patient reattending for further treatment, including to emergency medical care.[5] Thus, ensuring high quality care for people with acute dental problems is critical for both patient safety and service efficiency. Outcomes to evaluate the care provided for people with acute dental pain and/or infection are important.

Evidence-based clinical guidelines can improve the provision of quality healthcare and patient outcomes.[6] Guidelines for treating acute dental pain and infection are generally based on the principle that operative dental procedures (such as removal of a tooth or its pulp) are indicated to address the cause and prevent symptoms recurring.[7] Drugs such as analgesics and antibiotics have a limited role in dentistry and should usually only be used in addition to dental procedures.[8 9] Suboptimal treatment of dental pain and infection with drug prescriptions instead of dental procedures is common, including by general medical practitioners and in emergency departments.[10-12] The contribution of dentistry to global efforts to tackle antibiotic resistance[13]and opioid substance misuse disorder has been highlighted, with a call for the profession to improve its approach to stewardship of these drugs.[7 14 15]

Whilst a plethora of drug trials for the treatment of dental pain or infection have been published, there is little research on patient outcomes following urgent dental care for acute dental pain or infection.[5] A rise in the number of trials to evaluate dental antibiotic stewardship and opioid stewardship interventions is anticipated, with a focus on optimising care and judicious use of medicines for adults (where more than 90% of dental prescribing occurs).[16] To evaluate the effectiveness of these sorts of interventions and to enable improvements in the quality of urgent dental care, this study aimed to identify outcomes from the peer-reviewed literature for evaluating care for adults with acute dental pain and/or infection.

Objectives:

The research question was "What measures in the published literature have been employed to evaluate the outcome of care for adults with acute dental pain and/or infection?"

Methods:

Patient and public involvement

A coproduction team designed and delivered this systematic narrative review. Experts by experience of urgent dental care and/or complications of dental antibiotics (CC and CP) and academic dental professionals (LT, SH and WT) were involved in all stages of this study, from refining the research question and search terms which had been drafted by WT through to disseminating the results. Through discussion between the members of the coproduction team, involvement with each step of the review was allocated according to the skills they wished to develop and the time they had available to contribute at the relevant stages. Individual contributions are indicated in the following sections.

Eligibility criteria

Primary research studies published in peer-reviewed journals were included if they reported outcomes of care for adults (aged over 18-years) treated for acute dental pain and/or infection with advice, prescriptions, or interventions (such as dental extraction). There was no restriction on the year of dissemination.

Studies which included care for children or for people with other oral or dental conditions (such as cervicofacial infections treated as hospital inpatients or post-surgical pain control) were excluded. Studies of urgent dental care for traumatic injuries were excluded as this is a markedly different population and the subject of a separate study.[17] Reports which did not include the outcomes of care provided (or details of how those outcomes were measured) were also excluded, such as studies about the efficacy of local anaesthesia to facilitate the provision of dental procedures at point of care. Primary research studies not published in peer reviewed journals (such as conference abstracts, case studies and other grey literature) were

excluded as the research was seeking tried and tested outcomes for use in clinical trials. Studies not in the English language were excluded due to lack of translation facilities. Full details of the inclusion/exclusion criteria are detailed in Supplementary Material Table S1.

Population groups identified for subgroup analysis during the synthesis phase were dental vs other healthcare settings, and high-income vs low and middle-income countries (LMICs).

Information sources

On 29 November 2020, seven databases were searched from their earliest dates: CINAHL Plus, Dentistry and Oral Sciences, Ovid EMBASE, Ovid Medline, PyschINFO, Scopus and Web of Science.

Search strategy

The search strategy used to identify relevant papers from the database searches was developed in consultation with an information specialist at the University of Manchester. It consisted of 'population' AND 'intervention terms'. Population terms were: (Acute* OR Urgent OR Unschedul* OR Emergenc*) AND (Dental* OR Odontogenic OR Dentoalveolar) AND (Pain OR Toothache OR Pulpitis OR Infection OR Swell* OR Abscess OR Pericoronitis OR Osteitis OR Socket OR Periodontitis OR Implantitis OR Ulcer* OR Stomatitis). Intervention terms were: Patient Care OR Dental Care OR Procedure OR Treat* OR Endodont* OR Exodont* OR Extract* OR Extirpat* OR Incis* OR Drain* OR Debrid* OR Irrigat* OR Prescri* OR Antibiotic* OR Antimicrob* OR Antiseptic OR Analgesi* OR Advice OR Refer*

Limits included: "human" as animal and laboratory studies were not eligible for the review, and "English language" as justified in the 'eligibility criteria' section. There were no limits on the date of included studies.

Selection process

Titles and abstracts from the database searches (undertaken by WT) were transferred into Endnote X9 where duplicates were removed (by WT) and the title/abstracts were screened (independently by WT and SH) for potential inclusion. Full texts of all shortlisted studies

were assessed for eligibility (independently by WT and LT). Where necessary, corresponding authors were contacted to confirm whether the included population met our inclusion criteria. Disagreements at each stage of the process were resolved through discussion between the screeners.

Data collection process

The characteristics (study type, objective, and population) and outcomes, data source (patient-reported, clinician observed or administrative system) and data collection instrument were collected from each report by two reviewers (LT and SH) working independently. Disagreements at each stage of the process were resolved through discussion between the reviewers.

Data items – outcomes and other variables

All outcomes relating to the outcomes of care provided to adults with acute dental pain or infection were sought, together with details about the sources of data and timescales between urgent dental treatment received by the participants and completion of data collection. In addition, specific details about the types of studies (eg randomised controlled trial or questionnaire study) and population were sought, including age range of patients, type of healthcare setting (such as dental clinic or pharmacy), country in which the study took place, and whether a high-income or LMIC country (based on World Bank definitions[18]). Details about study type, patient age, healthcare setting and country for each included study are provided in Table 1, details about which countries were LMICs are highlighted (in bold) in Table 2. There was no restriction on timeframes for the outcomes and where missing data was identified this was recorded in the results tables. Where necessary, corresponding authors were contacted to provide details relating to the data items sought (such as the age of participants).

Quality assessment

The shortlisted studies were assessed using the Critical Appraisal Skills Programme (CASP) Checklist for RCTs.[19] For studies which used a design not valid for an RCT (as assessed via the CASP RCT checklist), the Quality Assessment Tool for Studies with Diverse Design (QATSDD) was used.[20] Quality assessment of all studies was undertaken by WT, with 30%

of studies (selected at random from across the CASP and QATSDD sets) independently assessed by CP. Discrepancies in relation to each element of the assessment framework were resolved through discussion between the assessors and, where differences were just one point, the scores were averaged.

Synthesis methods

All studies which had been selected for inclusion and which had passed the quality assessment were eligible for inclusion in synthesis. Outcome data collected were initially categorised by WT based on a framework advocated for antimicrobial stewardship interventions[21] as the outcomes identified in this study were intended to be employed in trials of stewardship interventions. All authors of the paper discussed and agreed adjustments to the category titles, which aligned the language with that used in a recently published international consensus of oral health outcomes.[22]

The tabular structure displays a summary of outcomes for each study, using the structure identified. Table 2 presents clinical outcomes ('signs/symptoms of dental pain or infection' and 'complications or harm') and patient-reported outcomes ('satisfaction with the outcome of care' and 'other') for each study with details of how the outcome was measured (such as numeric pain scale). Sources of data employed in each study and the timescales between treatment provided to participants and completion of data collection are presented in Table 3.

Results

Study selection

Of the 19,437 records identified from database searches, 27 studies were selected for inclusion (see Figure 1). One study was excluded as it was impossible to tell how the outcomes had been measured.[23] Another study[24] which may look like it should be included was excluded as it reported secondary analysis of data collected in other studies.[25 26]

Study characteristics

The studies dated between 1993 and 2020 and encompassed a heterogenous range of designs, from randomised controlled trials to questionnaire surveys. Most studies (n=23) took place in dental settings, one was in a hospital emergency department, another in a rural community

healthcare clinic and a third was in community pharmacy; the setting for one study was unclear. The earliest 14 studies all took place in high income countries (during the period 1993 to 2012). Of the 13 studies which took place between 2013 and 2020, seven were based in LMICs (Brazil, Egypt, India, Tanzania, and Turkey). Further characteristics of the included studies, including their objectives, are presented in Table 1.

Quality assessment

Following application of the inclusion/exclusion criteria, 11 studies were quality assessed using the CASP framework for RCTs (see Supplemental Material Table S2) and 16 using the QATSDD tool (see Supplemental Material Table S3). Many of the studies assessed using the QATSDD criteria scored poorly, for example due to failure to justify the sample size or provision of a rationale for the analytic method used, and few studies covered the QATSDD criterion about patients being involvement in the study design.

Results of individual studies

The outcomes recorded in each individual study are presented in Table 2, including details about how they were measured. Two categories of clinical outcomes and one of patient-report outcomes were identified. Clinical outcomes included: 'signs and symptoms of dental pain/infection', and 'complications or other harm' resulting from treatment or disease progression. Patient-reported outcomes included patient satisfaction with the outcome of care.

As also shown in Table 2, various approaches were used for measuring the clinical outcomes, including unidimensional pain scales (such as a visual analogue scale (VAS) or category pain scale), amount of rescue medication taken, and the presence of absence of various signs and symptoms such as swelling, trismus or pyrexia. Complications were assessed by recording whether unplanned visits had been required or whether the patient had experienced symptoms of drug allergy or other adverse effects (such as gastrointestinal symptoms and headaches).

Details about data sources for the outcomes and duration of data collection in each study are presented in Table 3. Most of the outcomes were reported by patients (n=20) through diaries, questionnaires or interviews. A minority of studies (n=7) employed clinical observations from in person monitoring or review during or after their treatment appointment. None of the

studies used a combination of patient-reported and clinician observed data. No studies employed data from healthcare administrative systems. Data collection in most studies took place over less than a week (n=17). In six studies, the duration of data collection was one week, and two of the remaining four studies data collection completed one year after the participant received urgent dental treatment.

Results of syntheses

Pain was the most commonly reported sign/symptom (see Table 2), including unstimulated/spontaneous pain (n=24), pain stimulated by percussion, chewing or thermal stimulus (n=7) or the need for additional pain relief through use of rescue medication (n=14). Complications or other harm related to the treatment provided included adverse outcomes (such as drug allergy or nausea) and progression of the acute dental condition requiring unplanned visits for additional treatment. Patient satisfaction was only recorded in studies in non-dental healthcare settings[27 28] and only one dental study included patient-reported outcomes.[29]

Comparing results between high-income countries and LMICs found just one difference in the outcomes reported: none of the studies undertaken in LMICs reported on swelling as a sign of infection, compared to 35% (n=7/20) of studies undertaken in high-income countries. There was also one difference found in data sources for the outcomes: none of the LMIC-based studies recorded clinician observed outcomes compared to 30% (n=6/20) of studies in high-income countries. No differences were found in data collection periods.

Discussion

A diverse range of measures were identified to assess the outcomes of care for adults presenting with acute dental pain and/or infection across a range of healthcare settings in high income and LMICs. Most were clinical outcomes, such as signs and symptoms of pain and infection and complications or other harms following treatment (such as drug allergy). Patient satisfaction was only reported in studies from non-dental settings. The range of outcomes and data collection periods were similar between high income countries and LMICs. Just one key difference was noted in their assessment: none of the LMIC studies reported clinician-observed data. This is the first study to focus comprehensively on outcomes relating to acute dental conditions and should be utilised when evaluating interventions for the care of adults presenting with acute dental pain or infection across health care settings internationally.

Measuring what matters to patients has been recognised as central to improving patient care and service delivery, with patients needing to be involved in decisions about what to measure.[30] For this reason, experts by experience of urgent dental care were key members of our coproduction team, including when devising the review's search strategy. Funding to reimburse their time for participating in the length process of a systematic review was welcomed by the experts by experience.

The range of healthcare settings included in this review (dental clinics, pharmacies, hospital emergency departments and community clinics) mean the findings of this study are widely generalisable and can be easily translated to different health care settings around the world. Even though limited to English language, studies from a wide range of countries were included, across both high-income countries and LMICs. Six papers were excluded due to language (including 50% in Japanese) which may have introduced additional outcomes and differences in cultural practices.

Restricting this paper to published studies relating to adults from the peer-reviewed literature means that additional measures in the grey literature may have been missed as well as meaning that it fails to conform completely to the new PRISMA 2020 guidelines for systematic reviews which were published during the course of our study.[31] The authors decided additional searches of the grey literature would not, however, meet the research questions or their intention to identify outcomes which had been successfully tried and tested. Studies including children were excluded from this review as the outcomes (especially patient-reported outcomes) are materially different.[32] Further, the trials for which these outcomes will be used by the authors relate to dental antibiotic stewardship and opioid stewardship for adult patients, which is the patient group where most overprescribing of these drugs occurs.[33 34]

The importance of valid, reliable, and feasible measures for improving the quality of oral health care, including patient-reported outcomes and experience measures has been recognised.[35] In 2020, an international consensus of patient-centred outcomes to measure adult oral health (focusing on caries and periodontal disease) was published and highlighted that multiple measures are required to capture the effect of oral health on the individual patient.[22] Where possible, we have adopted the terminology from this adult oral health standard set of outcomes when presenting our findings, such as 'complications or other harm resulting from treatment or disease progression' and 'unplanned visits.' However, whilst our

findings cover some of the same territory, there are important differences in the detail especially relating to timescales. For example, there is no mention of 'infection' in the oral health outcomes and 'dental pain' covers only the frequency of pain in the last six months and 'complications' within 30 days, whereas our study found that these outcomes were measured in hours and days for people with acute dental conditions. Quality of life indicators such as the ability to eat, sleep, speak or carry out usual work activities at home and in the workplace (productivity) are outcomes from the standard oral health set which could be useful for studies of the outcome of care for people with acute dental pain and/or infection but which were not employed in any of the studies within our review.[22]

Primary medical care and to a lesser extent primary dental care have been recent targets of global efforts to tackle antibiotic resistance through stewardship programmes by reducing unnecessary and inappropriate prescribing.[36 37] A hybrid umbrella/systematic review of measures to evaluate the effectiveness of antibiotic stewardship programmes, in primary medical and dental care respectively, found similar outcomes to this present review, including drug allergy, re-consultation rates and patient satisfaction.[38] Notably, the study about antibiotic stewardship measures found dental studies focused only on antibiotic use and the authors concluded that a range of metrics encompassing the wider measures employed in studies of medical care, including patient-reported outcomes, should also be utilised in dentistry. Our findings reiterate this idea that a diverse range of outcomes should be used to evaluate care for people with acute dental conditions. Clinical outcomes such as signs and symptoms of pain and infection, and complications (including unplanned dental visits) should be employed in future studies, together with patient-reported measures such as satisfaction with the outcome of care.

Most studies in the review used unidimensional pain scales which are recognised to work well for acute pain: visual analogue scale (VAS), Heft-Parker scale, numeric rating scale and category pain scale.[32] Interestingly, none used the unidimensional pain scales based on images: Faces Pain Scale or Wong-Baker Faces Pain Scale.[32]. Unsurprisingly none used the McGill Pain Scale or other multidimensional scales which are recognised to be more useful for chronic than acute pain.[32] Future research to compare the utility of pain scales based on images with the other unidimensional pain scales for use in urgent dental care settings would be useful.

Dental antibiotic and opioid prescribing are recent priorities for clinicians and policymakers around the world, with overprescribing identified as a problem driving the development and spread of antibiotic resistance[7] and substance misuse disorder[39], respectively. Prescribing rates and choices varying between countries, and solutions to tackle the problem of overprescribing need to be tailored to the local context.[14 40] A recent pilot trial of a clinical decision prescribing tool and targeted education to improve dental antibiotic and opioid prescribing in Australia demonstrated a 41% reduction in antibiotic usage and 59% reduction in opioids.[16] Clinical trials of antibiotic and opioid stewardship interventions are also planned in the UK[41] and US.[42] Further research to develop a set of core outcomes for studies relating to the care of adults with acute dental pain and infection would be useful in the evaluation of stewardship interventions, to enable direct comparisons between stewardship interventions internationally.[43]

Facilitating improvements in the quality of care for people with acute dental pain and/or infection is an important use for the outcomes identified in this study. As such, these measures will be useful in research, clinical and public health settings and future research should be directed towards their utilisation across various health care settings.

Other information

This systematic narrative review was registered in the PROSPERO International Register of Systematic Reviews (CRD42020210183) and contains details of the protocol for this study.

Data collection forms and other material used in the review are available (upon reasonable request) from the corresponding author.

Authors' contributions: WT was responsible for all aspects of the study including conception of the idea, acquisition of funding, and recruitment of the author team. Design of the study including agreeing search terms, inclusion/exclusion criteria and databases to be searched (following advice from the information specialist) was shared between all authors (CC, CP, LT, SH and WT). Database searches were undertaken by WT, study selection was undertaken by CP, LT, SH and WT (as detailed in the methods section). All authors were involved with interpretation of the final data and agreement about key points for this paper.

LT and WT drafted the paper and CP and SH critically reviewed. All authors approved the final version for publication and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the study were resolved.

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Tables

Table 1: Characteristics of included studies

Study	Study type	Objective	Population * (patient age, setting, country)
1. Fazakerley et al, 1993[44]	Comparative double-blind trial.	To evaluate the efficacy of cephradine, amoxicillin and phenoxymethylpenicillin in the treatment of dentoalveolar infections.	18-65 years. University dental clinic. United Kingdom.
2. Gibson et al, 1993[45]	Prospective survey.	To investigate the success of treatment in resolving the chief complaint of pain and to determine the compliance with further dental care for the original dental problem.	18 years or older. University dental clinic. Canada
3. Fouad et al, 1996[46]	Double-blind, placebo-controlled clinical trial.	To examine the effect of penicillin supplementation on the reduction of symptoms and the course of recovery of the localised acute apical abscess after emergency endodontic treatment.	18 years or older. University dental clinic. United States.
4. Penniston et al, 1996[47]	Prospective, randomized, double-blind, placebo-controlled clinical trial.	To compare the analgesic efficacy of ketorolac tromethamine following intraoral periapical infiltration injection or intramuscular injection of the drug.	18-65 years. University dental clinic. United States.
5. Adriaenssen et al, 1998[48]	Open, randomized, multicentre comparative study.	Comparison of the efficacy, safety and tolerability of azithromycin and co-amoxiclav in the treatment of acute periapical abscesses.	18 -75 years. Dental practices. Belgium.
6. Doroschak et al, 1999[49]	Randomized, double-blind, placebo-controlled study.	To determine if a combination of an NSAID and an opioid provide greater pain relief than either drug alone.	18-65 years. University dental clinic. United States.
7. Gallatin et al, 2000[50]	Prospective, double-blind, randomized study.	To evaluate pain reduction in untreated irreversible pulpitis using an intraosseous injection of Depo-Medrol.	18 years or older. University dental clinic. United States.
8. Houck et al, 2000[25]	Prospective, randomized blinded study.	To evaluate postoperative pain and swelling after performing a trephination procedure in symptomatic necrotic teeth with radiolucencies.	Adults*. University dental clinic. United States.
9. Nagle et al, 2000[51]	Prospective, randomized, double-blind study.	To determine the effect of penicillin on pain in untreated teeth diagnosed with irreversible pulpitis.	Adults* University dental clinic. United States.

10. Henry et al, 2001[26]	Prospective, randomized, double-blind, placebo-controlled study.	To determine the effect of penicillin on postoperative pain and swelling in symptomatic necrotic teeth.	18 years or older. University dental clinic. United States.
12. Hersh et al, 2003[52]	Randomized, double-blind, placebo-controlled clinical trial.	Efficacy and safety of a benzocaine intra-oral patch in patients presenting with spontaneous toothache pain	18-65 years. University dental clinic. United States.
13. Runyon et al, 2004[53]	Prospective, randomized, double-blind, placebo-controlled trial.	To determine if penicillin is necessary or beneficial in the treatment of undifferentiated dental pain without overt infection.	18 years or older. Emergency department. United States.
14. Campanelli et al, 2008[54]	Clinical study.	To record the objective and subjective systemic signs of emergency patients presenting with pulp necrosis and localized acute apical abscess.	18 years or older. University dental clinic. United States.
15. Cohen et al, 2009[28]	Cross-sectional survey.	The pharmacist's role in managing toothache pain from the perspective of the patient.	21 years or older. Community pharmacy. United States.
16. Wilson et al, 2013[27]	Retrospective questionnaire survey.	To record the levels of patient satisfaction with oral urgent treatment and to highlight areas for improvement in both training and service provision.	18 years or older. Rural community clinic.* Tanzania
17. Sethi et al, 2014[55]	Randomised clinical trial.	To compare and evaluate the effect of single oral dose of 100 mg tapentadol, 400 mg etodolac, or 10 mg ketorolac as a pre-treatment analgesic for the prevention and control of postoperative endodontic pain in patients with symptomatic irreversible pulpitis	18-60 years. Dental college clinic. India.
18. Pavithra et al, 2015[56]	Randomized double blind trial.	To compare and evaluate analgesic effectiveness of Ibuprofen and Aceclofenac in management of acute irreversible pulpitis.	20-50 years. Dental college clinic. India.
19. Bultema et al, 2016[57]	Prospective, double-blind randomized trial.	To compare liposomal bupivacaine versus bupivacaine for pain control in untreated, symptomatic irreversible pulpitis.	18 years or older. University dental clinic. United States.
20. Sebastian et al, 2016[58]	Prospective, randomized study.	To compare debridementversus no debridement on postoperative pain in emergency patients with symptomatic teeth, a pulpal diagnosis of necrosis, and aperiapical radiolucency.	18 years or older. University dental clinic. United States.
21. Santini et al, 2017[59]	Double blind, controlled parallel design.	To compare the overallanalgesic effectiveness of two combinations of opioid and non-opioid analgesics for acute periradicular abscess.	Over 18 years. Dental hospital. Brazil.

22. Taggar et al, 2017[60]	Randomized, double-masked, controlled, parallel-group trial.	To compare the analgesic effect of a single dose of ibuprofen sodium dihydrate with that of a comparable dose of ibuprofen acid in endodontic pain patients presenting with moderate to severe pain.	18-60 years. [Setting unclear]. United States.
23. Aaron et al, 2018[61]	Single centre prospective clinical Study.	To determine if dentists are successful in reducing pain caused by acute apical abscess in a National Health Service emergency setting and if different treatment strategies result in different levels of pain reduction.	20-68 years. Primary care dental clinic. United Kingdom.
24. Beus et al, 2018[29]	Prospective, randomized, single-blind study.	To compare the postoperative course of incision and drain with drain placement vs mock incision and drainage procedure with mock drain placement after endodontic debridement in swollen emergency patients with symptomatic teeth and a pulpal diagnosis of necrosis.	18 years or older. University dental clinic. United States.
25. Eren et al, 2018[62]	Single-blinded, single-centre, randomized controlled trial.	To evaluate three emergency procedures for their ability to alleviate clinical symptoms associated with symptomatic teeth having signs of (at least) partial irreversible pulpitis.	18-60 years. University dental clinic. Turkey.
26. Wolf et al, 2019[63]	Prospective randomised study.	To compare the outcomes of two emergency treatment procedures to alleviate pain from localized symptomatic apical periodontitis: complete chemo-mechanical disinfection of the root canal system, or removal of necrotic tissue from the pulp chamber without instrumentation of the root canals.	18 years or older. University dental clinic. Sweden
27. Al-Rawhani et al, 2020[64]	Randomized placebo-controlled double-blind trial.	To evaluate the effect of preoperative administration of a single, oral dose of 50 mg diclofenac potassium on postoperative pain in patients with symptomatic irreversible pulpitis (SIP) in mandibular molars.	18 years or older. University dental clinic. Egypt.
28. da Silva et al, 2020[65]	Double-blind, randomized clinical trial.	To compare the acetaminophen administration efficacy or its combination with codeine for pain control in acute apical abscesses cases.	18 years or older. University dental clinic. Brazil.

* Where not specified in the paper, authors were contacted to confirm participants were all over 18 years of age and case was for only people with acute dental pain or infection.

Table 2: Outcome measures employed in each included study.

	Signs/symptoms of dental pain or infection						Complications or harm		Patient-reported outcomes	
	Pain intensity - Unstimulated	Pain intensity - Stimulated	Pain Reduction	Rescue pain relief taken	Swelling	Other signs/ symptoms of infection	Adverse drug reaction	Unplanned visits	Satisfaction with outcome	Other
Fazakerley et al, 1993[44]	VAS				Numeric scale	Temperature Lymph nodes involved				
Gibson et al, 1993[45]	Yes/No			Yes/No				Yes/No		
Fouad et al, 1996[46]	VAS			Amount	Category scale	Fever, Trismus or Swallowing difficulty	Allergy GI Tract	Yes/No		
Penniston et al, 1996[47]	VAS, HP-VAS and Category Scale						Infection Pain			
Adriaenssen et al, 1998[48]	Category scale	Category scale			Yes/No	Gingival redness Bone loss	Headache			
Doroschak et al, 1999[49]	VAS, HP-VAS and Category Scale						GI tract Headache Euphoria Sedation			
Gallatin et al, 2000[50]	Category scale	Category scale		Amount						
Houck et al, 2000[25]	Numeric scale	Numeric scale		Amount & type	Numeric scale					
Nagle et al, 2000[51]	Numeric scale	Numeric scale		Amount						
Henry et al, 2001[26]	Numeric scale	Numeric scale		Amount & type	Numeric scale					
Hersh et al, 2003[52]			Verbal pain relief scale							

*Runyon et al, 2004[53]	VAS				Yes/No	Temperature Purulence Trismus				
Campanelli et al, 2008[54]	VAS					Malaise				
*Cohen et al, 2009[28]									Category scale	
***Wilson et al, 2013[27]**			**Category scale**						**Category scale**	**Cost of care**
Sethi et al, 2014[55]	**VAS**						**Nausea Vomiting Dizziness Headache Heartburn**			
Pavithra et al, 2015[56]	**VAS**									
Bultema et al, 2016[57]	VAS			Delayed opioid prescription			Numbness	Yes/No		
Sebastian et al, 2016[58]	HP-VAS			Delayed opioid prescription						
Santini et al 2017[59]	**VAS**			**Yes/No**			**Nausea Vomiting Dizziness Drowsiness Headache**			
Taggar et al, 2017[60]	VAS	Bite force to elicit pain	Time to 50% pain relief							
Aaron et al, 2018[61]	Modified pain quality assessment scale									
Beus et al, 2018[29]	HP-VAS			Amount and type	Perception of whether 'swelling becoming smaller'	Experience of bad taste or pus drainage				Perception of whether 'feeling better'

Eren et al, 2018[62]	**VAS**	**Yes/No on chewing and thermal stimulus**	**Amount**			
Wolf et al, 2019[63]	Numeric scale		Yes/No Opioid/ Non-opioid	Antibiotics prescribed	Yes/No	
Al-Rawhani et al, 2020[64]	**HP-VAS**		**Yes/No**			
da Silva et al, 2020[65]	**VAS**		**Yes/No**			

Nausea
Vomiting
Dizziness
Drowsiness
Headache

Abbreviations: VAS = Visual Analogue Scale; HP-VAS = Heft Parker Visual Analogue Scale

Studies highlighted in bold are those undertaken in LMICs.

*** Study undertaken in non-dental setting**

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Table 3: Data sources and data collection periods.

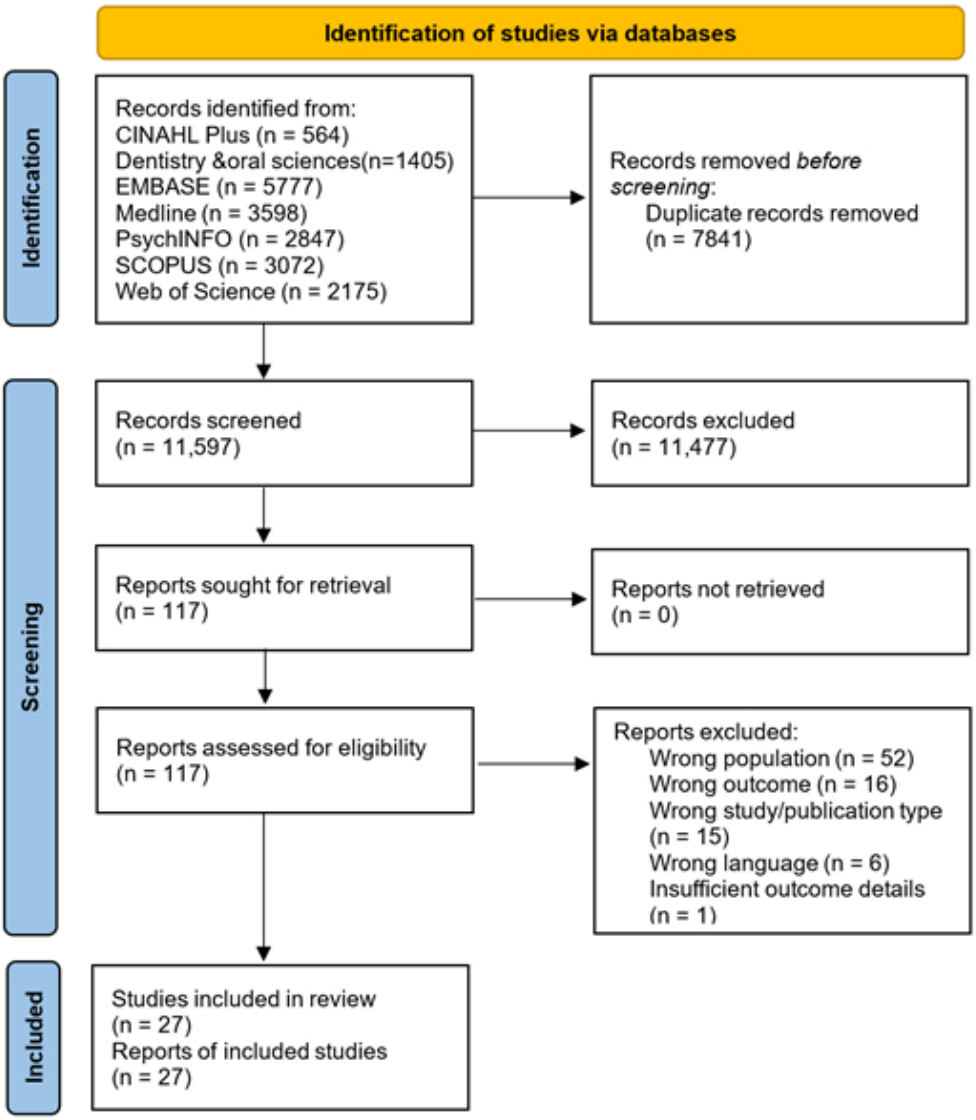
	Patient reported		Clinician observed	
	Patient diary	Questionnaires or interviews	In-person review	In-person monitoring
Fazakerley et al, 1993[44]			5 days	
Gibson et al, 1993[45]		2 days		
Fouad et al, 1996[46]	3 days			
Penniston et al, 1996[47]	6 hours			
Adriaenssenet al, 1998[48]			10 days	
Doroschak et al, 1999[49]	1 day			
Gallatin et al, 2000[50]	1 week			
Houck et al, 2000[25]	1 week			
Nagle et al, 2000[51]	1 week			
Henry et al, 2001[26]	1 week			
Hersh et al, 2003[52]				90 minutes
Runyon et al, 2004[53]			1 week	
Campanelli et al, 2008[54]			2 weeks	
Cohen et al, 2009[28]		1 year		
Wilson et al, 2013[27]		**1 year***		
Sethi et al, 2014[55]	**1 day**			
Pavithra et al, 2015[56]		**45 minutes**		
Bultema et al, 2016[57]	3 days			
Sebastian et al, 2016[58]	5 days			
Santini et al 2017[59]	**3 days**			
Taggar et al, 2017[60]				1 hour
Aaron et al, 2018[61]		1 day		
Beus et al, 2018[29]	4 days			
Eren et al, 2018[62]	**1 week**			
Wolf et al, 2019[63]		5 days		
Al-Rawhani et al, 2020[64]	**2 days**			
da Silva et al, 2020[65]	**3 days**			

Studies highlighted in bold are those undertaken in LMICs.

* Where not specified in the paper, authors were contacted to confirm the timescales.

Figure Legends:

Figure 1: PRISMA flow chart detailing selection of the included studies



PRISMA flow chart detailing selection of the included studies

350x400mm (38 x 38 DPI)

Supplemental Material

Table S1 – Inclusion/Exclusion Criteria

Inclusion criteria:

- Population:
  - Adults presenting with acute dental pain and/or infection
  - Any healthcare setting or service (not limited to dentistry)
- Intervention
  - Any care provided for the relief of acute dental pain or treatment of acute dental infection, including operative and pharmacological treatment and other non-pharmacological approaches (including advice only or referral to other services).
- Outcome
  - All outcomes measured and reported by the study which are related to the relief of acute dental pain or treatment of acute dental infection.
- Study/publication type
  - Primary research reported in peer reviewed journals
  - English language only

Exclusion criteria:

- Population
  - Animal studies
  - In-vitro / lab-based studies
  - People under the age of 18 years
  - People with other oral or dental conditions (eg emergency dental conditions such as cervico-facial infections requiring hospitalisation, dental trauma or haemorrhage following an extraction; oral cancer; or chronic conditions such as chronic facial pain, TMD or trigeminal neuralgia)
  - People attending for routine preventative care
  - People attending for postoperative pain following routine/scheduled dental care eg removal of third molars
  - People with unusual medical conditions eg glucose-6-dehydrogenase deficiency
  - Papers which include both adults and children
  - Papers which include non-acute as well as acute conditions
  - Paper which included non-dental as well as dental conditions
- Intervention
  - Approaches outside of conventional guidelines eg holistic or complementary therapies including acupuncture
- Outcomes
  - Outcomes which are not related to the relief of acute dental pain or treatment of acute dental infection.
  - Outcomes relating to local anaesthesia to enable treatment
- Study/publication type:
  - Systematic review
  - Guidelines and guideline development
  - Trial Protocol
  - Opinion piece/Commentary/Review articles/Case Reports/Letters
  - Qualitative studies
  - Studies if updates had subsequently been published
  - Manuscript not in English (e.g. abstract in English but not the rest)
  - No abstract available – or only an abstract available

Table S2 – Quality assessment of the studies using Critical Appraisal Skills Programme (CASP) Checklist for Randomised Controlled Trials

	a) Is the basic study design valid for an RCT?			b) Was the study methodologically sound?					c) What are the results?		d) Will the results help?		Overall
	1. Clear research question?	2. Random-isation?	3. All participants accounted for?	4a. Participants blinded?	4b. Investigators blinded?	4c. Analysts blinded?	5. Study groups similar at the start?	6. Same treatment for each group?	7. Comprehensive reporting?	8. Benefits vs harms/costs?	9. Locally applicable?	10. Better than existing care?	Include?
Fazakerley et al, 1993	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes
Fouad et al, 1996	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Yes	Can't tell	Yes
Houck et al, 2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nagle et al, 2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pavithra et al, 2015	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes
Santini et al, 2017	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Yes
Beus et al, 2018	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	No	Yes	Yes	Can't tell	Yes
Eren et al, 2018	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wolf et al, 2019	Yes	Yes	Yes	Can't tell	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Al-Rawhani et al, 2020	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes
da Silva et al, 2020	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table S3 – Quality assessment of studies which were not randomised controlled trials, using the Quality Assessment Tool for Studies with Diverse Designs (QATSDD)

	Explicit theoretical framework	Aims in main report	Setting described	Sample size considered	Sample of reasonable size	Data collection method	Choice of data collection tool(s)	Detailed recruitment data	Measuring tool assessed	Question and method fit - data collection	Question and method fit - analysis	Analysis method selected	Users involved in design	Strength/ limitation discussion	Total (% of maximum)
Scoring: 0 = No mention; 1=very slightly covered; 2=Moderately covered; 3=Completely covered. Where independent reviewer scores differed, averages are provided.															
Gibson et al, 1993	0	2	2	0	3	2	1	2	0	3	2	1	1	2	21 (53%)
Nusstein et al, 2002	1	3	2	0	0	3	2	3	1	2	3	1	0	1	22 (55%)
Campanelli et al, 2008	0	2	3	0	1	3	0	3	1	3	3	1	0	1	21 (53%)
Cohen et al, 2009	3	3	3	1	2	3	3	3	1	3	3	3	3	2	36 (90%)
Wilson et al, 2013	0	1	3	0	1	1	3	2	1	2	2	1	3	3	23 (58%)
Aaron et al, 2018	0	3	3	3	3	3	1	0	0	3	2	1	0	2	24 (60%)
Penniston et al, 1996	0	2	3	3	1	2	0	2.5	0	3	3	1	0	0	20.5 (51%)
Adriaenssen et al, 1998	2	1	3	3	3	2	1	2	0	1	2	0	0	0	20 (50%)
Doroschak et al, 1999	3	3	3	2	1	3	3	2.5	2	3	3	1	0	2	31.5 (79%)
Gallatin et al, 2000	3	3	1	0	1	3	1	3	0	3	2	1	0	1	22 (55%)
Henry et al, 2001	3	3	1	0	1.5	2.5	0	3	0	3	2	1	0	2	22 (55%)
Hersh et al, 2003	3	3	3	0	3	2	3	3	0	3	3	2	0	2	30 (75%)
Runyon et al, 2004	3	3	2	3	3	3	1	3	0	3	3	2	0	3	32 (80%)
Sethi et al, 2014	1	3	1	2	3	3	3	3	0	3	3	2	0	1	28 (70%)
Bultema et al, 2016	3	3	1	0	3	2	2	3	0	3	3	1	0	2	26 (65%)
Sebastian et al, 2016	2	3	1	0	3	2	1	3	0	2	2	1	0	1	21 (53%)
Taggar et al, 2017	3	3	1	1	3	3	1	3	0	2	2	1	0	3	26 (65%)

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Y
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Y
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Y
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Y
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Y
Synthesis of results	6	Specify the methods used to present and synthesise results.	Y
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Y
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Y
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Y
Interpretation	10	Provide a general interpretation of the results and important implications.	Y
OTHER			
Funding	11	Specify the primary source of funding for the review.	Y
Registration	12	Provide the register name and registration number.	Y

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8
Study characteristics	17	Cite each included study and present its characteristics.	9
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	9
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	10/11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	10+11
	23c	Discuss any limitations of the review processes used.	10+11
	23d	Discuss implications of the results for practice, policy, and future research.	11-13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	13
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	13
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1
Competing interests	26	Declare any competing interests of review authors.	1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	13

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

PRISMA 2020 Checklist

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TITLE PAGE

Title:

Outcomes to evaluate care for adults with acute dental pain and infection: a systematic narrative review.

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Competing interests statement

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organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Word count – 3479

ABSTRACT

Objective: To identify outcomes reported in peer-reviewed literature for evaluating the care of adults with acute dental pain or infection.

Design: Systematic narrative review.

Setting/Participants: Primary research studies published in peer-reviewed literature and reporting care for adults with acute dental pain or infection across healthcare settings. Reports not in English language were excluded.

Study selection: Seven databases (CINAHL Plus, Dentistry and Oral Sciences Source, EMBASE, MEDLINE, PsycINFO, Scopus, Web of Science) were searched from inception to December 2020. Risk of bias assessment used the Critical Appraisal Skills Programme checklist for randomised controlled trials and Quality Assessment Tool for Studies of Diverse Design for other study types.

Outcomes: Narrative synthesis included all outcomes of care for adults with acute dental pain or infection. Excluded were outcomes about pain management to facilitate treatment, prophylaxis of post-surgical pain/infection or traumatic injuries.

Results: Searches identified 19,437 records, and 27 studies (dating from 1993 to 2020) were selected for inclusion. Across dental, pharmacy, hospital emergency and rural clinic settings, the studies were undertaken in high-income (n=20) and low/middle-income (n=7) countries. Two clinical outcome categories were identified: signs and symptoms of pain/infection, and complications following treatment (including adverse drug reactions and reattendance for the same problem). Patient-reported outcomes included satisfaction with the care. Data collection methods included patient diaries, interviews and in-person reviews.

Discussion: A heterogenous range of study types and qualities were included: one study, published in 1947, was excluded only due to lacking outcome details. Studies from dentistry reported just clinical outcomes; across wider healthcare more outcomes were included.

Conclusions: A combination of clinical and patient-reported outcomes are recommended to evaluate care for adults with acute dental pain or infection. Further research is recommended to develop core outcomes aligned with the international consensus on oral health outcomes.

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Strengths and limitations of this study

- The first systematic review to examine outcome measures of care for adults with acute dental pain or infection across healthcare settings.
- The outcomes will be important for evaluating new dental antibiotic and opioid stewardship interventions, as these drugs are frequently overprescribed for adults with acute dental pain and infection, exacerbated by the COVID-19 pandemic.
- Studies about paediatric patients, studies about the post-operative management of pain, studies about local anaesthesia to facilitate dental treatment, studies about traumatic injuries and papers not in English language were excluded due to key differences in clinical management.
- Two independent reviewers extracted data and two different reviewers assessed the quality using either the Critical Appraisal Skills Programme (for the randomised controlled trials) or the Quality Assessment Tool for Studies with Diverse Designs.
- Reporting based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 guidelines, with searches of seven major electronic databases from their inception to December 2020.

MAIN TEXT

Introduction:

Acute dental pain has a significant impact on quality of life.[1 2] Timely intervention for the relief of dental pain and infection is essential to prevent worsening of ill health and reduce the risk of potentially life-threatening complications, such as sepsis, airway occlusion or analgesic overdose.[3 4] Failure of initial treatment to relieve dental pain and infection can result in patient reattending for further treatment, including to emergency medical care.[5] Thus, ensuring high quality care for people with acute dental problems is critical for both patient safety and service efficiency. Outcomes to evaluate the care provided for people with acute dental pain and/or infection are important.

Evidence-based clinical guidelines can improve the provision of quality healthcare and patient outcomes.[6] Guidelines for treating acute dental pain and infection are generally based on the principle that operative dental procedures (such as removal of a tooth or its pulp) are indicated to address the cause and prevent symptoms recurring.[7] Drugs such as analgesics and antibiotics have a limited role in dentistry and should usually only be used in addition to dental procedures.[8 9] Suboptimal treatment of dental pain and infection with drug prescriptions instead of dental procedures is common, including by general medical practitioners and in emergency departments.[10-12] The contribution of dentistry to global efforts to tackle antibiotic resistance[13]and opioid substance misuse disorder has been highlighted, with a call for the profession to improve its approach to stewardship of these drugs.[7 14 15]

Whilst a plethora of drug trials for the treatment of dental pain or infection have been published, there is little research on patient outcomes following urgent dental care for acute dental pain or infection.[5] A rise in the number of trials to evaluate dental antibiotic stewardship and opioid stewardship interventions is anticipated, with a focus on optimising care and judicious use of medicines for adults (where more than 90% of dental prescribing occurs).[16] To evaluate the effectiveness of these sorts of interventions and to enable improvements in the quality of urgent dental care, this study aimed to identify outcomes from the peer-reviewed literature for evaluating care for adults with acute dental pain and/or infection.

Objectives:

The research question was "What measures in the published literature have been employed to evaluate the outcome of care for adults with acute dental pain and/or infection?"

Methods:

Patient and public involvement

A coproduction team designed and delivered this systematic narrative review. Experts by experience (patients) of urgent dental care and/or complications of dental antibiotics (CC and CP) and academic dental professionals (LT, SH and WT) were involved in all stages of this study, from refining the research question and search terms which had been drafted by WT through to disseminating the results. Through discussion between the members of the coproduction team, involvement with each step of the review was allocated according to the skills they wished to develop and the time they had available to contribute at the relevant stages. Individual contributions are indicated in the following sections.

Eligibility criteria

Primary research studies published in peer-reviewed journals were included if they reported outcomes of care for adults (aged over 18-years) treated for acute dental pain and/or infection with advice, prescriptions, or interventions (such as dental extraction). There was no restriction on the year of dissemination.

Studies which included care for children or for people with other oral or dental conditions (such as cervicofacial infections treated as hospital inpatients or post-surgical pain control) were excluded. Studies of urgent dental care for traumatic injuries were excluded as this is a markedly different population and the subject of a separate study.[17] Reports which did not include the outcomes of care provided (or details of how those outcomes were measured) were also excluded, such as studies about the efficacy of local anaesthesia to facilitate the provision of dental procedures at point of care. Primary research studies not published in peer reviewed journals (such as conference abstracts, case studies and other grey literature) were

excluded as the research was seeking tried and tested outcomes for use in clinical trials. Studies not in the English language were excluded due to lack of translation facilities. Full details of the inclusion/exclusion criteria are detailed in Supplemental Material Table S1.

Population groups identified for subgroup analysis during the synthesis phase were dental vs other healthcare settings, and high-income vs low and middle-income countries (LMICs).

Information sources

On 29 November 2020, seven databases were searched from their earliest dates: CINAHL Plus, Dentistry and Oral Sciences Source, Ovid EMBASE, Ovid Medline, PyschINFO, Scopus and Web of Science.

Search strategy

The search strategy used to identify relevant papers from the database searches was developed in consultation with an information specialist at the University of Manchester. It consisted of 'population' AND 'intervention' terms. Population terms were: (Acute* OR Urgent OR Unschedul* OR Emergenc*) AND (Dental* OR Odontogenic OR Dentoalveolar) AND (Pain OR Toothache OR Pulpitis OR Infection OR Swell* OR Abscess OR Pericoronitis OR Osteitis OR Socket OR Periodontitis OR Implantitis OR Ulcer* OR Stomatitis). Intervention terms were: Patient Care OR Dental Care OR Procedure OR Treat* OR Endodont* OR Exodont* OR Extract* OR Extirpat* OR Incis* OR Drain* OR Debrid* OR Irrigat* OR Prescri* OR Antibiotic* OR Antimicrob* OR Antiseptic OR Analgesi* OR Advice OR Refer*. Full details of the search terms and limits employed with each database are detailed in Supplemental Material Table S2.

Limits included: "human" as animal and laboratory studies were not eligible for the review, and "English language" as justified in the 'eligibility criteria' section. There were no limits on the date of included studies.

Selection process

Titles and abstracts from the database searches (undertaken by WT) were transferred into Endnote X9 where duplicates were removed (by WT) and the title/abstracts were screened

(independently by WT and SH) for potential inclusion. Full texts of all shortlisted studies were assessed for eligibility (independently by WT and LT). Where necessary, corresponding authors were contacted to confirm whether the included population met our inclusion criteria. Disagreements at each stage of the process were resolved through discussion between the screeners.

Data collection process

The characteristics (study type, objective, and population) and outcomes, data source (patient-reported, clinician observed or administrative system) and data collection instrument were collected from each report by two reviewers (LT and SH) working independently. Disagreements at each stage of the process were resolved through discussion between the reviewers.

Data items – outcomes and other variables

All outcomes relating to the outcomes of care provided to adults with acute dental pain or infection were sought, together with details about the sources of data and timescales between urgent dental treatment received by the participants and completion of data collection. In addition, specific details about the types of studies (eg randomised controlled trial or questionnaire study) and population were sought, including age range of patients, type of healthcare setting (such as dental clinic or pharmacy), country in which the study took place, and whether a high-income or LMIC country (based on World Bank definitions[18]). Details about study type, patient age, healthcare setting and country for each included study are provided in Table 1, details about which countries were LMICs are highlighted (in bold) in Table 2. There was no restriction on timeframes for the outcomes and where missing data was identified this was recorded in the results tables. Where necessary, corresponding authors were contacted to provide details relating to the data items sought (such as the age of participants).

Quality assessment

The shortlisted studies were assessed using the Critical Appraisal Skills Programme (CASP) Checklist for RCTs.[19] For studies which used a design not valid for an RCT (as assessed via the CASP RCT checklist), the Quality Assessment Tool for Studies with Diverse Design

(QATSDD) was used.[20] Quality assessment of all studies was undertaken by WT, with 30% of studies (selected at random from across the CASP and QATSDD sets) independently assessed by CP. Discrepancies in relation to each element of the assessment framework were resolved through discussion between the assessors and, where differences were just one point, the scores were averaged.

Synthesis methods

All studies which had been selected for inclusion and which had passed the quality assessment were eligible for inclusion in synthesis. Outcome data collected were initially categorised by WT based on a framework advocated for antimicrobial stewardship interventions[21] as the outcomes identified in this study were intended to be employed in trials of stewardship interventions. All authors of the paper discussed and agreed adjustments to the category titles, which aligned the language with that used in a recently published international consensus of oral health outcomes.[22]

The tabular structure displays a summary of outcomes for each study, using the structure identified. Table 2 presents clinical outcomes ('signs/symptoms of dental pain or infection' and 'complications or harm') and patient-reported outcomes ('satisfaction with the outcome of care' and 'other') for each study with details of how the outcome was measured (such as numeric pain scale). Sources of data employed in each study and the timescales between treatment provided to participants and completion of data collection are presented in Table 3.

Results

Study selection

Of the 19,437 records identified from database searches, 27 studies were selected for inclusion (see Figure 1). One study, published in 1947, was excluded as it was impossible to tell how the outcomes had been measured.[23] Another study[24] which may look like it should be included was excluded as it reported secondary analysis of data collected in other studies.[25 26]

Study characteristics

The included studies dated between 1993 and 2020 and encompassed a heterogenous range of designs, from randomised controlled trials to questionnaire surveys. Most studies (n=23) took

place in dental settings, one was in a hospital emergency department, another in a rural community healthcare clinic and a third was in community pharmacy; the setting for one study was unclear. The earliest 14 studies all took place in high income countries (during the period 1993 to 2012). Of the 13 studies which took place between 2013 and 2020, seven were based in LMICs (Brazil, Egypt, India, Tanzania, and Turkey). Further characteristics of the included studies, including their objectives, are presented in Table 1.

Quality assessment

Following application of the inclusion/exclusion criteria, 11 studies were quality assessed using the CASP framework for RCTs (see Supplemental Material Table S3) and 16 using the QATSDD tool (see Supplemental Material Table S4). Many of the studies assessed using the QATSDD criteria scored poorly, for example due to failure to justify the sample size or provision of a rationale for the analytic method used, and few studies covered the QATSDD criterion about patients being involvement in the study design.

Results of individual studies

The outcomes recorded in each individual study are presented in Table 2, including details about how they were measured. Two categories of clinical outcomes and one of patient-report outcomes were identified. Clinical outcomes included: 'signs and symptoms of dental pain/infection', and 'complications or other harm' resulting from treatment or disease progression. Patient-reported outcomes included patient satisfaction with the outcome of care.

As also shown in Table 2, various approaches were used for measuring the clinical outcomes, including unidimensional pain scales (such as a visual analogue scale (VAS) or category pain scale), amount of rescue medication taken, and the presence of absence of various signs and symptoms such as swelling, trismus or pyrexia. Complications were assessed by recording whether unplanned visits had been required or whether the patient had experienced symptoms of drug allergy or other adverse effects (such as gastrointestinal symptoms and headaches).

Details about data sources for the outcomes and duration of data collection in each study are presented in Table 3. Most of the outcomes were reported by patients (n=20) through diaries, questionnaires or interviews. A minority of studies (n=7) employed clinical observations

from in person monitoring or review during or after their treatment appointment. None of the studies used a combination of patient-reported and clinician observed data. No studies employed data from healthcare administrative systems. Data collection in most studies took place over less than a week (n=17). In six studies, the duration of data collection was one week, and two of the remaining four studies data collection completed one year after the participant received urgent dental treatment.

Results of syntheses

Pain was the most commonly reported sign/symptom (see Table 2), including unstimulated/spontaneous pain (n=24), pain stimulated by percussion, chewing or thermal stimulus (n=7) or the need for additional pain relief through use of rescue medication (n=14). Complications or other harm related to the treatment provided included adverse outcomes (such as drug allergy or nausea) and progression of the acute dental condition requiring unplanned visits for additional treatment. Patient satisfaction was only recorded in studies in non-dental healthcare settings[27 28] and only one dental study included patient-reported outcomes.[29]

Comparing results between high-income countries and LMICs found just one difference in the outcomes reported: none of the studies undertaken in LMICs reported on swelling as a sign of infection, compared to 35% (n=7/20) of studies undertaken in high-income countries. There was also one difference found in data sources for the outcomes: none of the LMIC-based studies recorded clinician observed outcomes compared to 30% (n=6/20) of studies in high-income countries. No differences were found in data collection periods.

Discussion

A diverse range of measures were identified to assess the outcomes of care for adults presenting with acute dental pain and/or infection across a range of healthcare settings in high income and LMICs. Most were clinical outcomes, such as signs and symptoms of pain and infection and complications or other harms following treatment (such as drug allergy). Patient-reported outcomes relating to satisfaction were only used in studies from non-dental settings. The range of outcomes and data collection periods were similar between high income countries and LMICs. Just one key difference was noted in their assessment: none of the LMIC studies reported clinician-observed data. This is the first study to focus

comprehensively on outcomes relating to acute dental conditions and a lack of consensus in outcomes reported across the studies was found.

Due to the heterogenous range of studies identified for inclusion, a systematic narrative review was selected to enable synthesis of the results. This type of review is, however, more subjective, and open to potential bias than conventional systematic reviews. Core outcome sets (COS) can improve consistency in reporting and maximise the value derivable from studies.[30] Further research is indicated to develop a COS relating to the care of people presenting with acute dental pain or infection across health care settings internationally. Given the high rates of inappropriate antibiotic prescribing for people with acute dental conditions[16 31] and the increasing recognition of the important contribution dentistry can make to global efforts to tackle antibiotic resistance[7], this COS will be particularly important.

Measuring what matters to patients has been recognised as central to improving patient care and service delivery, with patients needing to be involved in decisions about what to measure.[32] For this reason, experts by experience of urgent dental care were key members of our coproduction team, including when devising the review's search strategy. Funding to reimburse their time for participating in the length process of a systematic review was welcomed by the experts by experience.

The range of healthcare settings included in this review (dental clinics, pharmacies, hospital emergency departments and community clinics) mean the findings of this study are widely generalisable and can be easily translated to different health care settings around the world. Even though limited to English language, studies from a wide range of countries were included, across both high-income countries and LMICs. Six papers were excluded due to language (including 50% in Japanese) which may have introduced additional outcomes and differences in cultural practices.

Restricting this paper to published studies relating to adults from the peer-reviewed literature means that additional measures in the grey literature may have been missed as well as meaning that it fails to conform completely to the new PRISMA 2020 guidelines for systematic reviews which were published during the course of our study.[33] The authors decided additional searches of the grey literature would not, however, meet the research questions or their intention to identify outcomes which had been successfully tried and tested. Studies including children were excluded from this review as the outcomes (especially

patient-reported outcomes) are materially different.[34] Further, the trials for which these outcomes will be used by the authors relate to dental antibiotic stewardship and opioid stewardship for adult patients, which is the patient group where most overprescribing of these drugs occurs.[35 36]

The importance of valid, reliable, and feasible measures for improving the quality of oral health care, including patient-reported outcomes and experience measures has been recognised.[37] In 2020, an international consensus of patient-centred outcomes to measure adult oral health (focusing on caries and periodontal disease) was published and highlighted that multiple measures are required to capture the effect of oral health on the individual patient.[22] Where possible, we have adopted the terminology from this adult oral health standard set of outcomes when presenting our findings, such as 'complications or other harm resulting from treatment or disease progression' and 'unplanned visits.' However, whilst our findings cover some of the same territory, there are important differences in the detail especially relating to timescales. For example, there is no mention of 'infection' in the oral health outcomes and 'dental pain' covers only the frequency of pain in the last six months and 'complications' within 30 days, whereas our study found that these outcomes were measured in hours and days for people with acute dental conditions. Quality of life indicators such as the ability to eat, sleep, speak or carry out usual work activities at home and in the workplace (productivity) are outcomes from the standard oral health set which could be useful for studies of the outcome of care for people with acute dental pain and/or infection but which were not employed in any of the studies within our review.[22]

Primary medical care and to a lesser extent primary dental care have been recent targets of global efforts to tackle antibiotic resistance through stewardship programmes by reducing unnecessary and inappropriate prescribing.[38 39] A hybrid umbrella/systematic review of measures to evaluate the effectiveness of antibiotic stewardship programmes, in primary medical and dental care respectively, found similar outcomes to this present review, including drug allergy, re-consultation rates and patient satisfaction.[40] Notably, the study about antibiotic stewardship measures found dental studies focused only on antibiotic use and the authors concluded that a range of metrics encompassing the wider measures employed in studies of medical care, including patient-reported outcomes, should also be utilised in dentistry. Our findings reiterate this idea that a diverse range of outcomes should be used to evaluate care for people with acute dental conditions. Clinical outcomes such as signs and

symptoms of pain and infection, and complications (including unplanned dental visits) should be employed in future studies, together with patient-reported measures such as satisfaction with the outcome of care.

Most studies in the review used unidimensional pain scales which are recognised to work well for acute pain: visual analogue scale (VAS), Heft-Parker scale, numeric rating scale and category pain scale.[34] Interestingly, none used the unidimensional pain scales based on images: Faces Pain Scale or Wong-Baker Faces Pain Scale.[34]. Unsurprisingly none used the McGill Pain Scale or other multidimensional scales which are recognised to be more useful for chronic than acute pain.[34] Future research to compare the utility of pain scales based on images with the other unidimensional pain scales for use in urgent dental care settings would be useful.

Dental antibiotic and opioid prescribing are recent priorities for clinicians and policymakers around the world, with overprescribing identified as a problem driving the development and spread of antibiotic resistance[7] and substance misuse disorder[41], respectively. Prescribing rates and choices varying between countries, and solutions to tackle the problem of overprescribing need to be tailored to the local context.[14 42] A recent pilot trial of a clinical decision prescribing tool and targeted education to improve dental antibiotic and opioid prescribing in Australia demonstrated a 41% reduction in antibiotic usage and 59% reduction in opioids.[16] Clinical trials of antibiotic and opioid stewardship interventions are also planned in the UK[43] and US.[44] Further research to develop a set of core outcomes for studies relating to the care of adults with acute dental pain and infection would be useful in the evaluation of stewardship interventions, to enable direct comparisons between stewardship interventions internationally.[45]

Standardising the reporting of metrics will facilitate improvements in the quality of care for people with acute dental pain and/or infection. The outcomes identified in this study (both clinical and patient reported) should form the basis on which to build international consensus on a COS as these measures will be useful in research, clinical and public health settings. Future research should be directed towards development and utilisation of this outcome set across health care settings where people with acute dental pain and infection present for treatment.

Other information

No human or animal participants were involved so no ethics approval was required for this systematic narrative review. It was, however, registered in the PROSPERO International Register of Systematic Reviews (CRD42020210183) which contains details of the protocol for this study.

Data collection forms and other material used in the review are available (upon reasonable request) from the corresponding author.

Contributorship statement: WT was responsible for all aspects of the study including conception of the idea, acquisition of funding, and recruitment of the author team. Design of the study including agreeing search terms, inclusion/exclusion criteria and databases to be searched (following advice from the information specialist) was shared between all authors (CC, CP, LT, SH and WT). Database searches were undertaken by WT, study selection was undertaken by CP, LT, SH and WT (as detailed in the methods section). All authors were involved with interpretation of the final data and agreement about key points for this paper. LT and WT drafted the paper and CP and SH critically reviewed. All authors approved the final version for publication and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the study were resolved.

Competing interests statement

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare: support from the National Institute for Health Research (North-West Research Design Service) to reimburse time of the experts by experience to coproduce the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Data sharing statement

All data relevant to the study are included in the article or uploaded as supplementary information. No additional data are available.

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Tables

Table 1: Characteristics of included studies

Study	Study type	Objective	Population * (patient age, setting, country)
Fazakerley et al, 1993[46]	Comparative double-blind trial.	To evaluate the efficacy of cephradine, amoxicillin and phenoxymethylpenicillin in the treatment of dentoalveolar infections.	18-65 years. University dental clinic, UK.
Gibson et al, 1993[47]	Prospective survey.	To investigate the success of treatment in resolving the chief complaint of pain and to determine the compliance with further dental care for the original dental problem.	18 years or older. University dental clinic, Canada.
Fouad et al, 1996[48]	Double-blind, placebo-controlled clinical trial.	To examine the effect of penicillin on the reduction of symptoms and the course of recovery of the localised acute apical abscess after emergency endodontic treatment.	18 years or older. University dental clinic, US.
Penniston et al, 1996[49]	Prospective, randomized, double-blind, placebo-controlled clinical trial.	To compare the analgesic efficacy of ketorolac tromethamine following intraoral periapical infiltration injection or intramuscular injection of the drug.	18-65 years. University dental clinic, US.
Adriaenssen et al, 1998[50]	Open, randomized, multicentre comparative study.	Comparison of the efficacy, safety and tolerability of azithromycin and co-amoxiclav in the treatment of acute periapical abscesses.	18 -75 years. Dental practices, Belgium
Doroschak et al, 1999[51]	Randomized, double-blind, placebo-controlled study.	To determine if a combination of an NSAID and an opioid provides greater pain relief than either drug alone.	18-65 years. University dental clinic, US
Gallatin et al, 2000[52]	Prospective, double-blind, randomized study.	To evaluate pain reduction in untreated irreversible pulpitis using an intraosseous injection of Depo-Medrol.	18 years or older. University dental clinic, US.
Houck et al, 2000[25]	Prospective, randomized blinded study.	To evaluate postoperative pain and swelling after performing a trephination procedure in symptomatic necrotic teeth with radiolucencies.	Adults*. University dental clinic, US.
Nagle et al, 2000[53]	Prospective, randomized, double-blind study.	To determine the effect of penicillin on pain in untreated teeth diagnosed with irreversible pulpitis.	Adults* University dental clinic, US.
Henry et al, 2001[26]	Prospective, randomized, double-blind, placebo-controlled study.	To determine the effect of penicillin on postoperative pain and swelling in symptomatic necrotic teeth.	18 years or older. University dental clinic, US.
Hersh et al, 2003[54]	Randomized, double-blind, placebo-controlled clinical trial.	Efficacy and safety of a benzocaine intra-oral patch in patients presenting with spontaneous toothache pain	18-65 years. University dental clinic, US.
Runyon et al, 2004[55]	Prospective, randomized, double-blind, placebo-controlled trial.	To determine if penicillin is necessary or beneficial in the treatment of undifferentiated dental pain without overt infection.	18 years or older. Emergency department, US.
Campanelli et al, 2008[56]	Clinical study.	To record the objective and subjective systemic signs of emergency patients presenting with pulp necrosis and localized acute apical abscess.	18 years or older. University dental clinic, US.

Cohen et al, 2009[28]	Cross-sectional survey.	The pharmacist's role in managing toothache pain from the perspective of the patient.	21 years or older. Community pharmacy, US.
Wilson et al, 2013[27]	Retrospective questionnaire survey.	To record the levels of patient satisfaction with oral urgent treatment and to highlight areas for improvement in both training and service provision.	18 years or older. Rural community clinic*, Tanzania
Sethi et al, 2014[57]	Randomised clinical trial.	To compare and evaluate the effect of an oral dose of 100 mg tapentadol, 400 mg etodolac, or 10 mg ketorolac as a pre-treatment analgesic for the prevention and control of postoperative endodontic pain in patients with irreversible pulpitis.	18-60 years. Dental college clinic, India.
Pavithra et al, 2015[58]	Randomized double blind trial.	To compare and evaluate analgesic effectiveness of Ibuprofen and Aceclofenac in management of acute irreversible pulpitis.	20-50 years. Dental college clinic, India.
Bultema et al, 2016[59]	Prospective, double-blind randomized trial.	To compare liposomal bupivacaine versus bupivacaine for pain control in untreated, symptomatic irreversible pulpitis.	18 years or older. University dental clinic, US.
Sebastian et al, 2016[60]	Prospective, randomized study.	To compare debridement versus no debridement on postoperative pain in emergency patients with symptomatic pulpal necrosis, and apical radiolucency.	18 years or older. University dental clinic, US.
Santini et al, 2017[61]	Double blind, controlled parallel design.	To compare the overall analgesic effectiveness of two combinations of opioid and non-opioid analgesics for acute periradicular abscess.	Over 18 years. Dental hospital, Brazil
Taggar et al, 2017[62]	Randomized, double-masked, controlled, parallel-group trial.	To compare the analgesic effect of a single dose of ibuprofen sodium dihydrate with that of a comparable dose of ibuprofen acid in endodontic pain patients presenting with moderate to severe pain.	18-60 years. [Setting unclear], US.
Aaron et al, 2018[63]	Single centre prospective clinical Study.	To determine if dentists are successful in reducing pain caused by acute apical abscess in a National Health Service emergency setting and if different treatment strategies result in different levels of pain reduction.	20-68 years. Primary care dental clinic, UK.
Beus et al, 2018[29]	Prospective, randomized, single-blind study.	To compare the postoperative course of incision and drain with drain placement vs mock incision and drainage procedure with mock drain placement after endodontic debridement in swollen emergency patients.	18 years or older. University dental clinic, US.
Eren et al, 2018[64]	Single-blinded, single-centre, randomized controlled trial.	To evaluate three emergency procedures for their ability to alleviate clinical symptoms associated with symptomatic teeth having signs of (at least) partial irreversible pulpitis.	18-60 years. University dental clinic, Turkey.
Wolf et al, 2019[65]	Prospective randomised study.	To compare the outcomes of two emergency treatment procedures to alleviate pain from localized symptomatic apical periodontitis.	18 years or older. University dental clinic, Sweden.
Al-Rawhani et al, 2020[66]	Randomized placebo-controlled double-blind trial.	To evaluate the effect of preoperative administration of a single, oral dose of 50 mg diclofenac on postoperative pain in patients with symptomatic irreversible pulpitis.	18 years or older. University dental clinic, Egypt.
da Silva et al, 2020[67]	Double-blind, randomized clinical trial.	To compare the acetaminophen administration efficacy or its combination with codeine for pain control in acute apical abscesses cases.	18 years or older. University dental clinic, Brazil.

* Where not specified in the paper, authors were contacted to confirm participants were all aged >18 years and care was for only people with acute dental pain or infection.

Table 2: Outcome measures employed in each included study.

	Signs/symptoms of dental pain or infection						Complications or harm		Patient-reported outcomes	
	Pain intensity - Unstimulated	Pain intensity - Stimulated	Pain Reduction	Rescue pain relief taken	Swelling	Other signs/ symptoms	Adverse drug reaction	Unplanned visits	Satisfaction	Other
Fazakerley et al, 1993[46]	VAS				Numeric scale	Temperature, Lymphadenopathy				
Gibson et al, 1993[47]	Yes/No			Yes/No				Yes/No		
Fouad et al, 1996[48]	VAS			Amount	Category scale	Fever, Trismus or Swallowing difficulty	Allergy GI Trac	Yes/No		
Penniston et al, 1996[49]	VAS, HP-VAS and Category Scale						Injection pain			
Adriaenssen et al, 1998[50]	Category scale	Category scale			Yes/No	Gingival redness, Bone loss	Headache			
Doroschak et al, 1999[51]	VAS, HP-VAS and Category Scale						GI trac Headache Euphoria Sedation			
Gallatin et al, 2000[52]	Category scale	Category scale		Amount						
Houck et al, 2000[25]	Numeric scale	Numeric scale		Amount & type	Numeric scale					
Nagle et al, 2000[53]	Numeric scale	Numeric scale		Amount						
Henry et al, 2001[26]	Numeric scale	Numeric scale		Amount & type	Numeric scale					
Hersh et al, 2003[54]			Verbal pain relief scale							
*Runyon et al, 2004[55]	VAS				Yes/No	Temperature, Purulence, Trismus				
Campanelli et al, 2008[56]	VAS					Malaise				
*Cohen et al, 2009[28]									Category scale	
*Wilson et al, 2013[27]			Category scale						Category scale	Cost of care
Sethi et al, 2014[57]	VAS						GI Trac Dizziness			

Pavithra et al, 2015[58]	VAS						Headache Heartburn		
Bultema et al, 2016[59]	VAS			Delayed prescription			Numbness	Yes/No	
Sebastian et al, 2016[60]	HP-VAS			Delayed prescription					
Santini et al 2017[61]	VAS			Yes/No			GI Tract Dizziness Drowsiness Headache		
Taggar et al, 2017[62]	VAS	Bite force to elicit pain	Time to 50% pain relief						
Aaron et al, 2018[63]	Modified pain quality assessment scale								
Beus et al, 2018[29]	HP-VAS			Amount and type	Patient perception: 'swelling becoming smaller'	Experience of bad taste or pus drainage			Patient perception: 'feeling better'
Eren et al, 2018[64]	VAS	Yes/No on chewing and thermal stimulus		Amount					
Wolf et al, 2019[65]	Numeric scale			Yes/No Opioid/ Non-opioid		Antibiotics prescribed		Yes/No	
Al-Rawhani et al, 2020[66]	HP-VAS			Yes/No					
da Silva et al, 2020[67]	VAS			Yes/No			GI Tract Dizziness Drowsiness Headache		

Abbreviations: VAS = Visual Analogue Scale; HP-VAS = Heft Parker Visual Analogue Scale. GI Tract = Nausea, vomiting and diarrhoea.

*** Study undertaken in non-dental setting**

Table 3: Data sources and data collection periods.

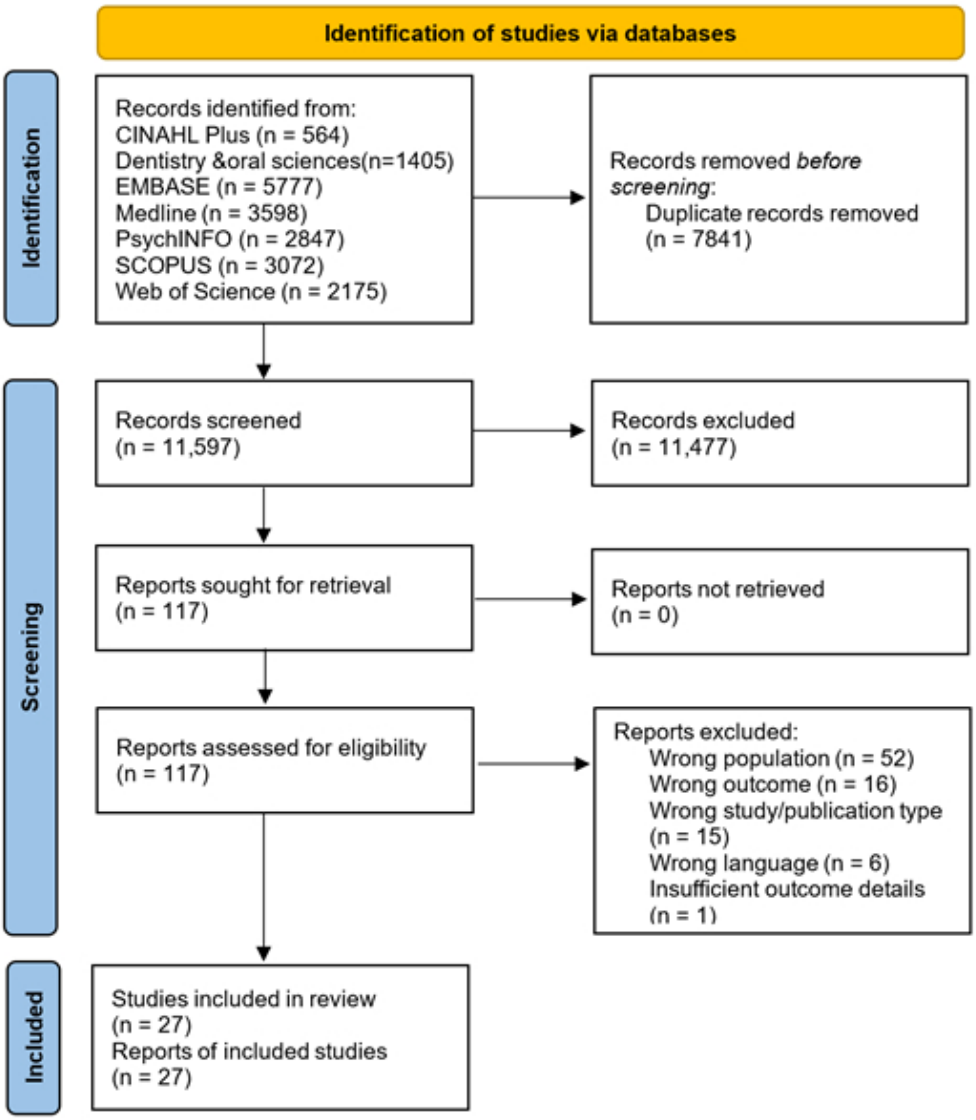
	Patient reported		Clinician observed	
	Patient diary	Questionnaires or interviews	In-person review	In-person monitoring
Fazakerley et al, 1993[46]			5 days	
Gibson et al, 1993[47]		2 days		
Fouad et al, 1996[48]	3 days			
Penniston et al, 1996[49]	6 hours			
Adriaenssenet al, 1998[50]			10 days	
Doroschak et al, 1999[51]	1 day			
Gallatin et al, 2000[52]	1 week			
Houck et al, 2000[25]	1 week			
Nagle et al, 2000[53]	1 week			
Henry et al, 2001[26]	1 week			
Hersh et al, 2003[54]				90 minutes
Runyon et al, 2004[55]			1 week	
Campanelli et al, 2008[56]			2 weeks	
Cohen et al, 2009[28]		1 year		
Wilson et al, 2013[27]		**1 year***		
Sethi et al, 2014[57]	**1 day**			
Pavithra et al, 2015[58]		**45 minutes**		
Bultema et al, 2016[59]	3 days			
Sebastian et al, 2016[60]	5 days			
Santini et al 2017[61]	**3 days**			
Taggar et al, 2017[62]				1 hour
Aaron et al, 2018[63]		1 day		
Beus et al, 2018[29]	4 days			
Eren et al, 2018[64]	**1 week**			
Wolf et al, 2019[65]		5 days		
Al-Rawhani et al, 2020[66]	**2 days**			
da Silva et al, 2020[67]	**3 days**			

Studies highlighted in bold are those undertaken in LMICs.

* Where not specified in the paper, authors were contacted to confirm the timescales.

Figure Legends:

Figure 1: PRISMA flow chart detailing selection of the included studies



PRISMA flow chart detailing selection of the included studies

350x400mm (38 x 38 DPI)

Supplemental Material

Table S1 – Inclusion/Exclusion Criteria

Inclusion criteria:

- Population:
  - Adults presenting with acute dental pain and/or infection
  - Any healthcare setting or service (not limited to dentistry)
- Intervention
  - Any care provided for the relief of acute dental pain or treatment of acute dental infection, including operative and pharmacological treatment and other non-pharmacological approaches (including advice only or referral to other services).
- Outcome
  - All outcomes measured and reported by the study which are related to the relief of acute dental pain or treatment of acute dental infection.
- Study/publication type
  - Primary research reported in peer reviewed journals
  - English language only

Exclusion criteria:

- Population
  - Animal studies
  - In-vitro / lab-based studies
  - People under the age of 18 years
  - People with other oral or dental conditions (eg emergency dental conditions such as cervico-facial infections requiring hospitalisation, dental trauma or haemorrhage following an extraction; oral cancer; or chronic conditions such as chronic facial pain, TMD or trigeminal neuralgia)
  - People attending for routine preventative care
  - People attending for postoperative pain following routine/scheduled dental care eg removal of third molars
  - People with unusual medical conditions eg glucose-6-dehydrogenase deficiency
  - Papers which include both adults and children
  - Papers which include non-acute as well as acute conditions
  - Paper which included non-dental as well as dental conditions
- Intervention
  - Approaches outside of conventional guidelines eg holistic or complementary therapies including acupuncture
- Outcomes
  - Outcomes which are not related to the relief of acute dental pain or treatment of acute dental infection.
  - Outcomes relating to local anaesthesia to enable treatment
- Study/publication type:
  - Systematic review
  - Guidelines and guideline development
  - Trial Protocol
  - Opinion piece/Commentary/Review articles/Case Reports/Letters
  - Qualitative studies
  - Studies if updates had subsequently been published
  - Manuscript not in English (e.g. abstract in English but not the rest)
  - No abstract available – or only an abstract available

Table S2 – Search terms for each database

Database	Population search terms	Boolean Operator	Intervention search terms	Limitations employed
CINAHL Plus (EBSCO Host)	((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or Implantitis or Ulcer* or Stomatitis))	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*)	English Language Academic Journals
Dentistry and Oral Science Sources (EBSCO Host)	((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or Implantitis or Ulcer* or Stomatitis))	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*)	English Language Academic Journals
EMBASE (Ovid Online)	((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or	English Language Human

	Implantitis or Ulcer* or Stomatitis)).mp		Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*).mp	
Medline (Ovid Online)	((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or Implantitis or Ulcer* or Stomatitis)).mp	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*).mp	English Language Human
PsychINFO (Ovid Online)	((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or Implantitis or Ulcer* or Stomatitis)).mp	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*).mp	English Language Human
Scopus	Search within article title, abstract, key words: '((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*)	Published Articles English Language Human

	Implantitis or Ulcer* or Stomatitis))’			
Web of Science	((Acute* or Urgent or Unschedul* or Emergenc*) AND (Dent* or Odontogenic or Dentoalveolar) AND (Pain or Toothache or Pulpitis or Infection or Swell* or Abscess or Pericoronitis or Osteitis or Socket or Periodontitis or Implantitis or Ulcer* or Stomatitis))	AND	(Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer* or Patient Care or Dental Care or Procedure or Treat* or Endodont* or Exodont* or Extract* or Extirpat* or Incis* or Drain* or Debrid* or Irrigat* or Prescri* or Antibiotic* or Antimicrob* or Antiseptic or Analgesi* or Advice or Refer*)	Articles English Language

Table S3 – Quality assessment of the studies using Critical Appraisal Skills Programme (CASP) Checklist for Randomised Controlled Trials

	a) Is the basic study design valid for an RCT?			b) Was the study methodologically sound?					c) What are the results?		d) Will the results help?		Overall
	1. Clear research question?	2. Random-isation?	3. All participants accounted for?	4a. Participants blinded?	4b. Investigators blinded?	4c. Analysts blinded?	5. Study groups similar at the start?	6. Same treatment for each group?	7. Comprehensive reporting?	8. Benefits vs harms/costs?	9. Locally applicable?	10. Better than existing care?	Include?
Fazakerley et al, 1993	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes
Fouad et al, 1996	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Yes	Can't tell	Yes
Houck et al, 2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nagle et al, 2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pavithra et al, 2015	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes
Santini et al, 2017	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Yes
Beus et al, 2018	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	No	Yes	Yes	Can't tell	Yes
Eren et al, 2018	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wolf et al, 2019	Yes	Yes	Yes	Can't tell	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Al-Rawhani et al, 2020	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes
da Silva et al, 2020	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table S3 – Quality assessment of studies which were not randomised controlled trials, using the Quality Assessment Tool for Studies with Diverse Designs (QATSDD)

	Explicit theoretical framework	Aims in main report	Setting described	Sample size considered	Sample of reasonable size	Data collection method	Choice of data collection tool(s)	Detailed recruitment data	Measuring tool assessed	Question and method fit - data collection	Question and method fit - analysis	Analysis method selected	Users involved in design	Strength/ limitation discussion	Total (% of maximum)
Scoring: 0 = No mention; 1=very slightly covered; 2=Moderately covered; 3=Completely covered. Where independent reviewer scores differed, averages are provided.															
Gibson et al, 1993	0	2	2	0	3	2	1	2	0	3	2	1	1	2	21 (53%)
Nusstein et al, 2002	1	3	2	0	0	3	2	3	1	2	3	1	0	1	22 (55%)
Campanelli et al, 2008	0	2	3	0	1	3	0	3	1	3	3	1	0	1	21 (53%)
Cohen et al, 2009	3	3	3	1	2	3	3	3	1	3	3	3	3	2	36 (90%)
Wilson et al, 2013	0	1	3	0	1	1	3	2	1	2	2	1	3	3	23 (58%)
Aaron et al, 2018	0	3	3	3	3	3	1	0	0	3	2	1	0	2	24 (60%)
Penniston et al, 1996	0	2	3	3	1	2	0	2.5	0	3	3	1	0	0	20.5 (51%)
Adriaenssen et al, 1998	2	1	3	3	3	2	1	2	0	1	2	0	0	0	20 (50%)
Doroschak et al, 1999	3	3	3	2	1	3	3	2.5	2	3	3	1	0	2	31.5 (79%)
Gallatin et al, 2000	3	3	1	0	1	3	1	3	0	3	2	1	0	1	22 (55%)
Henry et al, 2001	3	3	1	0	1.5	2.5	0	3	0	3	2	1	0	2	22 (55%)
Hersh et al, 2003	3	3	3	0	3	2	3	3	0	3	3	2	0	2	30 (75%)
Runyon et al, 2004	3	3	2	3	3	3	1	3	0	3	3	2	0	3	32 (80%)
Sethi et al, 2014	1	3	1	2	3	3	3	3	0	3	3	2	0	1	28 (70%)
Bultema et al, 2016	3	3	1	0	3	2	2	3	0	3	3	1	0	2	26 (65%)
Sebastian et al, 2016	2	3	1	0	3	2	1	3	0	2	2	1	0	1	21 (53%)
Taggar et al, 2017	3	3	1	1	3	3	1	3	0	2	2	1	0	3	26 (65%)

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Y
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Y
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Y
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Y
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Y
Synthesis of results	6	Specify the methods used to present and synthesise results.	Y
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Y
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Y
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Y
Interpretation	10	Provide a general interpretation of the results and important implications.	Y
OTHER			
Funding	11	Specify the primary source of funding for the review.	Y
Registration	12	Provide the register name and registration number.	Y

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8
Study characteristics	17	Cite each included study and present its characteristics.	9
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	9
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	10/11
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	10+11
	23c	Discuss any limitations of the review processes used.	10+11
	23d	Discuss implications of the results for practice, policy, and future research.	11-13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	13
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	13
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1
Competing interests	26	Declare any competing interests of review authors.	1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	13

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