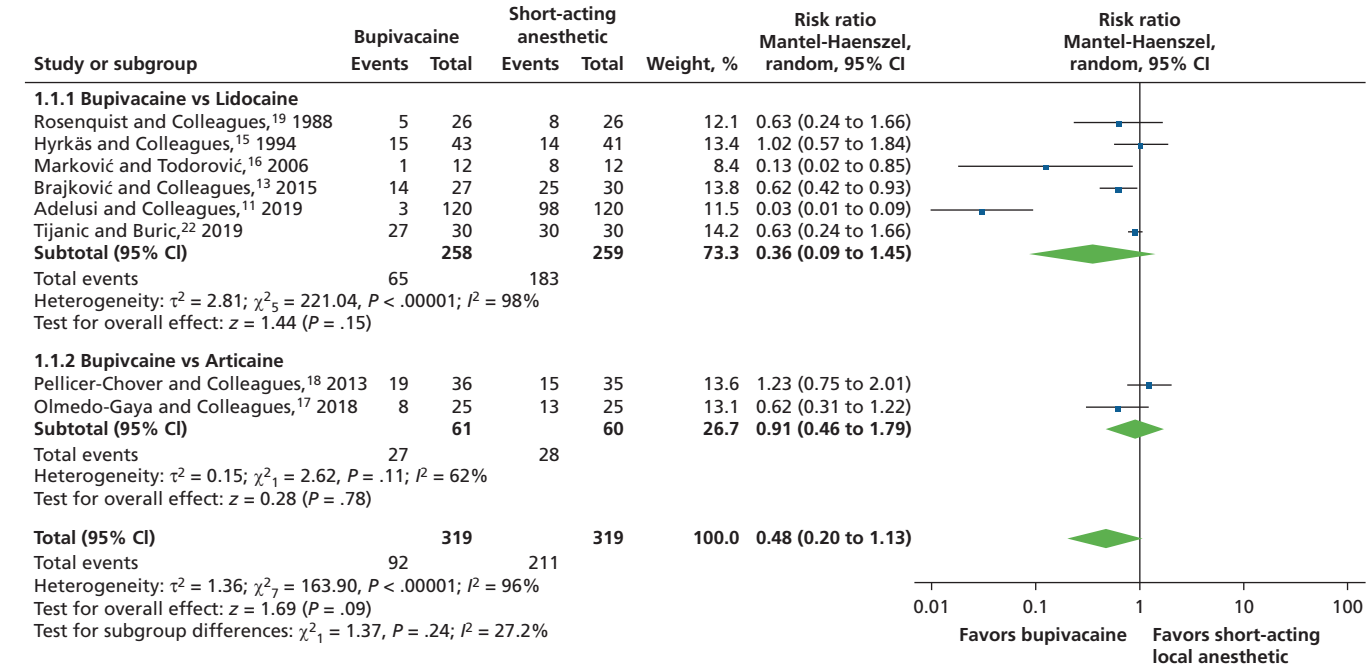
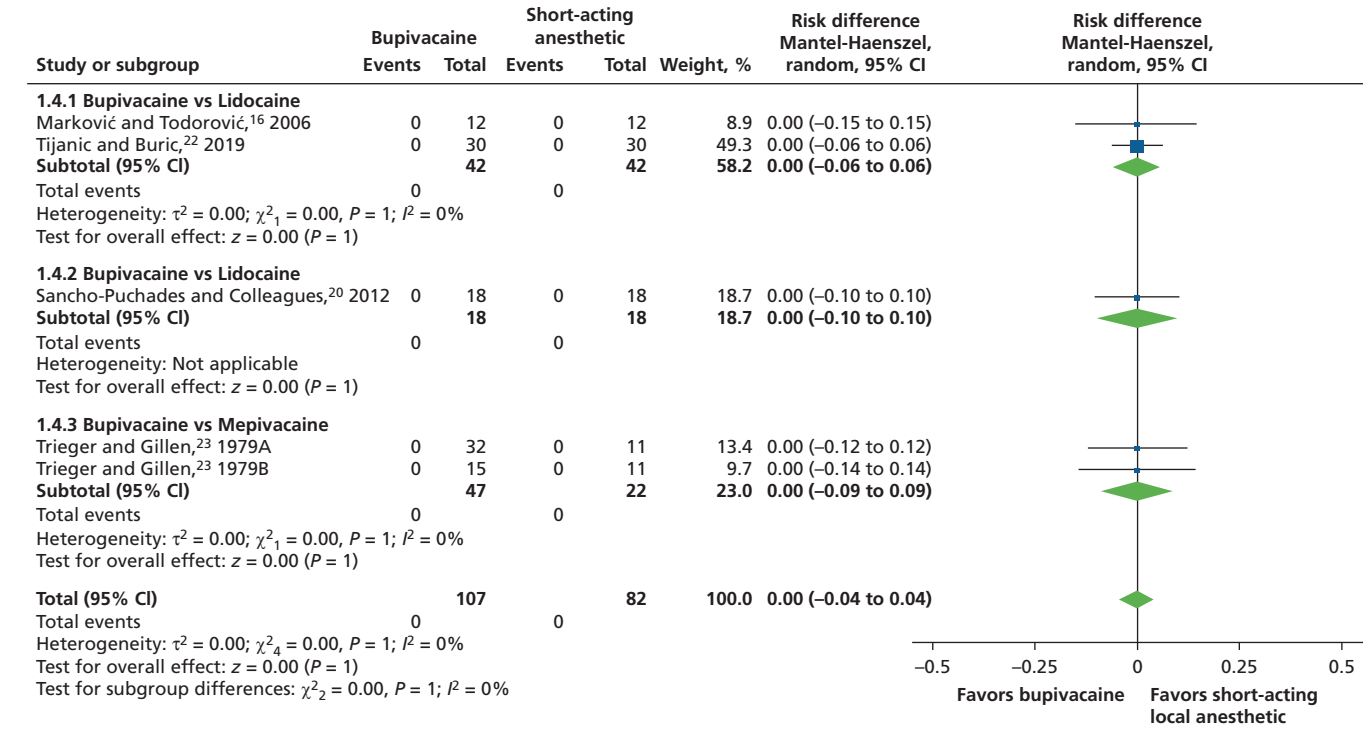
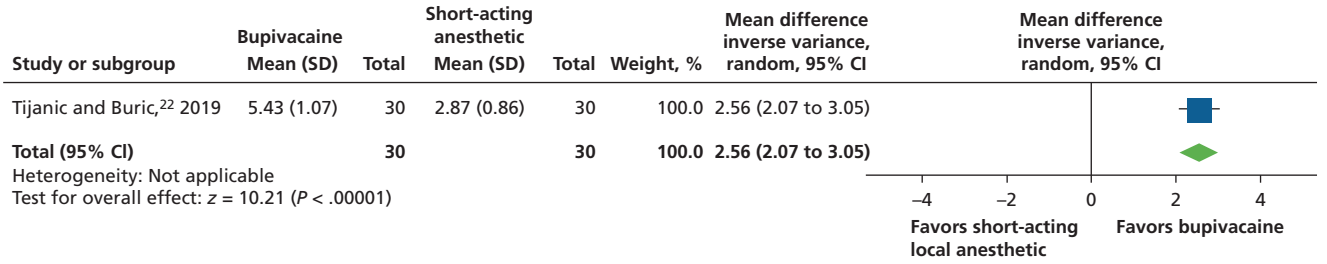


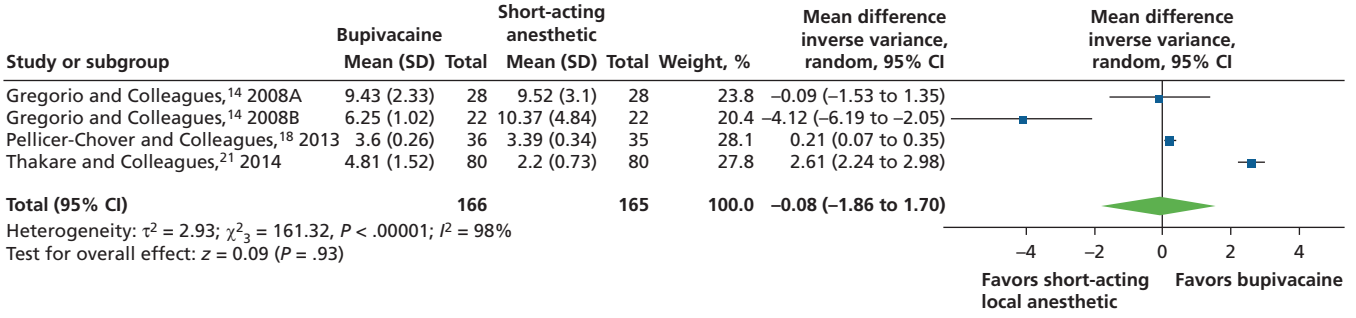
eFigure 1. Forest plot of bupivacaine vs short-acting local anesthetics for acute dental pain: use of rescue analgesia at longest follow-up.



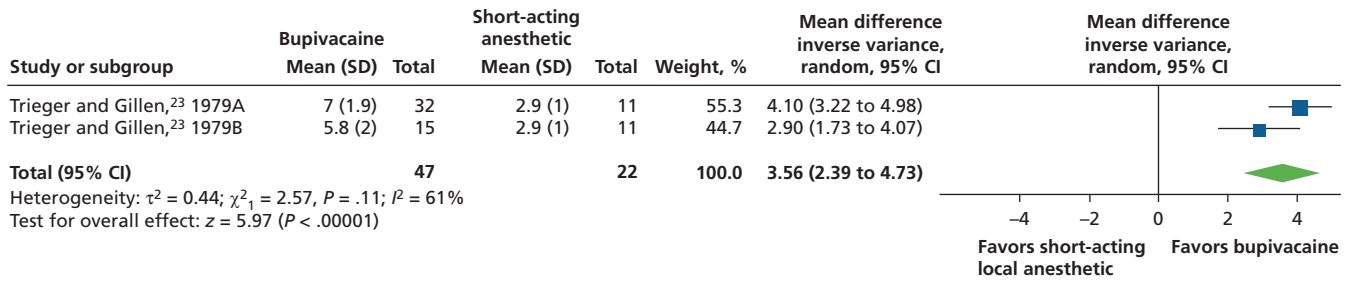
eFigure 2. Bupivacaine vs short-acting local anesthetics for acute dental pain: any adverse effect. $P = 1$ is an artifact of the software system.



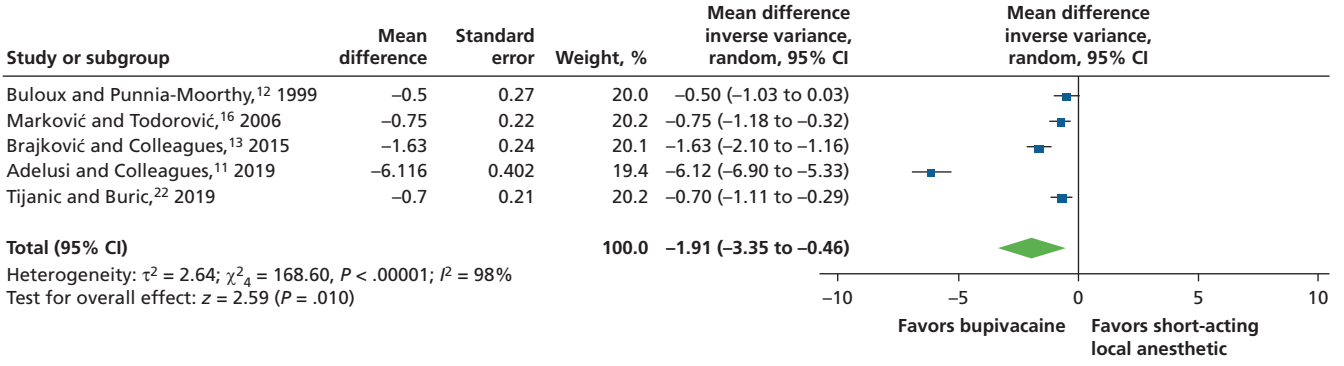
eFigure 3. Bupivacaine vs short-acting local anesthetic for acute dental pain: time (hours) to analgesic consumption.



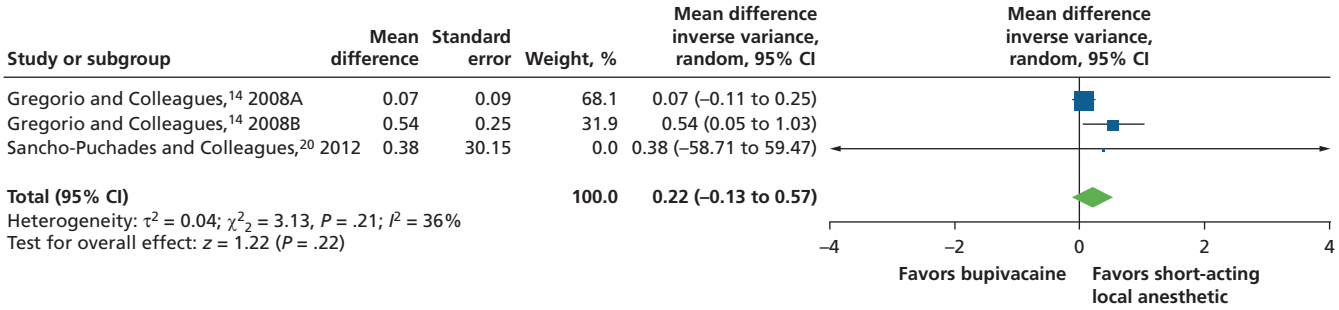
eFigure 4. Bupivacaine vs short-acting local anesthetic for acute dental pain: time (hours) to analgesic consumption.



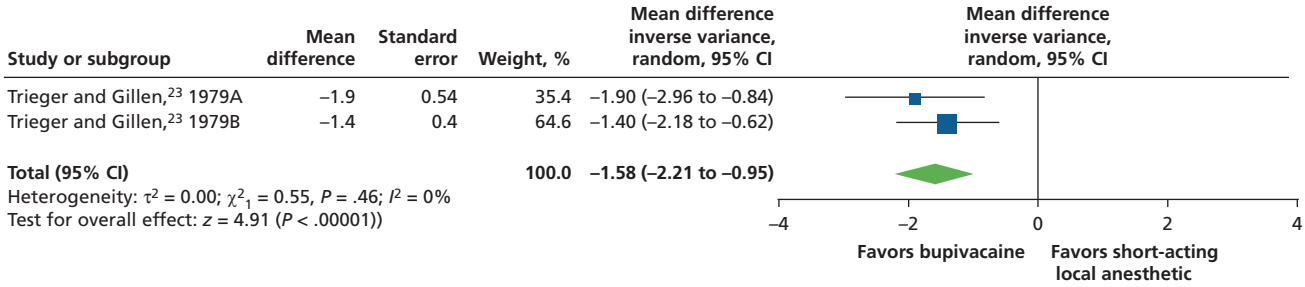
eFigure 5. Bupivacaine vs short-acting local anesthetic for acute dental pain: time (hours) to analgesic consumption.



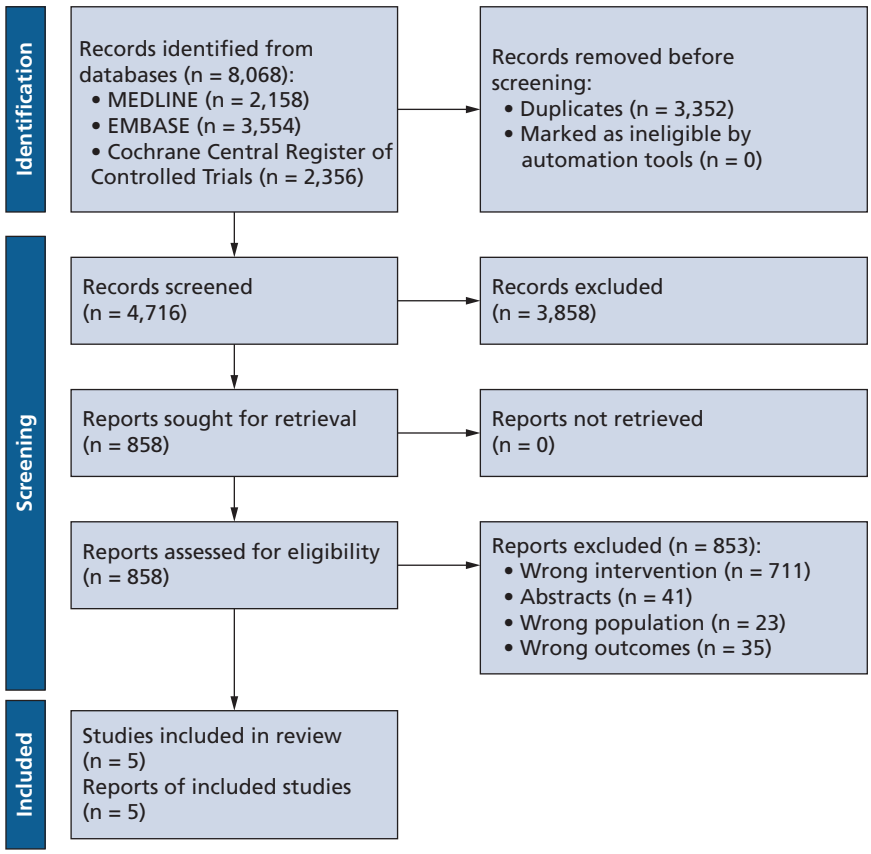
eFigure 6. Bupivacaine vs short-acting local anesthetic for acute dental pain: amount of analgesic consumption (doses).



eFigure 7. Bupivacaine vs short-acting local anesthetic for acute dental pain: amount of analgesic consumption (doses).



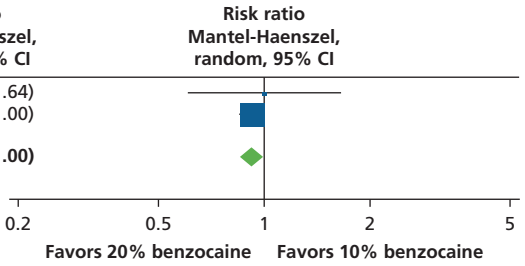
eFigure 8. Bupivacaine vs short-acting local anesthetic for acute dental pain: amount of analgesic consumption (doses).



eFigure 9. Study identification and selection flowchart of the studies in systematic review 2 including benzocaine, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement.[10]

Study or subgroup	10% Benzocaine Events	Total	20% Benzocaine Events	Total	Weight, %	Risk ratio Mantel-Haenszel, random, 95% CI
Gangarosa and Colleagues,[25] 1989	7	9	7	9	2.6	1.00 (0.61 to 1.64)
Hersh and Colleagues,[26] 2013	188	233	199	228	97.4	0.92 (0.85 to 1.00)
Total (95% CI)		**242**		**237**	**100.0**	**0.93 (0.86 to 1.00)**
Total events	195		206			

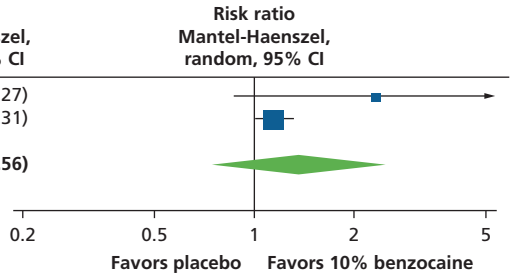
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_1 = 0.10$, $P = .76$; $I^2 = 0\%$
Test for overall effect: $z = 1.90$ ($P = .06$)



eFigure 10. 10% benzocaine vs 20% benzocaine: amount of responders at 20 minutes.

Study or subgroup	10% Benzocaine Events	Total	Placebo Events	Total	Weight, %	Risk ratio Mantel-Haenszel, random, 95% CI
Gangarosa and Colleagues,[25] 1989	7	9	3	9	25.9	2.33 (0.87 to 6.27)
Hersh and Colleagues,[26] 2013	188	223	81	115	74.1	1.15 (1.00 to 1.31)
Total (95% CI)		**242**		**124**	**100.0**	**1.38 (0.74 to 2.56)**
Total events	195		84			

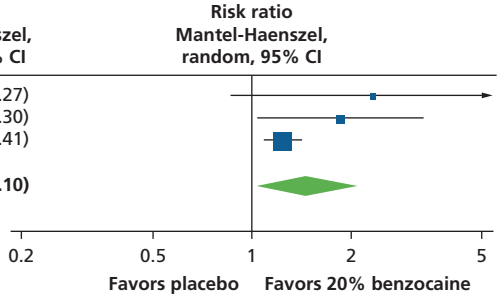
Heterogeneity: $\tau^2 = 0.13$; $\chi^2_1 = 2.00$, $P = .16$; $I^2 = 50\%$
Test for overall effect: $z = 1.02$ ($P = .31$)



eFigure 11. 10% benzocaine vs placebo: amount of responders at 20 minutes.

Study or subgroup	20% Benzocaine Events	Total	Placebo Events	Total	Weight, %	Risk ratio Mantel-Haenszel, random, 95% CI
Gangarosa and Colleagues,[25] 1989	7	19	3	9	11.0	2.33 (0.87 to 6.27)
Hersh and Colleagues,[28] 2005	13	15	7	15	24.7	1.86 (1.04 to 3.30)
Hersh and Colleagues,[26] 2013	199	228	81	115	64.3	1.24 (1.09 to 1.41)
Total (95% CI)		**252**		**139**	**100.0**	**1.47 (1.03 to 2.10)**
Total events	219		91			

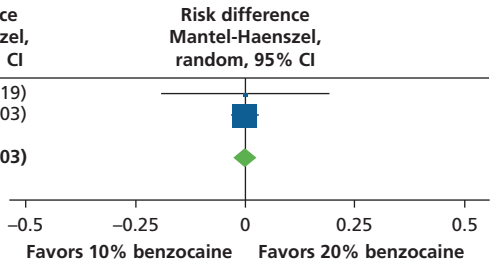
Heterogeneity: $\tau^2 = 0.05$; $\chi^2_2 = 3.38$, $P = .18$; $I^2 = 41\%$
Test for overall effect: $z = 2.11$ ($P = .03$)



eFigure 12. 20% benzocaine vs placebo: amount of responders at 20 minutes.

Study or subgroup	10% Benzocaine Events	Total	20% Benzocaine Events	Total	Weight, %	Risk difference Mantel-Haenszel, random, 95% CI
Gangarosa and Colleagues,[25] 1989	0	9	0	9	2.3	0.00 (–0.19 to 0.19)
Hersh and Colleagues,[26] 2013	6	223	6	228	97.7	–0.00 (–0.03 to 0.03)
Total (95% CI)		**242**		**237**	**100.0**	**–0.00 (–0.03 to 0.03)**
Total events	6		6			

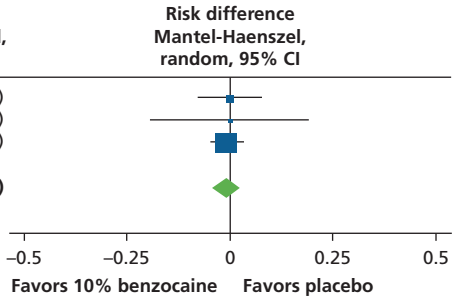
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_1 = 0.00$, $P = 1$; $I^2 = 0\%$
Test for overall effect: $z = 0.04$ ($P = .97$)



eFigure 13. 10% benzocaine vs 20% benzocaine: any adverse effect. $P = 1$ is an artifact of the software system.

Study or subgroup	10% Benzocaine Events	Total	Placebo Events	Total	Weight, %	Risk difference Mantel-Haenszel, random, 95% CI
Sveen and Colleagues,[29] 1982	0	24	0	25	20.3	0.00 (–0.08 to 0.08)
Gangarosa and Colleagues,[25] 1989	0	9	0	9	3.2	0.00 (–0.19 to 0.19)
Hersh and Colleagues,[26] 2013	6	233	4	115	76.5	–0.01 (–0.05 to 0.03)
Total (95% CI)		**266**		**149**	**100.0**	**–0.01 (–0.04 to 0.03)**
Total events	6		4			

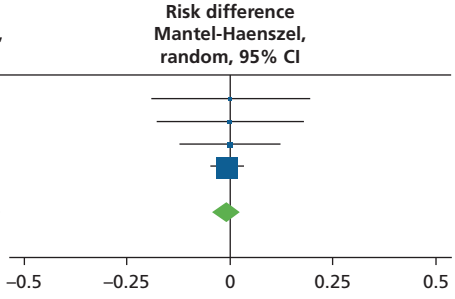
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_2 = 0.05$, $P = .98$; $I^2 = 0\%$
Test for overall effect: $z = 0.40$ ($P = .69$)



eFigure 14. 10% benzocaine vs placebo: any adverse effect.

Study or subgroup	20% Benzocaine Events	Total	Placebo Events	Total	Weight, %	Risk difference Mantel-Haenszel, random, 95% CI
Gangarosa and Colleagues,[25] 1989	0	9	0	9	3.5	0.00 (–0.19 to 0.19)
Hersh and Colleagues,[27] 1993	0	10	0	10	4.3	0.00 (–0.17 to 0.17)
Hersh and Colleagues,[28] 2005	0	15	0	15	8.9	0.00 (–0.12 to 0.12)
Hersh and Colleagues,[26] 2013	6	228	4	115	83.3	–0.01 (–0.05 to 0.03)
Total (95% CI)		**262**		**149**	**100.0**	**–0.01 (–0.04 to 0.03)**
Total events	6		4			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_3 = 0.03$, $P = 1$; $I^2 = 0\%$
Test for overall effect: $z = 0.38$ ($P = .70$)



eFigure 15. 20% benzocaine vs placebo: any adverse effect. $P = 1$ is an artifact of the software system.

eTable 1. PRISMA* checklist.

SECTION AND TOPIC	ITEM NO.	CHECKLIST ITEM	LOCATION WHERE ITEM IS REPORTED
Title			
Title	1	Identify the report as a systematic review.	Page (P) 1
Abstract			
Abstract	2	See the PRISMA 2020 for abstracts checklist.	P1
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P3
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P3-4
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.	P4, appendix
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	Appendix
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.	P4
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.	P4
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 (for example, for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P4
	10b	List and define all other variables for which data were sought (for example, participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P4
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.	P5
Effect measures	12	Specify for each outcome the effect measure(s) (for example, risk ratio, mean difference) used in the synthesis or presentation of results.	P5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (for example, tabulating the study intervention characteristics and comparing against the planned groups for each synthesis [item no. 5]).	P5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	P5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	P5
	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.	P5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (for example, subgroup analysis, meta-regression).	P6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	P6

* PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[10]

eTable 1. Continued

SECTION AND TOPIC	ITEM NO.	CHECKLIST ITEM	LOCATION WHERE ITEM IS REPORTED
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	P6
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.	P7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Not applicable
Study characteristics	17	Cite each included study and present its characteristics.	P7
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix
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 (for example, confidence/credible interval), ideally using structured tables or plots.	Not applicable
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	P7
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (for example, confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P7-11
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Appendix
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Appendix
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Appendix
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Appendix
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P11-12
	23b	Discuss any limitations of the evidence included in the review.	P12
	23c	Discuss any limitations of the review processes used.	P13
	23d	Discuss implications of the results for practice, policy, and future research.	P12
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.	P3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not applicable
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P1
Competing interests	26	Declare any competing interests of review authors.	P1
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.	Not applicable

eTable 2. Sample search strategy.

DATABASE	SEARCH STRATEGY
Ovid MEDLINE E-published Ahead of Print, In-Process, and Other Non-Indexed Citations, Ovid MEDLINE Daily, and Ovid MEDLINE 1946 to Present	1 (pain* and (dental or teeth or tooth or oral or mouth or odont* or endodont*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (58334)
	2 (pain/ or acute pain/ or exp pain, postoperative/) and (dental or teeth or tooth or oral or mouth or odont* or endodont*).ti,ab. (11066)
	3 1 or 2 (58338)
	Annotation: dental pain limiter
	4 Toothache/ or Pulpitis/ or exp periapical periodontitis/ (10036)
	5 (toothache* or odontalg* or pulpitis or apical periodontitis or periapical abscess or endodont*).mp. (30122)
	6 4 or 5 (31297)
	Annotation: endodontic population
	7 3 and 6 (3406)
	Annotation: endodontic dental pain
	8 Molar, Third/ (6670)
	9 exp Tooth Extraction/ (20340)
	10 (((third or wisdom or impact* or unerupt*) adj3 (teeth or tooth or molar)) or ((teeth or tooth or molar) adj3 (extract* or remov* or surg*))).mp. (44553)
	11 or/8-10 (45201)
	Annotation: third molar extraction
	12 3 and 11 (3905)
	Annotation: third molar extraction pain
	13 7 or 12 (6947)
	14 3 and (6 or 11) (6947)
	Annotation: logic check: dental pain and (endodontic or third molar)
	15 random:.tw. or placebo:.mp. or double-blind:.tw. (1291591)
	16 ((treatment or control) adj3 group*).ab. (624172)
	17 (allocat* adj5 group*).ab. (26592)
	18 ((clinical or control*) adj3 trial).ti,ab,kw. (297366)
	19 or/15-18 (1798368)
	Annotation: modified HIRU RCT filter
	20 14 and 19 (2275)
	21 exp animals/ not humans.sh. (4768153)
	22 20 not 21 (2258)
	23 (dh or dt or pc or rh or rt or su or th).fs. (7033700)
	24 exp Analgesia/ (44555)
	25 exp Analgesics/ (538503)
	26 analges*.mp. (197813)
	27 treat*.mp. (6135100)
	28 therap*.mp. (6259786)
	29 intervention*.mp. (1088700)
	30 manag*.mp. (1565947)
	31 prevent*.mp. (2435611)
	32 (surgery or surgical).mp. (3112981)

eTable 2. Continued

DATABASE	SEARCH STRATEGY
	33 exp Drug Therapy/ (1377452)
	34 exp Therapeutics/ (4661006)
	35 (antibiotic* or opioid* or steroid*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (841008)
	36 or/23-35 (14241897)
	37 22 and 36 (2158)
	38 "28858553".fc_acno. (1)
	39 "27769675".fc_acno. (1)
	40 "27461787".fc_acno. (1)
	41 "32318443".fc_acno. (1)
	42 "32065309".fc_acno. (1)
	43 "29959306".fc_acno. (1)
	44 or/38-43 (6)
	45 37 and 44 (6)

eTable 3. Risk of bias assessment of the studies in systematic review 1 including local anesthetics.

STUDY, YEAR	RANDOMIZATION	DEVIATIONS FROM THE INTENDED INTERVENTION	MISSING OUTCOME DATA	MEASUREMENT OF OUTCOME	SELECTION OF THE REPORTED RESULTS
Use of Rescue Analgesia					
Rosenquist and Colleagues,[19] 1988	Probably low	Probably low	Low	Low	Probably low
Hyrkas and Colleagues,[15] 1994	Low	Low	Low	Low	Low
Markovic and Todorović,[16] 2006	Probably low	Low	Low	Low	Low
Pellicer-Chover and Colleagues,[18] 2013	Low	Low	Low	Low	Low
Brajkovic and Colleagues,[13] 2015	Low	Low	High	Low	Low
Olmedo-Gaya and Colleagues,[17] 2018	Low	Low	Low	Low	Probably high
Adelusi and Colleagues,[11] 2019	Probably low	Low	Low	Low	Low
Tijanic and Buric,[22] 2019	Low	Low	Low	Low	Low
Time to Analgesic Consumption					
Trieger and Gillen,[23] 1979A	Probably high	Probably high	Low	High	Low
Trieger and Gillen,[23] 1979B	Probably high	Probably high	Low	High	Low
Gregorio and Colleagues,[14] 2008A	Low	Low	Low	Low	Low
Gregorio and Colleagues,[14] 2008B	Low	Low	Low	Low	Low
Trullenque-Eriksson and Guisado-Moya,[24] 2010	Probably high	Low	High	Low	High
Pellicer-Chover and Colleagues,[18] 2013	Low	Low	Low	Low	Low
Thakare and Colleagues,[21] 2014	Low	High	Low	Probably low	Low
Olmedo-Gaya and Colleagues,[17] 2017	Low	Low	Low	Low	High
Tijanic and Buric,[22] 2019	Low	Low	Low	Low	Low
Amount of Analgesic Consumption					
Trieger and Gillen,[23] 1979A	Probably high	Probably high	Low	High	High
Trieger and Gillen,[23] 1979B	Probably high	Probably high	Low	High	High
Bouloux and Punnia-Moorthy,[12] 1999	Low	Low	Low	Low	Probably high
Markovic and Todorović,[16] 2006	Probably low	Low	Low	Low	High
Gregorio and Colleagues,[14] 2008A	Low	Low	Low	Low	Low
Gregorio and Colleagues,[14] 2008B	Low	Low	Low	Low	Low
Sancho-Puchades and Colleagues,[20] 2012	Low	Low	Probably low	Low	High
Brajkovic and Colleagues,[13] 2015	Low	Low	High	Low	Low

eTable 3. Continued

STUDY, YEAR	RANDOMIZATION	DEVIATIONS FROM THE INTENDED INTERVENTION	MISSING OUTCOME DATA	MEASUREMENT OF OUTCOME	SELECTION OF THE REPORTED RESULTS
Adelusi and Colleagues,[11] 2019	Probably low	Low	Low	Low	Probably high
Tijanic and Buric,[22] 2019	Low	Low	Low	Low	Low
Any Adverse Effect					
Trieger and Gillen,[23] 1979A	Probably high	Probably high	Probably low	High	High
Trieger and Gillen,[23] 1979B	Probably high	Probably high	Probably low	High	High
Markovic and Todorović,[16] 2006	Probably low	Low	Probably low	Low	High
Sancho-Puchades and Colleagues,[20] 2011	Low	Low	Probably low	Low	Low
Tijanic and Buric,[22] 2019	Low	Low	Low	Low	Low

eTable 4. Characteristics of the studies in systematic review 2 comparing benzocaine formulations to each other and placebo.

STUDY, YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PARTICIPATNS RANDOMIZED	AGE, Y, MEAN (SD or SE)	SEX, FEMALE, %	POPULATION	INTERVENTIONS
Sveen and Colleagues,[29] 1982	Parallel group	United States	49	26.2 (Not reported)	48.98	Pulpitis or toothache or its complications	7.5% benzocaine, placebo
Gangarosa and Colleagues,[25] 1989	Parallel group	United States	27	28 (SD, 6)	70.37	Pulpitis or toothache or its complications	20% benzocaine, 10% benzocaine, placebo
Hersh and Colleagues,[27] 1993	Parallel group	United States	20	30 (SE, 2.25)	55	Pulpitis or toothache or its complications	20% benzocaine, placebo
Hersh and Colleagues,[28] 2005	Parallel group	United States	30	30.25 (SD, 8.63)	50	Pulpitis or toothache or its complications	20% benzocaine, placebo
Hersh and Colleagues,[26] 2013	Parallel group	United States	576	31.1 (SD, 12.7)	52.08	Pulpitis or toothache or its complications	20% benzocaine, 10% benzocaine, placebo

eTable 5. Risk of bias assessment on studies in systematic review 2 including benzocaine.

STUDY, YEAR	RANDOMIZATION	DEVIATIONS FROM THE INTENDED OUTCOME	MISSING OUTCOME DATA	MEASUREMENT OF OUTCOME	SELECTION OF THE REPORTED RESULTS
Amount of Responders at 20 Minutes					
Gangarosa and Colleagues,[25] 1989	Low	Low	Low	Low	Low
Hersh and Colleagues,[28] 2005	Low	Low	Low	Low	Low
Hersh and Colleagues,[26] 2013	Probably low	Low	Low	Low	Low
Any Adverse Effect					
Sveen and Colleagues,[29] 1982	Low	Low	Low	Low	High
Gangarosa and Colleagues,[25] 1989	Low	Low	Low	Low	Probably low
Hersh and Colleagues[27] 1993	Probably low	Low	Low	Low	Probably low
Hersh and Colleagues,[28] 20052005	Low	Low	Low	Low	Probably low
Hersh and Colleagues,[26] 2013	Probably low	Low	Low	Low	Low

eTable 6. 10% benzocaine vs 20% benzocaine for pulpitis and toothache.

OUTCOME	FOLLOW-UP, MIN	PARTICIPANTS (RANDOMIZED CONTROLLED TRIALS), NO.	RELATIVE EFFECT* (95% CI)	ANTICIPATED ABSOLUTE EFFECTS, % (95% CI)			CERTAINTY	WHAT HAPPENS
				With 20% Benzocaine	With 10% Benzocaine	Difference		
Amount of Responders Assessed With Proportion of Participants Who Had a Reduced Pain Intensity Score at 2 Consecutive Time Points	20-30	479 (2)	Risk ratio, 0.93 (0.86 to 1.00)	86.9	80.8 (74.8 to 86.9)	–6.1 (–12.2 to 0.0)	Moderate†	There is probably a negligible benefit of 20% benzocaine compared with 10% benzocaine with regard to the amount of responders from 20-30 min.
Any Adverse Effect Assessed With Proportion of Participants Experiencing Any Adverse Effect‡	90-120	479 (2)	Not estimable	2.5	2.5	0.0 (–3.0 to 3.0)	Low‡,§	There may be no difference between 10% and 20% benzocaine with regard to incidence of adverse effects.

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
† Using a threshold of 8.69% (based on 10% of the risk with 20% benzocaine), the lower bound of the 95% CI indicates an important effect favoring 20% benzocaine, whereas the upper bound suggests that there is no difference between these interventions. Therefore, the authors rated down 1 level owing to imprecision. ‡ All reported incidents of adverse effects were categorized as mild adverse effects (not specified). § Using a threshold of 0.25% (based on 10% of the risk with 20% benzocaine), the lower bound of the 95% CI suggests an important benefit of 10% benzocaine, whereas the upper bound suggests an important benefit of 20% benzocaine. Therefore, the authors rated down 2 levels owing to imprecision.

eTable 7. 10% benzocaine vs placebo for pulpitis and toothache.

OUTCOME	FOLLOW-UP, MIN	PARTICIPANTS (RANDOMIZED CONTROLLED TRIALS), NO.	RELATIVE EFFECT* (95% CI)	ANTICIPATED ABSOLUTE EFFECTS (95% CI)			CERTAINTY	WHAT HAPPENS
				Placebo	With 10% Benzocaine	Difference		
Amount of Responders Assessed With Proportion of Participants Who Had a Reduced Pain Intensity Score for at Least 2 Consecutive Time Points	20-30	366 (2)	Risk ratio, 1.38 (0.74 to 2.56)	67.7	93.5 (50.1 to 100)	25.7 (–17.6 to 105.7)	Low†,‡	10% benzocaine may increase the amount of responders at 20 to 30 min when compared with no treatment (placebo) by an important amount.
Adverse Effects Assessed With Proportion of Participants Experiencing Any Adverse Effect§	10-120	415 (3)	Not estimable	2.7	2.3	–1.0 (–4.0 to 3.0)	Low¶	There may be an important difference favoring 10% benzocaine when compared with no treatment (placebo) with regards to incidence of adverse effects.

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
† There is moderate statistical heterogeneity ($I^2 = 50\%$, $P = .16$). However, the CIs of the effect estimates overlap, so the authors did not rate down for inconsistency.
‡ Using a threshold of 6.77% (based on 10% of the baseline risk, that is, the risk with no treatment [placebo]), the lower bound of the 95% CI suggests an important benefit of no treatment (placebo), whereas the upper bound suggests an important benefit of 10% benzocaine. Therefore, the authors rated down 2 levels owing to imprecision. § All reported incidents of adverse effects were categorized as mild or moderate adverse effects (not specified). ¶ Using a threshold of 0.27% (based on 10% of the baseline risk, that is, the risk with no treatment [placebo]), the lower bound of the 95% CI suggests an important benefit of 10% benzocaine, whereas the upper bound suggests an important benefit of no treatment (placebo). Therefore, the authors rated down 2 levels owing to imprecision.

eTable 8. 20% benzocaine vs placebo for pulpitis and toothache.

OUTCOME	FOLLOW-UP, MIN	PARTICIPANTS (RANDOMIZED CONTROLLED TRIALS), NO.	RELATIVE EFFECT* (95% CI)	ANTICIPATED ABSOLUTE EFFECTS (95% CI)			CERTAINTY	WHAT HAPPENS
				Placebo	With 20% Benzocaine	Difference		
Amount of Responders Assessed With Proportion of Participants Who Had a Reduced Pain Intensity Score for at Least 2 Consecutive Time Points	20-30	391 (3)	Risk ratio, 1.47 (1.03 to 2.10)	65.5	96.2 (67.4 to 100)	30.8 (2.0 to 72.0)	Low†,‡	20% benzocaine may increase the amount of responders at 20 to 30 min when compared with no treatment (placebo) by an important amount.
Adverse Effects Assessed With Proportion of Participants Experiencing any Adverse Effect§	10-120	411 (4)	Not estimable	2.7	2.3	–1.0 (–4.0 to 3.0)	Low¶	There may be an important difference favoring 20% benzocaine over no treatment (placebo) with regards to incidence of adverse effects.

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
† There is moderate statistical heterogeneity ($I^2 = 41\%$, $P = .18$). However, the 95% CIs of the effect estimates overlap, so the authors did not rate down for inconsistency. ‡ Using a threshold of 6.55% (based on 10% of the baseline risk, that is, the risk with no treatment [placebo]), the lower bound of the 95% CI suggests a negligible benefit of 20% benzocaine, whereas the upper bound suggests an important benefit of 20% benzocaine. Therefore, the authors rated down 2 levels owing to imprecision. § All reported incidents of adverse effects were categorized as mild or moderate adverse effects (not specified). ¶ Using a threshold of 0.27% (based on 10% of the baseline risk, that is, the risk with no treatment [placebo]), the lower bound of the 95% CI suggests an important benefit of 20% benzocaine, whereas the upper bound suggests an important benefit of no treatment (placebo). Therefore, the authors rated down 2 levels owing to imprecision.