Is there an association between crown discoloration and pulp necrosis in traumatized permanent teeth? A meta-analysis

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Abstract: The present study aimed to identify the scientific evidence regarding the association between crown discoloration and pulp necrosis in traumatized permanent teeth. A systematic literature search was conducted in the PubMed/Medline, Lilacs/BBO, Scopus, Web of Science, Cochrane Library databases, and grey literature. Quality assessment and bias control were carried out according to the Fowkes and Fulton guidelines. Meta-analysis was performed, and the odds ratio was calculated with a 95% confidence interval. The quality assessment of the evidence was determined for the meta-analysis outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. From 2,702 studies identified, five articles met the inclusion criteria. One among these showed no methodological soundness and was excluded from the meta-analysis, and the remaining four studies were included in the meta-analysis. The total number of traumatized permanent teeth evaluated in the meta-analysis was 367. The results showed a positive association between crown discoloration and pulp necrosis in permanent teeth. Teeth with crown discoloration showed 23 times more chance to present pulp necrosis than teeth without crown discoloration (OR 23.82 [1.25, 452.87]; p = 0.03), with a very low certainty of evidence. There is a significant association between crown discoloration and pulp necrosis of traumatized permanent teeth. Due to the very low strength of evidence according to GRADE, this result should be viewed with caution.

Keywords: Dental Pulp Necrosis; Dentition, Permanent; Tooth Injuries; Tooth Discoloration.

Introduction

A common complication of dental trauma is pulp necrosis.[1,2,3] Its prevalence rate in traumatized permanent teeth varies from 26.9 to 73.3%,[1,2,4,5,6] depending mainly on the type of dental trauma and the stage of root development. Among immature permanent teeth, pulp necrosis ranges from 13.0 to 66.7% and in mature permanent teeth, between 42.0 to 87.0%.[2,4,6] Signs of trauma that indicate diagnosis of pulp necrosis may manifest in the subsequent weeks, months, or years after the injury.[3,7]

Regular controls for monitoring the state of the pulp after dental trauma are necessary for an early detection of complications.[2] As a result, a follow-up protocol is very important for a correct diagnosis.[8]

The following criteria are proposed by studies for the classification of non-vital pulp after dental trauma: abscess/fistula, periapical bone rarefaction, inflammatory root resorption, arrested root development, persistent crown discoloration, and loss of pulpal sensibility (sensitive tests).[9,10] Traumatized teeth that show persistent crown discoloration or loss of pulpal sensibility are only considered necrotic when associated with one of the following signs: a) abscess/fistula, or b) obvious periapical bone rarefaction, or c) inflammatory external root resorption.[1,6,9,10,11]

Loss of sensibility and color change can be temporary,[7,12] indicating pulp damage, but they do not determine a definitive pulp necrosis diagnosis[10] since revascularization and regeneration/repair of the traumatized pulp can occur.[13]

Dental trauma is more frequent in maxillary central incisors,[2,5,6,8] and post-traumatic complications can result in esthetic compromise.[14] Due to its compromising oral esthetics, crown discoloration is a clinical alteration that afflicts the patient[15] and raises doubts in the clinician. Even in cases where there is no evidence of pulp necrosis, color change suggests alteration of the pulpal tissue[10] with uncertainties regarding the prognosis,[16] which might progress to necrosis. When facing this clinical alteration, the clinician needs to establish a follow-up schedule. This involves the interval between consultations and the actual time of tooth monitoring, which is not well defined in the literature or in the guideline of The International Association of Dental Traumatology (IADT)[17] for permanent teeth. Knowledge concerning the association or not of crown discoloration with pulp necrosis can help optimize a specific follow-up protocol for teeth with crown discoloration, aiming for immediate endodontic treatment in cases of necrosis or upkeep of follow-ups in cases of maintenance of pulp vitality. Thus, the aim of the present systematic review was to verify if there is an association between crown discoloration and pulp necrosis in traumatized permanent teeth.

Methodology

Focused question

The present systematic review was designed in order to answer the following focused question: Is there an association between crown discoloration and pulp necrosis in traumatized permanent teeth?

Protocol and registry

The present systematic review with meta-analysis was reported according to the PRISMA protocol[18] and the Maia and Antonio guideline.[19] The developed protocol was registered in the PROSPERO database under the number CRD42017068650.

Literature search strategy

An electronic search was performed in the databases PubMed/Medline, Lilacs/BBO, Scopus, Web of Science, Cochrane Library, and also in the grey literature catalogs ProQuest, OpenGrey, Capes Thesis Bank, and Google Scholar (Table 1) on March 2018 and updated on August 2019. MeSH terms, synonyms, related terms, and free terms were used and combined with the Boolean operators 'AND' and 'OR', respecting each databases' rules. No language or date of publication restrictions were applied. When necessary, articles were read in full to determine the selection. A manual search was also performed in the reference lists of all included studies to identify possible studies that were not retrieved through the electronic search.

Eligibility criteria

The Population, Exposure, Comparisons, and Outcome (PECO)[20] strategy was used to identify observational studies in traumatized permanent teeth (P) with (E) or without (C) pulp necrosis and the association with crown discoloration (O). The following types of articles were excluded from the present review: literature reviews, conference abstracts, letters, *in vitro* studies, case reports; studies with follow-up of less than one month; studies with malignancies included in the sample; studies where the crown discoloration was identified after endodontic treatment; sample overlap; studies that did not present

Table 1. Search strategy used in the systematic review.

PubMed	**#1** "dentition, permanent"[MeSH Terms]) OR "permanent dentition"[Title/Abstract]) OR "permanent teeth"[Title/Abstract]) OR "permanent tooth"[Title/Abstract]) OR "tooth injuries"[MeSH Terms]) OR "tooth injuries"[Title/Abstract]) OR "dental lesions"[Title/Abstract]) OR "dental injuries"[Title/Abstract]) OR "dental trauma"[Title/Abstract]) OR "traumatic injury"[Title/Abstract]) OR injuries[Title/Abstract]) OR injury[Title/Abstract]) OR trauma[Title/Abstract]) OR traumatized[Title/Abstract]) OR traumatic[Title/Abstract **#2** "dental pulp necrosis"[MeSH Terms]) OR "dental pulp necrosis"[Title/Abstract]) OR necrotic[Title/Abstract]) OR pulp[Title/Abstract]) OR pulps[Title/Abstract]) OR pulpal[Title/Abstract]) OR necrosis[Title/Abstract]) OR necroses[Title/Abstract] **#3** "dental pulp"[MeSH Terms]) OR "dental pulp"[Title/Abstract]) OR dental[Title/Abstract]) OR pulp[Title/Abstract]) OR vitality[Title/Abstract] **#4** crowns[MeSH Terms]) OR "crowns, dental"[Title/Abstract]) OR coronal[Title/Abstract]) OR discolouration[Title/Abstract]) OR discoloration[Title/Abstract]) OR discolored[Title/Abstract]) OR colour[Title/Abstract]) OR color[MeSH Terms]) OR color[Title/Abstract]) **#1 AND #2 AND #3 AND #4**
Lilacs	**#1** MH: "permanent dentition" OR MH: "permanent teeth" OR MH: "permanent tooth" OR MH: "dentição permanente" OR MH: "Tooth Injuries" OR MH: "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR injuries OR "traumatismos de los dientes" OR "injúria traumática" OR "lesion traumática" **#2** MH: "dental pulp necrosis" OR MH: necrotic OR MH: pulp OR MH: pulps OR MH: pulpal OR necrosis OR necroses **#3** "dental pulp" OR dental OR pulp OR vitality OR MH: "pulp vitality" OR "vital pulp" OR MH: "vitalidade pulpar" OR MH: "vitalidad pulpar" **#4** crown OR crowns OR coronal OR discolouration" OR discolour OR discolor OR color OR colour OR descoloração**#1 AND #2 AND #3 AND #4**
Scopus	**#1** ((TITLE-ABS-KEY ("dentition permanent")) OR (TITLE-ABS-KEY (" tooth injuries ")) OR (TITLE-ABS-KEY ("dental lesions")) OR (TITLE-ABS-KEY ("dental injuries")) OR (TITLE-ABS-KEY ("dental trauma")) OR (TITLE-ABS-KEY ("traumatic injury")) OR (TITLE-ABS-KEY (injuries)) OR (TITLE-ABS-KEY (injury)) OR (TITLE-ABS-KEY (" trauma ")) OR (TITLE-ABS-KEY (" traumatized ")) OR (TITLE-ABS-KEY (" traumatic ")) **#2** (TITLE-ABS-KEY ("dental pulp necrosis")) OR (TITLE-ABS-KEY ("pulp necrosis")) OR (TITLE-ABS-KEY (necrotic)) OR (TITLE-ABS-KEY (pulp)) OR (TITLE-ABS-KEY (" pulps ")) OR (TITLE-ABS-KEY (" pulpal ")) OR (TITLE-ABS-KEY (necrosis)) OR (TITLE-ABS-KEY (necroses)) **#3** ((TITLE-ABS-KEY ("dental pulp")) OR (TITLE-ABS-KEY ("pulp vitality")) OR (TITLE-ABS-KEY (pulp)) OR (TITLE-ABS-KEY (vitality)) **#4** ((TITLE-ABS-KEY (crowns)) OR(TITLE-ABS-KEY (crown)) OR (TITLE-ABS-KEY (coronal)) OR (TITLE-ABS-KEY (discoloration)) OR (TITLE-ABS-KEY (discoloured)) OR (TITLE-ABS-KEY (colour)) OR (TITLE-ABS-KEY (color)) **#1 AND #2 AND #3 AND #4**
Web of Science	**#1** TS=("permanent dentition" OR "tooth injuries" OR "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR injuries OR injury OR trauma OR trauma OR traumatized OR traumatic **#2** TS=("dental pulp necrosis" OR necrotic OR pulp OR pulps OR pulpal OR necrosis OR necroses) **#3** TS=("dental pulp" OR dental OR pulp OR vitality) **#4** TS=(crown OR crowns OR coronal OR discolouration OR discoloured OR discolored OR colour OR color) **#1 AND #2 AND #3 AND #4**

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Cochrane	**#1** MeSH descriptor: ["Permanent Dentition"] explode all trees
	#2 MeSH descriptor: [Tooth injuries] explode all trees
	#3 "dental trauma": ti,ab,kw
	#4 "traumatic injury": ti,ab,kw
	#5 "dental lesions": ti,ab,kw
	#6 "dental injury": ti,ab,kw
	#7 #1 or #2 or #3 or #4 or #5 or #6 or
	#8 MeSH descriptor: [Dental pulp necrosis] explode all trees
	#9 pulp: ti,ab,kw
	#10 necrosis: ti,ab,kw
	#11 #8 or #9 or #10
	#12 MeSH descriptor: [Dental pulp] explode all trees
	#13 "pulp vitality": ti,ab,kw
	#14 dental: ti,ab,kw
	#15 pulp: ti,ab,kw
	#16 vitality: ti,ab,kw
	#17 #13 or #14 or #15 or #16
	#18 MeSH descriptor: [Tooth crown] explode all trees
	#19 MeSH descriptor: [Tooth Discoloration] explode all trees\
	#20 coronal: ti,ab,kw
	#21 color: ti,ab,kw
	#22 colour: ti,ab,kw
	#23 #18 or #19 or #20 or #21 or #22
	#24 #7 and #11 and #17 and #23
OpenGrey	"traumatic dental" OR trauma AND "pulp necrosis" AND "dental pulp" AND "vitality" AND discolored
ProQuest	**#1** all("permanent dentition" OR "tooth injuries" OR "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR trauma OR traumatized OR traumatic)
	#2 all("dental pulp necrosis" OR "necrotic" OR "pulps" OR "Pulp necrosis" OR Necroses)
	#3 all("dental pulp" OR "pulp vitality" OR pulp OR vital OR vitality)
	#4 all(crown OR coronal OR discolouration OR discoloration OR discoloured)
	#1 AND #2 AND #3 AND #4
Banco de teses e dissertações Capes	all("permanent dentition" OR "tooth injuries" OR "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR trauma OR traumatized OR traumatic) AND all("dental pulp necrosis" OR "necrotic" OR "pulps" OR "Pulp necrosis" OR Necroses) AND all("dental pulp" OR "pulp vitality" OR pulp OR vital OR vitality) AND all(crown OR coronal OR discolouration OR discoloration OR discoloured)
Google Scholar	"dental trauma" AND "pulp necrosis" AND pulp AND discoloration filetype:pdf

traumatized teeth without crown discoloration; studies in which clinical and/or radiographic signs of pulp necrosis have not been reported; studies on avulsed teeth and their replantation, and studies with pulp necrosis diagnosed only by the presence of crown discoloration.

The eligibility criteria were used by two independent reviewers (BSM and NAA) to select the studies based on titles and abstracts from the databases, grey literature, and manual searches. When the title and abstract did not provide enough information, the full text was analyzed with the objective of determining its eligibility. Studies that appeared in more than one database were considered only once. After applying the eligibility criteria, the results of both reviewers were compared, and the study was only discarded in case of both reviewers' consensus. Any disagreement was resolved through discussion with a third review author (MC).

The Mendeley Desktop© software (version 1.17.1, 2008–2017 Mendeley Ltd., Elsevier Inc., USA) was used for management and selection of the references.

Data extraction

Two reviewers (BSM and NAA) read the full articles and extracted the information independently. The following data were extracted from each eligible study: authors, year of publication, study country, study design, number of participants included in the study, age of the participants in years, study methods (evaluation criteria), results (number of traumatized permanent teeth, number of teeth with pulp necrosis, number of teeth without pulp necrosis, number of teeth with and without crown discoloration). Disagreements between the reviewers were solved by discussion with a third review author (MC). In studies with missing data, the authors were contacted by e-mail for further data details or for additional information.

Quality assessment and risk of bias

The methodological quality and bias control of eligible studies was carried out independently by the two reviewers (BSM and NAA) in accordance with the guidelines and critical appraisal described by Fowkes and Fulton.[21] Any differences between the two examiners were resolved with a third reviewer (MC).

This quality assessment enables the classification of cross-sectional, cohort, controlled trial, and case-control studies. The checklist contains questions on study design, study sample representativeness, control group characteristics, quality of measurements and outcomes, completeness, and distorting influences. When verifying the criteria for each guideline, the importance of failures concerning their expected effects on the results was scored as "major" (++) or "minor" (+) problem, and "no problem" (0). For items where the checklist question was not applicable, 'NA' was registered. For this evaluation, the authors elaborated a standardization for each item of the checklist (Table 2).

The corresponding authors were contacted in order to clarify doubts. Disagreements between the reviewers regarding the quality assessment and risk of bias were resolved by consensus with a third review author.

Summary measures and meta-analysis

In the quantitative analysis, only studies with "NO" as a response in the Summary Questions were included. The criteria used for traumatized teeth where the association between the presence or absence of pulp necrosis and the presence or absence of permanent crown discolorations. For the diagnosis of pulp necrosis, clinical (abscess and/or fistula) and/or radiographic signs were considered (periapical bone rarefaction or inflammatory external root resorption). For conventional pulp tests (electric pulp test and cold pulp test), the negative response was considered only with the presence of a radiographic sign.

The extracted data were analyzed using the RevMan software (Review Manager v. 5.3, The Cochrane Collaboration; Copenhagen, Denmark) to assess the relationship between pulp necrosis and crown discoloration in permanent teeth. The prevalence of crown discoloration (events) and the total number of teeth with (case) and without (control) pulp necrosis were used to calculate the odds ratio with a 95% confidence interval (CI).

Table 2. Domains and Risk of Bias considered in accordance with the items of the guidelines and critical appraisal described by Fowkes and Fulton.[21]

Guideline	Checklist	Description
Study design appropriate to objective?	Objective	If they agreed (0) was assigned.
Study sample representative?	Source of sample	[0] when well described [+] partial information [++] when not informed
	Sampling method	[0] probabilistic [+] not probabilistic [++] not reported
	Sample size	For studies without the sample calculation, 145 teeth were considered as an ideal sample size according to Moccelini et al.[22] [0] did sample calculation [+] with sample >145 [++] with sample <145
	Entry criteria/ exclusions	[0] inclusion and exclusion criteria [+] only one of the criteria [++] criteria not reported
	Non-respondents	[0] completed clinical records/sheets [+] incomplete/partially clinical records [++] does not report the data of the patient's clinical records/how many patients did not participate in the follow-up
Control group acceptable?	Definition of controls	[0] the comparison group was adequate [+] the comparison group showed small failures (e.g. just clinical evaluation) [++] the comparison group was not adequate, which could cause distortions (when the evaluation used to collect information regarding pulp necrosis was different for the comparison group)
	Source of controls	[0] all participants from the same source and the source is representative [+] the characteristics for both groups showed small distortions (e.g. root development) [++] the source of the comparison was not adequate for the purpose of the study (different source of sample and/or the distribution of the sample characteristics was distinct between the groups)
	Comparable characteristics	[0] equivalent degree of eruption of the sample [+] small range of degree of eruption [++] not reported or the degree of eruption was not adequate for the purpose of the study
Quality of measurements and outcomes?	Validity	[0] with complete data about criteria for evaluation and diagnosis [+] only partial data [++] the studies did not provide the adequate criteria for evaluation of sequelae
	Reproducibility	[0] reported kappa value and in the case of only one examiner performing the intra-rate evaluation [+] for a study with more than one examiner, if only the inter-rater evaluation was performed [++] for studies in which the reliability of the Cohen's kappa and intra-class correlations (ICCs) measurements was not performed, inter-rater (if more than one examiner) and/or intra-rate (if only one or more than one examiner)
	Quality control	[0] for studies that presented measures for data quality control in which they described the statistical methods, and that standardized procedures and training were adopted to ensure the quality of information obtained through patient records [+] study performed without only one/or two the factors [++] for studies that did not present measures for data quality control (monitoring), and who did not describe statistical methods in which standardization and training procedures were not adopted and reported to ensure the quality of information obtained through patient records, since they may have deficiencies in completeness

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		[0] for studies that performed standardization of the electric pulp testing and radiographic examination
	Compliance	[+] for studies that did not perform standardization of the electric pulp testing (if performed) or radiographic examination
		[++] for studies that did not perform standardization of the radiographic examination and electric pulp testing (if both were performed)
		[0] all required data provided (frequency, number, p value)
	Missing data	[+] incomplete data not affecting completion
Completeness?		[++] incomplete results, and exclusion of important data that compromise completion
	Confounding factors	[0] (dental caries) if used as an exclusion factor and in the confounding of statistical analysis or article discussion
		[+] when used only in the discussion
		[++] if the research did not mention the considered factor (dental caries)
	Distortion reduced by analysis	[0] used multiple regression and when the confounding factor was excluded
		[+] did not perform multiple regression, however, when the confounding factor was excluded
		[++] did not perform multiple regression to reduce influences and did not use confounding factors
Summary	Bias - Are the results erroneously biased in a certain direction?	
	Confounding - Are there any serious confounding or other distorting influences?	"YES" or "NO" answers were assigned to each question. If the answers to the three questions were "NO", the article could be judged as solid (low risk of bias).
Questions	Chance - Is it likely that the results occurred by chance?	

Random effect models were employed because the studies were not functionally equivalent and the objective was to generalize the results from the meta-analysis (type of exam used for the diagnose of pulp necrosis and mean age were different between studies).[23] Heterogeneity was tested using the I^2 index and, if necessary, sensitivity analyses were conducted to estimate and verify the influence of studies, one by one, on the subgroup and pooled results when heterogeneity was substantial or considerable (50–100%, $p < 0.05$).[24] Only studies free of bias were included in the meta-analysis. If some of the information needed for the meta-analysis was absent from any of the selected studies, the authors were contacted to provide the missing data.

Quality of evidence

The assessment of quality of evidence was determined for the meta-analysis outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[25] Observational studies start as low evidence, and the quality of the body of evidence decreases to very low if serious or very serious issues related to risk of bias, inconsistency, indirectness, imprecision, and publication bias are detected. On the other hand, the quality of evidence could increase if the influence of all plausible confounding factors would reduce a demonstrated effect, or suggest a spurious effect, and if the magnitude of effect is large or very large. As a result, the quality of the evidence can vary from very low to high.

Results

A flow diagram (Figure 1) describes the study selection process. The search identified a total of 2,702 titles/abstracts stemming from databases. After removal of duplicates, 1,207 studies remained and were analyzed (reading of titles and abstracts) according to the study criteria. Five studies[5,12,26,27,28] were included for qualitative synthesis, while four[5,12,27,28] were used for the final meta-analysis.

Data extraction

The main characteristics of included studies are presented in Table 3. The descriptive observational study design was adopted for all studies,[5,12,26,27,28] and all studies were conducted in university settings.[5,12,26,27,28] Two studies were conducted in Brazil,[5,28] one in Sweden,[12] one in the US,[26] and one in Nigeria.[27] Two studies evaluated teeth with intrusive luxation[5,28] and one with root fracture,[12] the other studies did not report the type of dental trauma evaluated. The study of Oginni et al.[27] did not inform the number and age of patients. Only one study by Holcomb and Gregory[26] did not provide/confirm information or answer the contact by e-mail.

Quality assessment and risk of bias

The quality assessment and bias control of the 5 selected studies are presented in Table 4 according to the guideline described by Fowkes and
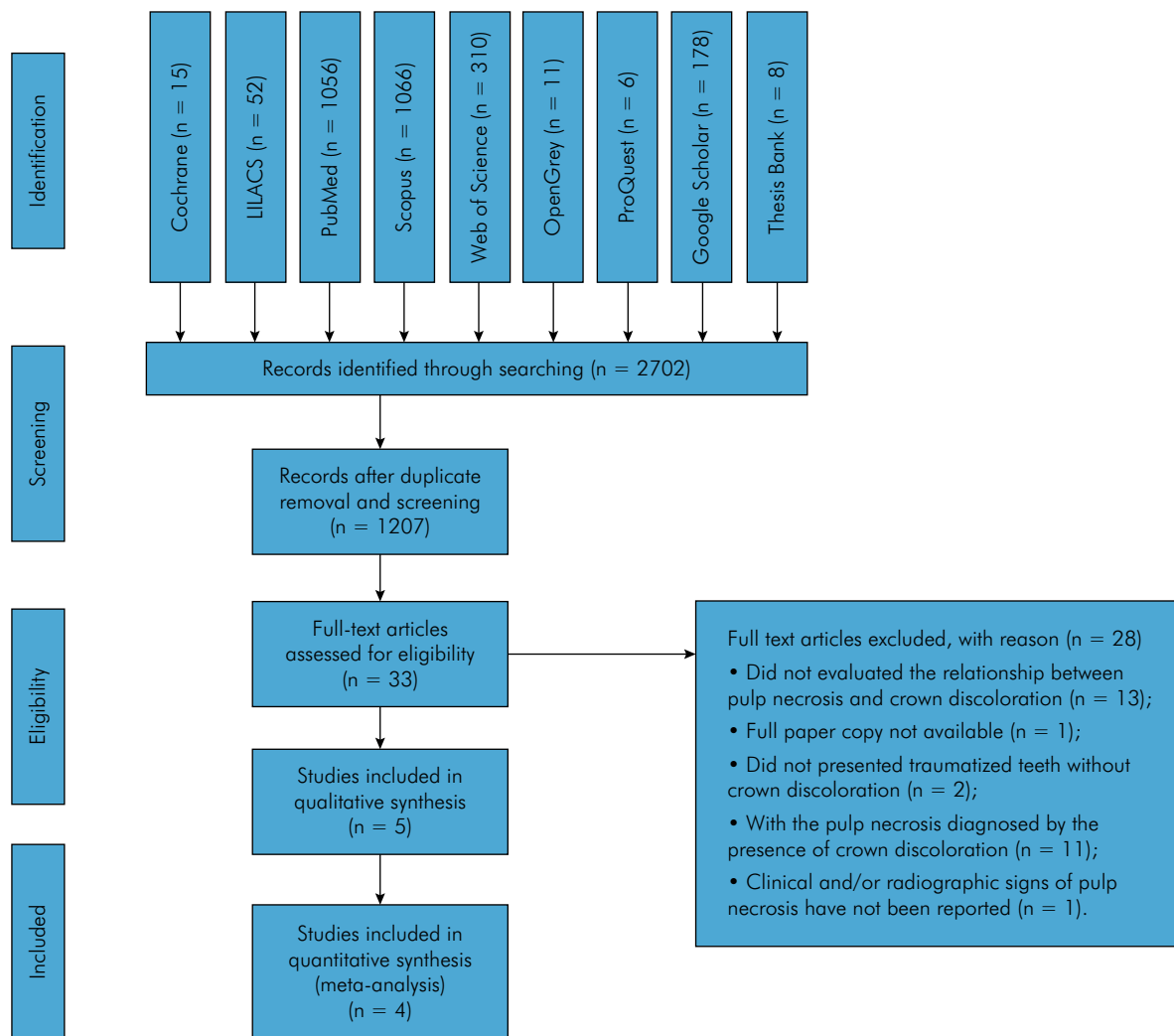

Figure 1. Flowchart diagram of literature search and selection criteria according to the PRISMA statement.

Table 3. Data extracted from the included studies.

Author, year, country	Sample size	Source of study	Age range (years)	Type of dental trauma	Follow-up	N of traumatized teeth*	Exam for pulp necrosis diagnosis	Description of teeth	Statistical analysis and study result
Holcomb and Gregory, 1967[26], USA	34	United States Naval Academy	7–16	NI	The teeth were evaluated over a four-year interval	40	Electric pulp testing, clinical and/or radiographic	Of the forty teeth, only three showed pulp necrosis; of these, two presented crown discoloration.	Descriptive analysis.
Malmgren and Hübel, 2012[12], Sweden	39	Department of Paediatric Dentistry at the Eastman Institute in Stockholm	7–19	Root fracture	The follow-up period ranged from 1 to 9 years	42	Electric pulp testing, clinical and/or radiographic	Only one tooth maintained crown discoloration and showed pulp necrosis during follow-up.	Descriptive analysis and Chi-squared test (p < 0.05). No significant difference was found in prognosis between teeth with and without discoloration (p = 0.76).
Neto et al., 2009[5], Brazil	12	Center of Buccodental Trauma (CENTRAU) of the University of Ceará	7–14 years and 8 months	Intrusive luxation	Follow-ups at 2 weeks, 1, 3, and 6 months and annually.	15	Thermal pulp testing, clinical and/or radiographic	Eleven teeth showed pulp necrosis, one tooth presented crown discoloration.	Descriptive analysis and relative risk.
Oginni et al., 2009[27], Nigeria	NI	Oral Diagnosis Unit and the Conservative Clinic of the Dental Hospital, Obafemi Awolowo University Ile-Ife	NI	NI	The teeth were evaluated sometime after the traumatic injury.	276	Electric pulp testing, clinical and/or radiographic	All teeth evaluated presented pulp canal obliteration. Seventy-five teeth showed pulp necrosis and all of these teeth presented crown discoloration.	Descriptive analysis, chi-squared test (p<0.05) and Mantel–Haenszel. No differences were found between teeth with a negative response to the sensitivity test and periapical bone rarefaction (pulp necrosis) and yellow, grey or normal color.
Soares et al., 2018[28], Brazil	25	Dental Trauma Surveillance Center (DTSC) of the Federal University of Rio de Janeiro,	6-12	Intrusive luxation	Followed for a minimum period of three months after initial attendance	34	Electric pulp testing, clinical and/or radiographic	Twelve teeth presented pulp necrosis and none of the evaluated teeth showed crown discoloration.	Descriptive analysis, chi-squared test (p<0.05) and logistic regression analysis (p < 0.05).

*Total calculated by the author; NI: not informed.

Fulton.[21] Regarding *sample*, Moreira Neto et al.[5] and Oginni et al.,[27] in the item source of sample, described partial information and it was considered a minor problem. All studies used convenience sampling and it was also considered a minor problem. Regarding the item *sample size*, Holcomb and Gregory,[26] Malmgren

Table 4. Quality assessment Fowkes and Fulton.[21]

Guideline	Checklist	Holcomb and Gregory, 1967[26]	Malmgren and Hübel, 2012[12]	Moreira Neto et al., 2009[5]	Oginni et al., 2009[27]	Soares et al., 2018[28]
		Objective				
Study design appropriate to the objective?	Prevalence	0	0	0	0	0
	Prognosis	NA	NA	NA	NA	NA
	Treatment	NA	NA	NA	NA	NA
	Cause	NA	NA	NA	NA	NA
Study sample representative?	Source of sample	0	0	+	+	0
	Sampling method	+	+	+	+	+
	Sample size	++	++	++	+	++
	Entry criteria/exclusions	+	0	0	0	0
	Non-respondents	+	0	0	0	0
Control group acceptable?	Definition of controls	0	0	0	0	0
	Source of controls	0	0	0	0	0
	Matching/randomization	NA	NA	NA	NA	NA
	Comparable characteristics	0	0	0	0	0
Quality of measurements and outcomes?	Validity	0	0	0	0	0
	Reproducibility	++	++	0	0	0
	Blindness	N A	NA	NA	NA	NA
	Quality control	+	0	0	0	0
Completeness?	Compliance	+	0	0	0	0
	Dropouts	NA	NA	NA	NA	NA
	Deaths	NA	NA	NA	NA	NA
	Missing data	0	+	0	0	0
Distorting influences?	Extraneous treatments	NA	NA	NA	NA	NA
	Contamination	NA	NA	NA	NA	NA
	Changes over time	NA	NA	NA	NA	NA
	Confounding factors	++	0	0	0	0
	Distortion reduced by analysis	++	+	0	0	0
Summary questions	Bias – Are the results erroneously biased in a certain direction?	YES	NO	NO	NO	NO
	Confounding – Are there any serious confounding or other distorting influences?	YES	NO	NO	NO	NO
	Chance – Is it likely that the results occurred by chance?	YES	NO	NO	NO	NO

0: no problem; +: minor problem; ++: major problem; NA: not applicable

and Hübel,[12] Moreira Neto et al.[5] and Soares et al.[28] did not perform sample size calculation and the sample was <145 teeth, and it was considered a major problem, and Oginni et al.[27] did not perform the sample size calculation and the sample was > 145 teeth, and it was considered a minor problem.

The article of Holcomb and Gregory[26] did not mention the exclusion criteria, and it was considered a minor problem. In the item *non-respondents*, Holcomb and Gregory[26] described partial information in the clinical records, and it was considered a minor problem.

In *quality of measurements and outcomes*, in the item *reproducibility*, Holcomb and Gregory[26] and Malmgren and Hübel[12] did not perform Cohen's kappa reliability test and intra-class correlations (ICCs), and it was considered a major problem. For the item *quality of control*, Holcomb and Gregory[26] did not describe any statistical methods and presented deficiencies in completeness of the information obtained through patient records, and it was considered a minor problem.

In *completeness*, in the item *compliance*, Holcomb and Gregory[26] did not perform standardization of the radiographic examination, and it was considered a minor problem. For the item *missing data*, Malmgren and Hübel[12] in the discussion showed incomplete data without affecting completion, and it was considered a minor problem.

In relation to *distorting influences*, in the item *confounding factors*, Holcomb and Gregory[26] did not mention dental caries, which was considered a factor, and the item was considered a major problem. For the item *distortion reduced by analysis*, Holcomb and Gregory[26] did not perform a multiple regression and did not include confounding factors, and it was considered a major problem. Malmgren and Hübel[12] did not perform a multiple regression, but the authors excluded teeth with dental caries, and it was considered a minor problem.

Lastly, the questions regarding "*Bias*", "*Chance*" and "*Confounding*" for the four studies[5,12,27,28] were answered with a NO. For the study of Holcomb and Gregory[26] the three questions were answered with a YES. Therefore, the articles by Malmgren and Hübel,[12] Moreira Neto et al.,[5] Oginni et al.,[27] and Soares et al.[28] were classified with high methodological quality and Holcomb and Gregory[26] had no methodological soundness (Table 4).

Meta-analysis and quality of evidence

The meta-analysis was conducted only with the data available in the studies included in the present systematic review. The Holcomb and Gregory[26] study was classified as having serious confounding or other distorting influences, and was excluded from the meta-analysis. Four studies were included in the quantitative synthesis.[5,12,27,28]

The heterogeneity of the four studies was substantial but not significant (I^2=56% p = 0.11). In an attempt to reduce heterogeneity, sensitivity analysis was performed by removing the studies one by one.[24] During this stage, the heterogeneity ranged from 0% to 74%. However, the removal of these studies from the analysis nullified the heterogeneity without altering the overall significance of the result. Thus, the final meta-analysis included the four studies.

The pooled meta-analysis showed a positive association between crown discoloration and pulp necrosis in permanent teeth. Teeth with crown discoloration presented 23 times higher chance to present pulp necrosis than teeth without crown discoloration (OR 23.84 [1.23, 464.06]; p=0.04) (Figure 2), with a very low quality of evidence (Table 5).
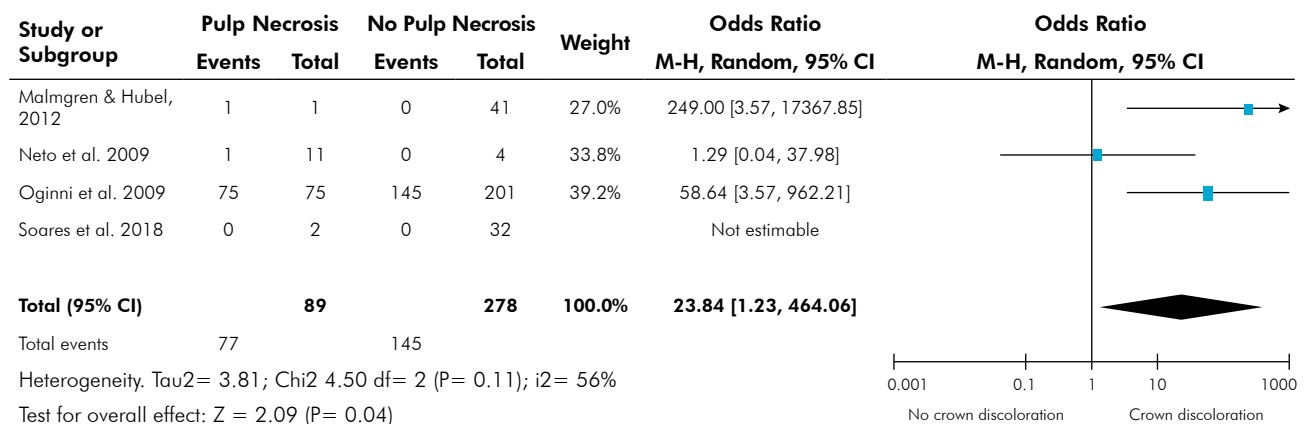
Study or Subgroup	Pulp Necrosis		No Pulp Necrosis		Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total			
Malmgren & Hubel, 2012	1	1	0	41	27.0%	249.00 [3.57, 17367.85]	
Neto et al. 2009	1	11	0	4	33.8%	1.29 [0.04, 37.98]	
Oginni et al. 2009	75	75	145	201	39.2%	58.64 [3.57, 962.21]	
Soares et al. 2018	0	2	0	32		Not estimable	
Total (95% CI)		89		278	100.0%	23.84 [1.23, 464.06]	
Total events	77		145				

Heterogeneity. Tau2= 3.81; Chi2 4.50 df= 2 (P= 0.11); i2= 56%

Test for overall effect: Z = 2.09 (P= 0.04)

0.001 0.1 1 10 1000

No crown discoloration   Crown discoloration

Figure 2. Forest plot the association between pulp necrosis and crown discoloration in traumatized permanent teeth.

Table 5. Evidence profile. Association of crown discoloration and pulp necrosis in traumatized permanent teeth.

n studies	Study design	Certainty assessment					n of patients		Effect		Certainty
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Crown discoloration	No crown discoloration	Relative (95% CI) OR 23.82	Absolute (95% CI)	
							77 cases	145 controls		-	⊕○○○
3	observational studies	not serious	serious [b,c]	not serious	very serious [a,d]	very strong association	-	0.0%	(1.25 to 452.87)	0 fewer per 1.000 (from 0 fewer to 0 fewer)	Very low

CI: Confidence interval; OR: Odds ratio; a. Total number of events is less than that requested by GRADE for the evaluation of studies with an odds ratio. b. Some variation in the effect estimates across studies with overlap of confidence intervals associated with the effect estimates. c. Heterogeneity higher than 50% but not significant. d. Lower and higher confidence intervals greater than 25% of OR.

Discussion

Crown discoloration is a common sequela after trauma,[29] easily identified by the patient due to esthetic impairment,[15] and therefore, it is common for the patient to seek dental care to treat this alteration.[30] This sequela indicates loss of pulp vitality when associated with at least one more sign of necrosis (periapical bone rarefaction, external inflammatory reabsorption).[9,10] However, in many cases, crown discoloration is the only sign of alteration after dental trauma, leaving the dentist uncertain because, despite suggesting pulp necrosis, it is still not an indication for endodontic treatment.[9] In order to elucidate this question, the present systematic review and meta-analysis showed that there is an association between crown discoloration of the traumatized permanent tooth and pulp necrosis.

Although the definitive diagnosis of pulp necrosis is only confirmed by clinical observation of the pulp after endodontic access of the tooth or by histological analysis,[31] the literature agrees that for the beginning of endodontic treatment, the absence of pulp vitality can be identified through periapical radiolucency signs, abscess/fistula,[32] and external inflammatory root resorption[33] regardless of the history of trauma. Thus, for traumatized teeth, the discoloration of the crown alone is insufficient to confirm pulp necrosis according to Andreasen[9] and Malmgren and Rübel,[12] since in the first year after dental trauma, the prognosis of the pulp is uncertain.[6]

Although the literature presents a significant number of studies evaluating crown discoloration and pulp necrosis of traumatized permanent teeth, most do not meet the eligibility criteria of the present study for not distinguishing among necrotic teeth with and without discoloration, or not reporting association data. Among the five studies included, the study by Oginni et al.[27] reported the absence of association between crown discoloration and pulp necrosis and the other studies presented descriptive data.

Another important aspect worth highlighting is the time of crown discoloration after trauma, that is, whether it was transient or permanent. For the present review, only permanent crown discolorations were considered (at the end of follow-up) and there was no distinction of color shades. Discoloration is defined as transient when it is identified soon after the trauma, remaining altered during the period of pulp healing.[34] Transient discoloration is described as a favorable prognostic sign in the study by Malmgren and Rübel,[12] where 8 of the 9 traumatized teeth with color change and negative response to the sensitivity tests at the beginning of follow-up returned to their normal color within the period from 4 to 6 months and responded positively to the sensitivity tests. The permanent color change is defined at the end of the follow-up (there is no period stipulated in the literature), attributed to a possible pulp infection with necrotic tissue autolysis and extravasation of the products into the dentine.[9,34]

Other aspects such as the age of the patient at the time of trauma, the type of dental trauma, the stage of root development,[8,10,31] and the combination of types of dental trauma[10,35] are factors that influence the sequelae and prognosis of the traumatized tooth. Dental trauma is more frequent in children and adolescents,[2] and immature permanent teeth have a better prognosis, with a better healing process compared to mature permanent teeth[2,35] after dental trauma such as pulp exposure, root fracture, and luxation injury.[2,17,35]

Several factors that may influence the prognosis of the traumatized permanent tooth can be found in the analyzed studies in this systematic review and may have influenced the relationship between pulp necrosis and crown discoloration. In addition, the high heterogeneity, confirmed in the meta-analysis, could have influenced the results. Malmgren and Hübel[12] evaluated 7 to 19-year-old patients with intra-alveolar root fracture. Of the 42 teeth evaluated, only one had crown discoloration and pulp necrosis. Full root formation with closed apex occurred in 80.9%, with half-closed apex in 14.3%, and full root formation with an open apex in two teeth (4.8%).[12] Root fracture is a rare trauma in permanent teeth and has shown good prognosis.[2,36] Moreira Neto et al.[5] assessed the treatment approach of teeth with severe intrusion. Of the fifteen traumatized permanent teeth, 73.3% had an incomplete root formation and 26.6% had a complete root formation at the time of trauma. Of the immature teeth, four teeth were vital with pulp canal obliteration and without color change. All mature teeth presented pulp necrosis and no crown discoloration. The early stage of root development (immature) had a positive effect in that sample.[5] Intrusive luxation is a very severe injury and the healing process may be accompanied by a high number of post-trauma complications, principally pulp necrosis.[2,5] In the study by Moreira Neto et al.,[5] eleven teeth presented pulp necrosis and one, crown discoloration. Moreover, of the all teeth evaluated, 66.6% showed an additional injury, which increases the risk of pulp necrosis.[5] Oginni et al.[27] did not discriminate the types of dental trauma, however, all teeth presented pulp canal obliteration and 27.2% were necrotic. The study by Soares et al.[28] evaluated only luxation injury and no tooth showed discoloration.

Crown discoloration was not considered in any of the four studies as a criterion for the diagnosis of pulp necrosis. The studies performed the diagnosis of pulp necrosis in different ways, and the teeth that presented a negative response to the electric or thermal pulp test were associated with another clinical/radiographic sign of pulp necrosis (abscess/fistula and/or periapical bone rarefaction and/or external inflammatory resorption).[5,12,26,27,28] Only in the studies by Moreira Neto et al.[5] and Oginni et al.,[27] the measurements reliability for the radiographic diagnosis were measured, which may justify the heterogeneity of the included studies.

Although radiographic examination is of great importance after dental trauma and can indicate, in many cases, endodontic treatment, Andreasen and Kahler[13] report that traumatic teeth during the pulp healing process can present radiographic changes that can generate diagnostic confusion. In some cases, a periapical radiolucency or pronounced expansion of the periodontal ligament may be identified.[34] Transient apical breakdown (TAB), a temporary process with evident resorption of the apex[37] or periapical region may lead to an overdiagnosis[9] and should be differentiated from periapical replacement resorption[37] and periapical bone rarefaction.[35] In addition, in the study by Andreasen,[34] TAB was concomitantly identified with color and sensibility changes after luxation injuries, which returned to their normal conditions during the follow-up period.

The assessment of the methodological quality of the studies included in the systematic review is very important because it is related to the critical and detailed evaluation of the studies.[38] All primary studies included in that systematic review showed observational analytical design that allowed the guide described by Fowkes and Fulton[21] to properly assess the methodological quality and risk of bias. Only the study by Holcomb and Gregory[26] did not show methodological soundness, because it had problems in one of the three summary questions (confounding factors), since there was no confirmation of the exclusion of teeth with caries.

The studies by Malmgren and Hübel,[12] Moreira Neto et al.,[5] Oginni et al.[27] and Soares et al.[28] were considered to have good methodological quality, and were included in the quantitative analysis; however, the heterogeneity was considered substantial. The heterogeneity observed between studies may be related to the variability between the characteristics of the previously mentioned samples and diagnostic tests.[24]

Although the meta-analysis included four studies, Soares et al. [28] results were not computed in the effect size (OR 23.84) because no event (tooth discoloration) was described in this study results. The only rate effect that computes results with no events is the risk difference (RD). However, RD could not be applied in the present meta-analysis since it requires the incidence in the exposed and unexposed groups, which was not available in the included studies as they all had cross-sectional designs and no prospective analysis. Although no events were reported, the authors opted to maintain Soares et al. [28] in the quantitative analysis to provide results that were representative of the studies.

Although the results of the present systematic review and meta-analysis showed a positive association between crown discoloration and pulp necrosis, some aspects need to be analyzed with caution before the indication of endodontic treatment: a) crown discoloration is not a pathognomonic sign of necrosis,[9] b) part of the studies did not differentiate between open and closed teeth, c) transient and permanent discolorations are not clearly identified, and d) the level of evidence in the studies is very low.

Among the options of a) initiating endodontic treatment having only crown discoloration as a sign of pulpal alteration and b) follow up teeth with discoloration until another clinical and/or radiographic sign of pulp necrosis is identified, the latter seems to be more prudent and reduce the risk of unnecessary endodontics. Andreasen and Kahler[39] emphasize that clinicians should consider signs and symptoms in addition to radiographic evaluations before intervention with pulp therapy.

In this sense, although the follow-up advocated by the IADT for traumatized permanent teeth is dependent on the type of trauma,[17] based on the present systematic review, after identifying a crown discoloration on a permanent tooth with trauma, irrespective of the shade, the clinician should recommend a specific clinical and radiographic follow-up, that is, with shorter intervals between visits. Thus, in cases where the tooth with crown discoloration is actually necrotic, the final diagnosis through other clinical/radiographic signs could be performed early and endodontic treatment initiated immediately, favoring the prognosis of the treatment. On the other hand, in cases where no clinical/radiographic signs that confirm pulp necrosis are identified, the tooth would remain in follow-up, without endodontic intervention. It is important that further studies determine a specific follow-up protocol for traumatized teeth with crown discoloration.

One limitation of the present systematic review and meta-analysis was that the studies included did not have the same objective as the present study and did not report confirmation of the diagnosis of pulp necrosis after endodontic access (gold standard). Therefore, because the GRADE method indicated a very low quality of the evidence, more prospective and retrospective studies are needed specifically designed to evaluate the present association and, thus, support the current evidence. Further research is also needed to determine a specific protocol for monitoring traumatized permanent teeth with crown discoloration.

In conclusion, there seems to be an association between the clinical sign of crown discoloration and pulp necrosis in traumatized permanent teeth. However, these data need to be carefully evaluated in view of the low quality of the evidence. In addition, specific monitoring of the teeth with crown discoloration is fundamental to minimize damages and favor the prognosis.

Acknowledgments

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