

Effectiveness of single- versus multiple-visit endodontic treatment of teeth with apical periodontitis: a systematic review and meta-analysis

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Abstract

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Aim The clinical question this review aimed to answer is: does single-visit root canal treatment without calcium hydroxide dressing, compared to multiple-visit treatment with calcium hydroxide dressing for 1 week or more, result in a lower healing (success) rate (as measured by clinical and radiographic interpretation)?

Methodology CENTRAL, MEDLINE, EMBASE and HEALTH STAR databases were used. Reference lists from identified articles were scanned. A forward search was undertaken on the authors of the identified articles. Papers that had cited these articles were also identified through Science Citation Index to identify potentially relevant subsequent primary research.

Review methods The included studies were randomized controlled clinical trials (RCTs) comparing

healing rate of single- and multiple-visit root canal treatment in humans. The outcome measured was healing of radiographically detectable lesions. Data in those studies were independently extracted.

Results Only three RCTs were identified and included in the review, covering 146 cases. Sample size of all three studies was small; none demonstrated a statistically significant difference in healing rates. Risk differences of included studies were combined using the inverse variance-weighted method ($RD_{\text{Pooled}} = -6.3\%$; 95% CI: $-20.3-7.8$).

Conclusion Based on the current best available evidence, single-visit root canal treatment appeared to be slightly more effective than multiple visit, i.e. 6.3% higher healing rate. However, the difference in healing rate between these two treatment regimens was not statistically significant ($P = 0.3809$).

Keywords: evidence-based dentistry, one-step endodontics, therapeutic efficacy, treatment effectiveness.

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Introduction

It has been established beyond doubt that apical periodontitis is caused by bacteria within root canals

(Kakehashi *et al.* 1965, Moller *et al.* 1981). Logically, the treatment of apical periodontitis should be removal of the cause, i.e. bacterial eradication. Mechanical debridement combined with antibacterial irrigation (0.5% sodium hypochlorite) can render 40–60% of the treated teeth bacteria-negative (Byström & Sundqvist 1983, Sjögren *et al.* 1997). In addition to mechanical debridement and antibacterial irrigation, dressing the canal for 1 week with calcium hydroxide has been shown to increase the percentage of bacteria-negative

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teeth to around 70% (Law & Messer 2004). By extrapolation, the regimen including calcium hydroxide dressing between appointments should provide a higher healing rate, because bacteria are further reduced. Thus, the healing rate of multiple-visit treatment should be higher than single-visit treatment (without calcium hydroxide dressing).

Single-visit root canal treatment has become common practice and offers several advantages such as a reduced flare-up rate (Walton & Fouad 1992, Imura & Zuolo 1995, Albashaireh & Alnegrish 1998), good patient acceptance and practice management considerations. One survey study reported that almost 70% of endodontists would treat teeth with a necrotic pulp and chronic apical abscess in one visit (Whitten *et al.* 1996). Another survey showed that around 70% of undergraduate teaching institutions in the USA encourage single-visit root canal treatment (Qualtrough *et al.* 1999). However, the fact that various practices are widely adopted does not indicate that the practices are biologically sound and/or appropriate. The argument for single-visit treatment relies heavily on convenience, patient acceptance and reduced postoperative pain. On the other hand, bacterial eradication cannot be predictably maximized without calcium hydroxide dressing between appointments; thus, the potential for healing may be compromised (Spångberg 2001). The issue is very controversial, and opinions vary greatly as to the relative risks and benefits of single- versus multiple-visit root canal treatment. The direct evidence comparing healing rates following single- and multiple-visit root canal treatment should provide insight as to which regimen is more effective.

Randomized controlled clinical trials (RCTs) are generally considered the most reliable method for assessing the efficacy of treatments (Elwood 1998), because they can minimize confounders and maximize control over the trial environment. RCTs are high in the hierarchy of quality of evidence (Greenhalgh 2001) because they can establish the most convincing causal relationship compared with other types of clinical studies, e.g. cohort, case-control, and cross-sectional survey. However, individual RCTs are often small and lack statistical power, owing mainly to their high cost and high degree of long-term commitment required. A meta-analysis is a statistical methodology in which data from individual RCTs are considered and analysed together (Upton & Cook 2002); by combining data they improve the ability to study the consistency of results, i.e. they give increased power.

There has been a growing international interest in the development of measures to help ensure that practice decision-making is better informed by the results of relevant and reliable research (evidence-based) (Sutton 2000). A systematic review is one of those measures. It is an evaluation and interpretation of all available research evidence relevant to a particular question. A concerted attempt is made to identify all relevant primary research, a standardized appraisal of study quality is made and the studies of acceptable quality are systematically and quantitatively synthesized (Glasziou 2001).

This systematic review addresses the choices (single- or multiple-visit root canal treatment) clinicians face in dental practice, and aims to provide the current best available evidence upon which clinical decisions regarding root canal treatment can be based. The clinical question to be answered in this systematic review was framed in terms of a PICO question {problem (P), intervention (I), comparison (C), and outcome (O)} as follows: in patients undergoing root canal treatment for apical periodontitis (teeth with an infected root canal system), does single-visit treatment without calcium hydroxide dressing, compared to multiple-visit treatment with calcium hydroxide dressing for 1 week or more, result in a lower healing (success) rate (as measured by clinical and radiographic interpretation)?

Materials and methods

Literature search

Randomized controlled trials and controlled clinical trials of single- versus multiple-visit root canal treatment conducted in humans were identified. The Cochrane Controlled Trials Register (CENTRAL) was searched using the term ENDODONTICS, SINGLE, ONE, TWO, MULTIPLE, VISITS, APPOINTMENTS. The optimum search strategy for detecting controlled trials formulated by the Cochrane Collaboration as outlined in the Cochrane Reviewers' Handbook (Alderson *et al.* 2004) was combined with the above-mentioned terms and used to search MEDLINE from 1966 to August 2004 (Table 1). A similar search was undertaken on EMBASE (1988–2004) and HealthSTAR. No language restriction was applied to the search. A total of 196 studies were subjected to the preliminary analysis. Two reviewers scanned all titles and abstracts (Edwards *et al.* 2002), where available, and decided whether or not they were related to healing rate of single- or multiple-visit root canal treatment. Where information

Table 1 MEDLINE (Ovid) search strategy developed to find article-related single-visit endodontics

Search history	Results
1 Endodontics/or apicectomy/or dental implantation, endosseous, endodontic/or dental pulp capping/or pulpectomy/or pulpotomy/or 'root canal therapy'/or dental pulp devitalization/or 'root canal obturation'/or retrograde obturation/or 'root canal preparation'/or tooth replantation/	16 064
2 One.mp. {mp=title, original title, abstract, name of substance, mesh subject heading}	1 349 112
3 Single.mp. {mp=title, original title, abstract, name of substance, mesh subject heading}	523 388
4 Two.mp. {mp=title, original title, abstract, name of substance, mesh subject heading}	1 771 618
5 Multiple.mp. {mp=title, original title, abstract, name of substance, mesh subject heading}	336 124
6 Visit\$.mp. {mp=title, original title, abstract, name of substance, mesh subject heading}	51 432
7 Appointment\$.mp {mp=title, original title, abstract, name of substance, mesh subject heading}	8983
8 2 or 3 or 4 or 5	3 050 842
9 6 or 7	59 289
10 1 and 8 and 9	210
11 Limit 10 to human	196

from the title and abstract was not adequate in determining the paper's relevance, they were automatically included in subsequent analysis. A total of 173 studies were excluded from the list, and the 23 remaining articles were subjected to stricter exclusion criteria.

Inclusion and exclusion

The full text articles of the remaining studies were then obtained and reviewed by the two reviewers, and the inclusion criteria (Table 2) were applied independently.

Table 2 Inclusion and exclusion criteria used in the analysis

Inclusion criteria

1. Subjects had a noncontributory medical history
2. Subjects presented with mature teeth with infected necrotic root canals and radiographic evidence of periapical bone loss (as an indication of preoperative canal infection)
3. All selected root canals had not received any endodontic treatment previously
4. Subjects underwent nonsurgical root canal treatment during the study
5. The outcome measure was the number of teeth that showed radiographic evidence of healing

Exclusion criteria

1. Inclusion of test teeth without infected necrotic root canal systems and/or radiographic evidence of periapical bone loss (hence no preoperative canal infection)
2. Subjects were not randomly assigned to single- or multiple-visit treatment
3. Study carried out on failed, endodontically treated teeth (retreatment cases)
4. No comparison between single- and multiple-visit endodontics within the same study
5. No healing rate presented

Reference lists from identified articles were scanned to identify other potentially relevant articles [one more article was identified (Friedman *et al.* 1995)]. A forward search was undertaken on the authors of the identified articles. Papers that had cited these articles were also identified through Science Citation Index (<http://www.isinet.com>), to identify potentially relevant subsequent primary research (Glasziou 2001) [one more article was identified (Farzaneh *et al.* 2004)].

Data extraction

A systematic data extraction sheet constructed by The Critical Appraisal Skills Programme (CASP) (Learning and Development, Public Health Resource Unit NHS, UK) (<http://www.phru.nhs.uk/casp/casp.htm>, last accessed 28 June 2004) and CONSORT guidelines (Begg *et al.* 1996, Newcombe 2004) were adapted by the reviewers who independently extracted the data. Authors of two studies were contacted to acquire additional information not available in the published article.

Meta-analysis

Between-study heterogeneity was assessed using standard chi-square test or *Q*-statistic. The principal measure of treatment effect was risk difference, which is defined as the risk in the experimental group minus the risk in the control group. For the purpose of this study it is given as the difference in healing rates between single- and multiple-visit treatment. Risk difference is a measure of the impact of the treatment on the number of events (healing), as it takes into account the prevalence of the event, i.e. how common it is. This is in contrast to

odds ratio, which is a measure of the association between treatment and outcome, but does not give an indication of the impact of the intervention, i.e. the same odds ratio can give a different impact depending on how common the event is (Sutton 2000). The fixed effect method for combining study estimates was used and an overall estimate was produced. Risk differences of included studies were combined using the inverse variance-weighted method, by which each study was given a weight directly proportional to its precision (Sutton 2000) (Comprehensive Meta Analysis Version 1.0.25; Biostat, Englewood, NJ, USA). The level of statistical significance was set at 0.05.

Results

Included and excluded studies

Only three small RCTs met our inclusion criteria (Table 2): that is, Trope *et al.* (1999), Weiger *et al.* (2000) and Peters & Wesselink (2002). Five studies (Soltanoff 1978, Rudner & Oliet 1981, Oliet 1983, Friedman *et al.* 1995, Farzaneh *et al.* 2004) that compared healing rate of single- and multiple-visit root canal treatment were excluded, mainly because their patient allocations were not randomized. Other studies were excluded because of different reasons as shown in Table 3.

Data summary of included studies

Randomization could well be the single most important design feature of a study investigating therapeutic efficacy because it is the only way to control for confounders that are not known or not measured (Alderson *et al.* 2004). Randomization was explicitly stated in Trope *et al.* (1999) and Peters & Wesselink (2002), but not reported by Weiger *et al.* (2000). Randomization was, however, implicitly stated using the term 'minimization', which is one of the several patient randomization systems. Overall, randomization was reasonably adequate in all three studies, even though it was not detailed and was not as stringent as required by CONSORT guidelines.

The differences between subjects of treatment groups at entry to the trial might act as a significant confounder. The differences in severity of apical periodontitis (high PAI score) might affect healing time and/or chance of healing. Trope *et al.* (1999) solved the problem of differences in severity of apical periodontitis by baseline adjustment, using a periapical index (PAI),

Table 3 Studies excluded from and included in systematic review (see Table 2)

Excluded studies	Exclusion criteria	Included studies
Wolch (1975)	5	Trope <i>et al.</i> (1999)
Soltanoff (1978)	1, 2	Weiger <i>et al.</i> (2000)
Ashkenaz (1979)	4	Peters & Wesselink (2002)
Fujita & Nagasawa (1979)	4	
Pekruhn (1981)	5	
Rudner & Oliet (1981)	2	
Lipton (1982)	Unable to locate, after repeated attempts	
Oliet (1983)	2	
Pekruhn (1986)	1, 2, 3, 4	
Petrovic <i>et al.</i> (1990)	4	
Yamada (1992)	5	
Jurcak <i>et al.</i> (1993)	1, 4	
Fava (1994)	5	
Friedman <i>et al.</i> (1995)	2	
Sjögren <i>et al.</i> (1997)	4	
Kenrick (2000)	5	
Soares & Cesar (2001)	4	
Wolcott (2002)	5	
McFarland (2003)	5	
Field <i>et al.</i> (2004)	1, 2, 4	
Farzaneh <i>et al.</i> (2004)	2	
Kvist <i>et al.</i> (2004)	5	

and including only subjects with PAI score 3 or more. The PAI scoring system is a 5-point scale radiographic interpretation designed to determine the absence, presence or transformation of a disease state as score 1 is healthy periapical tissue and score 5 is severe apical periodontitis with exacerbating features (Ørstavik *et al.* 1986). Healing was judged as a decrease in the PAI score over time. Even though differences in subjects could be balanced, it also decreased their sample size (almost 50% reduction in the single-visit group) and statistical power was decreased a great deal. Weiger *et al.* (2000) implemented a minimization technique to dynamically balance different tooth types between the two treatment groups. Peters & Wesselink (2002) did not mention any attempts to balance differences between subjects of the two treatment groups.

Sample size ranged from 17 to 36 teeth per treatment group. None of the papers reported rationale for the sample size. Endodontic treatment performed in all studies seemed to be standard. Sodium hypochlorite was used as an irrigant with concentration 1–2.5%. However, effects of different NaOCl concentrations on

outcomes have not been demonstrated. Calcium hydroxide was used with different duration (1–4 weeks). Again, duration of calcium hydroxide dressing seems to be inconsequential once a 1-week duration is reached (Sjögren *et al.* 1991).

Assessment of healing

One-year follow-up time is the soonest possible to determine whether or not the lesion has healed (Ørstavik 1996). Follow-up time in all three studies was adequate, with patients followed for 1–5 years. The follow-up period in some instances, however, is less than ideal as many cases do not show complete healing for 4–5 years. In the study of Weiger *et al.* (2000), cases were mostly followed until complete healing occurred regardless of time interval (6 months–5 years). Trope *et al.* (1999) used 1 year as a cut off point, which might appear to be a shortcoming in cases where the lesion had not completely healed. However, this study utilized a different scoring system (PAI score) (Ørstavik *et al.* 1986), and the teeth with a decreased PAI score were deemed healed, even though they might not have normal PDL width.

Internal validity or observation consistency is an extremely important issue in randomized controlled trials; without it, systematic bias is ensured. Radiographic interpretation is very subject to human visual perception. Trope *et al.* (1999) was the only paper exercising an extensive calibration of evaluators. Calibration was implicitly stated in Peters & Wesselink (2002) by brief mentioning of κ score. Blinding is

another technique to minimize systematic bias; all three studies clearly stated, although without specific details, the use of blinding.

A low recall rate affects study credibility a great deal because lost samples are not accounted for and their treatment results cannot be obtained. This does not seem to apply here, as all three studies presented a very high recall rate (92–100%).

Meta-analysis

Outcomes of individual studies and a summary of meta-analysis results are shown in Tables 4 and 5 and Fig. 1. No studies demonstrated a statistically significant difference in healing rate (therapeutic efficacy) between single- and multiple-visit treatment. Meta-analysis was performed on the combined data. The outcome measure (healing rate) was based on binary data, i.e. healed/not-healed. A comparison was made between single- and multiple-visit groups, thus outcome measures were comparative binary outcomes (Sutton 2000). Between-study heterogeneity was assessed using the standard chi-square test or *Q*-statistic. The three studies were homogeneous [Test of Homogeneity Cochran *Q* (ChiSq) = 1.724, d.f. = 2, *P* = 0.4222]. A graphical informal test (Forest plot) also confirmed the homogeneity (Fig. 1). Thus, fixed effect methods for combining study estimates were used and overall estimate was produced. Risk differences of included studies were combined using the inverse variance-weighted method ($RD_{\text{Pooled}} = -6.3\%$; 95% CI: $-20.3-7.8$). Based on the

Table 4 Data summary of included studies

Citation	<i>N</i> (total)	Observation time (years)	Number of teeth (not healed/total) in single-visit group	Number of teeth (not healed/total) in multiple-visit group	Healing rate (%), single versus multiple visit
Trope <i>et al.</i> (1999)	41	1	8/22	5/19	64 vs. 74
Weiger <i>et al.</i> (2000)	67	0.5–5	6/36	9/31	83 vs. 71
Peters & Wesselink (2002)	38	4.5	4/21	5/17	81 vs. 71
Combined three studies	146	NA	18/79	19/67	77 vs. 71

NA, not applicable.

Table 5 Meta-analysis data summary

Citation	Risk difference (%)	95% CI		Weight (%)	<i>P</i> -value
		Lower	Upper		
Trope <i>et al.</i> (1999)	10	-18.2	38.3	48.25 (24.8)	0.491
Weiger <i>et al.</i> (2000)	-12.4	-32.5	7.7	95.20 (49)	0.226
Peters & Wesselink (2002)	-10.4	-37.8	17	51.14 (26.2)	0.455
Combined three studies	-6.3	-20.3	7.8	NA	0.381

Negative value indicates the difference is in favour of single-visit endodontics. NA, not applicable.

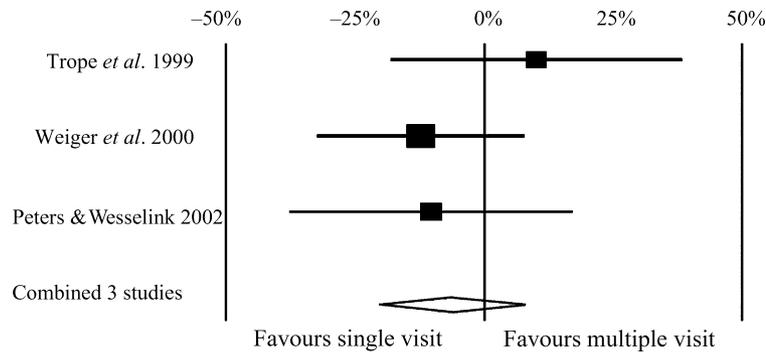


Figure 1 Forest plot. Horizontal line shows the 95% confidence interval; the shorter the line, the higher the precision of the study. Negative and positive value of risk difference is used to indicate the differences in direction of the value. Black boxes indicate the mean risk difference; their sizes are proportional to their sample size. The transparent diamond is the pooled result, with horizontal tips indicating 95% confidence interval, and the vertical tips indicating pooled risk difference. The vertical line at 0% indicates no healing rate difference between the two treatment regimens.

current best available evidence, single-visit root canal treatment appeared to be slightly more effective than multiple visit, i.e. a 6.3% higher healing rate. However, the difference in healing rate between the two treatment regimens was not statistically significant ($P = 0.3809$).

Discussion

Three small studies are not strong evidence for making clinical decisions

A wide confidence interval (28.1%) of pooled risk difference indicated low statistical power or low precision, in other words, the impact of single-visit treatment was weak on providing better treatment outcomes. Even though the 95% confidence interval of pooled risk difference was wide, it was narrower than individual studies indicating a higher precision (Fig. 1).

Publication bias (the tendency that positive studies are more likely to be published than negative ones) cannot be ruled out. However, a publication bias test (e.g. the funnel plot) was not performed because it would be unrealistic to perform such a test accurately on the very small number of RCTs. Another potential source of bias is differences in characteristics of subjects between the single- and multiple-visit groups. In clinical studies, these differences always exist, but imbalances in factors that are not prognostic cannot fairly be considered sources of bias (Burton *et al.* 2004). In root canal treatment, there is only one consensual preoperative prognostic factor, that is, a radiographically detectable lesion or the presence of apical periodontitis. This potential bias did not apply here because a radiographically detectable

lesion was present in all subjects as part of the inclusion criteria. Other potential prognostic factors, e.g. lesion size, pulpal status, symptoms and tooth type have never been proven. The impact of those factors is contradictory or inconclusive at most (Friedman 1998). Operators in all three studies were experienced endodontists; thus extrapolation of the results of this review to general practitioners may not be entirely appropriate. A large number of cross-sectional studies indicated that technical quality of root canal treatment in many countries is frequently low (Dugas *et al.* 2003). The focus of root canal treatment should be on the highest possible technical standard with good bacterial control rather than completing treatment in the shortest number of appointments.

Sample size in all three studies was unjustifiably but understandably small. This demonstrates an important limitation of RCTs in dentistry. The proper sample size should be calculated prior to trial. The sample size (power statistics) depends on the healing rate difference that is considered clinically significant. The higher the difference, the smaller the sample size. The highest possible healing rate difference could be taken from the study of Sjögren *et al.* (1997), that is 26% (94% vs. 68% healing rates in negative and positive cultured teeth, respectively). The sample size required for this difference at $P = 0.05$ and 80% power is 64 in total (32/group) (Sokal & Rohlf 1995), which is the smallest sample size possible. On the other hand, the Toronto study (Farzaneh *et al.* 2004) judged differences between outcomes of <10% to be trivial; if we were to conduct the trial anticipating a 10% difference, the upper limit of the sample size should then be 430 in total (90% vs.

80% expected healing rate) or 622 in total (80% vs. 70% expected healing rate) at $P = 0.05$, 80% power. It took two endodontists 5 years to recruit 67 patients in one of the included studies (Weiger *et al.* 2000), so that, an individual study that can detect the small difference (10%) in healing rate of single- and multiple-visit endodontics is never likely to become available.

When a study shows no statistically significant difference between treatment modalities ($P > 0.05$), either there is genuinely no difference between the treatments or there were too few subjects to demonstrate such a difference if it existed. It does not tell us which. The meta-analysis showed no statistically significant difference ($P = 0.381$) in healing rate of the two treatment regimens. The upper 95% confidence interval of the pooled risk difference was 7.8% in favour of multiple visit (Table 5), indicating that if a larger trial was conducted, there would be only a 2.5% chance that a difference larger than 7.8% would be found. As <10% difference is considered to be clinically unimportant (Farzaneh *et al.* 2004), it is highly unlikely that a larger trial would find a larger, significant difference in favour of multiple-visit root canal treatment. The nonsignificant result demonstrated here could thus be considered definitive in the sense that single-visit treatment is not likely to lead to a lower healing rate than multiple-visit treatment (<10% healing rate differential), although it must be acknowledged that the level of evidence is weak.

Of the additional studies that were excluded due to lack of randomization, similar differences of 10% or less were also found (Soltanoff 1978, Rudner & Oliet 1981, Oliet 1983, Friedman *et al.* 1995, Farzaneh *et al.* 2004).

The biological argument is not supported by clinical evidence

The biological benefit of multiple-visit treatment is that bacterial load can be further reduced by an antibacterial dressing between appointments. Based on clinical outcomes, no additional benefit is provided by the use of an inter-appointment antibacterial dressing such as calcium hydroxide. Probably, elimination of bacteria is not strictly necessary, and maximum reduction of bacteria and effective canal filling may be sufficient in terms of healing, rather than complete eradication.

In a study that examined the influence of infection at the time of root filling on the outcome of treatment (Sjögren *et al.* 1997), 68% of teeth which were infected at the time of root filling, healed after the treatment. Similar results have also been reported in other studies

(Sundqvist *et al.* 1998, Katebzadeh *et al.* 2000). While infection at the time of root filling will adversely affect the outcome of treatment, the presence of a pathogen, alone, is not sufficient for persistence of disease. There must be other factors that occur in combination to result in persistence of endodontic disease (Sundqvist & Figdor 2003), and calcium hydroxide dressing might not be able to affect these factors.

Clinical recommendations based on results

When clinicians are faced with choices of which treatment regimen should be offered to patients, the central issues that should be considered are which regimen does more good than harm, which regimens are worth the effort, and cost of using them (Sackett 2000), and probably which regimen gives higher patient and operator satisfaction. This review addressed only the first question (treatment effectiveness). The other three questions still remain open for further research.

In terms of therapeutic efficacy, current best available evidence failed to demonstrate a difference between the two treatment regimens. The worst-case scenario of healing rate of single-visit endodontics was 7.8% (upper 95% CI, Table 5) less than with multiple-visit treatment. In view of public health policy decisions, this can be considered insignificant, especially when contrasted with the lower end of 95% CI (20.3% higher healing rate in favour of single visit, Table 5). On the other hand, as clinicians dealing with individual patients, we will strive for the best possible bacterial control, in an effort to maximize prospects for healing.

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