

# **Single- or multiple visit root-canal treatment: Systematic Review and Meta-Analysis**

## **Abstract**

Increasing data indicates that single-visit root-canal treatment, which has a range of practical advantages, might be as or even more effective than the over multiple visit treatments. This systematic review of the literature aims compare both strategies with regards to risk of postoperative pain and complications.

## **Registration**

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## **Contributions**

FS and GG drafted the manuscript, contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. FS developed the search strategy. FS and GG performed data extraction and analysis. FS provided statistical expertise. Both authors read, provided feedback and approved the final manuscript.

## **Amendments**

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

## **Support**

The authors' institutions support the execution of this study and no external funding has been received

## **Introduction**

Rationale

Single-visit root-canal treatment has a number of advantages over conventional multi-visit treatment, for example the reduced number of visits, reduced workload (e.g. for repeated placement of rubberdam, anaesthetics or intermediary restorations) and lower material costs (for medication, anaesthetics, intermediary restoration etc.). However, it might be disadvantageous both with regards to short and long term outcomes. The former include mainly postoperative inflammation of peri-apical tissues, leading to mild to severe pain, or swelling (1, 2). Both pain and swelling have been associated with instrumentation or irrigation transporting medications, infected debris and (with it) bacteria into the peri-apical tissues, or inadequate instrumentation and disinfection leading to bacterial persistence within or bacterial recontamination of the root-canal system and periapex (1, 2). The latter factors as well as root-filling quality and coronal seal are associated with long-term complications including persisting

inflammation and infection, resulting in abscess, sinus tracks, pain, and radiographic signs of peri-apical bone resorption (3, 4). For both short and long-term outcomes, the preoperative condition of the tooth (tooth type, vitality, symptoms, peri-apical conditions) are of further relevance, but beyond the hands of the clinician (4)

A number of reviews have focussed on comparing single- versus multiple visit root-canal treatment (3, 5-8), either being outdated by now (3, 6), investigating only short-term pain as outcome (5), combining controlled trial data with uncontrolled trials or expert opinions to reflect the breadth of evidence (7) or pooling short- and long-term outcomes, thereby not allowing to weigh them against each other (8). The present reviews aim to comprehensively compare the available data on short- and long-term complications of single- versus multiple visit root-canal treatment. Our primary objective is to answer the question: In patients needing root-canal treatment, is single-visit treatment significantly more effective than multiple visit treatment with regards to risk of long-term failure? The secondary objective is to compare treatments with regards to risk of postoperative pain. Moreover, we will investigate moderators of risks using subgroup or meta-regression analysis. Last, we aim to assess how statistically robust current evidence is with regards to type I or II errors using trial sequential analysis, which could guide the conduct of further studies and help to derive clinical recommendations from our findings.

## **Methods**

### **Eligibility criteria**

This systematic review will include trials that:

- are randomized controlled trials, or controlled trials without indication of treatment allocation having a clinical reason (i.e. without perceived risk of indication bias, as decided by both authors). Sensitivity analyses will be performed to account for the introduced risk of bias.
- compare single-visit with multiple visit root-canal treatment in permanent teeth with closed apices, regardless of pre-operative conditions (again, sensitivity analyses will be performed to account for different conditions)
- report on risk of long-term complications or risk of short-term pain. Long-term was defined as minimum 1 year.

### ***Outcomes***

The primary outcome is risk of complications, defined as clinically and/or radiographically determined need to re-treat (non-surgical or surgical treatment, or extraction) after 1 year or later. Need to re-treat could be due to severe pain, abscess or sinus, or development, persistence or aggravation of peri-apical lesions etc. No standard as to how peri-apical lesions

were assessed or categorized was set. A minimum time threshold to separate risk of complications from risk of short-term pain was used (see below).

The secondary outcomes are

- risks of any short-term pain (<1 year after treatment), either after obturation or after instrumentation or after both. One of the outcome measures for complications was postoperative discomfort (binary, yes/no). For comparison of treatments, we considered only pain after obturation, not after instrumentation without obturation during multiple visit treatment.
- risks of short-term flare-ups (<1 year after treatment), defined as severe pain, swelling etc. leading to or being in perceived need of re-treatment.

## **Information sources**

### *Electronic searches*

We will have searched Medline via PubMed, and will search Embase via Ovid and Cochrane Central. Moreover, opengrey.eu will be searched to identify accepted, but not published studies. In addition, reference lists of identified full-texts will be screened and cross-referenced. We will contact study authors if required to obtain full-texts. Neither authors nor journals will be blinded to reviewers.

## **Search strategy**

The following search (9) will be developed for each database:

Search (patients) AND (((((((first OR second OR third)) OR (1st OR 2nd OR 3rd)) OR (one OR two OR three)) OR single) OR multiple) OR multi)) AND (((endodontic\*) OR root canal therapy) OR root canal)) AND ((visit\* OR appointment\* OR session\*))

## **Study records**

### *Data management*

A piloted spreadsheet will be used for data extraction and management.

### *Selection process*

Two authors will independently screen titles and then compare findings. Where there is disagreement, titles will be included to obtain full texts. Full texts will be assessed independently after de-duplication. Studies will be included after agreement with consensus in cases of disagreement being reached through discussion.

### *Data collection process*

Data extraction will be performed independently by two reviewers. Disagreements will be resolved through discussion.

### **Data items**

The following items will be collected: Author names, year, sample, sample, setting, tooth type, pulp vitality, preoperative pain, periapical lesions, instrumentation type, obturation type, irrigation, medication, intermediate restoration, no of visits, evaluation method, findings.

### **Outcomes and prioritisation**

The study findings for our primary and secondary outcomes and outcome measures will be extracted.

### **Data synthesis**

#### *Data synthesis*

The statistical unit will be the tooth. While this could lead to artificially narrow confidence intervals in case of multiple teeth being treated in one patient, we expect most studies to not have a significant degree of clustering (10). Random-effects meta-analysis will be performed using random-effect model via Comprehensive Meta-Analysis 2.2.64 (Biostat, Englewood, NJ, USA), with Odds Ratios (OR) or Standardized Mean Differences (SMD) and 95% confidence intervals (95% CI) being calculated as effect estimates. In studies reporting on more than two treatments, groups will be combined if possible, or separated if factorial design was used, or groups omitted in case they do not follow clinical standards to avoid unit-of-analysis conflicts. Heterogeneity will be assessed using Cochran's Q and  $I^2$ -statistics (11). Funnel plot analysis and Egger test will be performed to assess small study effects or publication bias for analyses with five or more trials being present (12, 13). OR or SMD will be adjusted (ORa, SMDa) to check the impact of possible publication bias (14).

#### *Subgroup analyses*

We might carry out subgroup or meta-regression analyses for different settings, medications, tooth type, pulp conditions, pain, peri-apical conditions. A sensitivity analysis will be performed, excluding studies with unclear randomization, which might indicate selection bias (see above). For meta-regression, the unrestricted maximum-likelihood method will be used, and Bonferroni adjustments applied to correct for multiple testing (21, 24).

### **Confidence in data**

Selection bias (sequence generation, allocation concealment), performance and detection bias (blinding of participants, operators, examiners), attrition bias (loss-to-follow-up and

missing values or participants) and reporting bias (selective reporting, unclear withdrawals, missing outcomes) will be recorded, assessed and classified according to Cochrane guidelines (13).

In addition, trial sequential analysis (TSA) will be performed to assess if quantitative findings are robust, and to calculate the required information size (RIS), i.e. the cumulative sample size needed to yield significant differences between probiotic and control therapy (15, 16). RIS will be calculated based on type I error risk of  $\alpha=0.05$  and a type II error risk of  $\beta=0.20$  (equivalent to a power of 0.80). The control event proportion (i.e. event incidence in control group) and the relative risk reduction (RRR) will be used to estimate RIS. RRR will be based on an a priori defined worthwhile interventional effect of 20%. RIS will be diversity adjusted (DARIS). To assess if differences yielded by conventional meta-analysis are robust, TSA additionally estimates trial sequential monitoring boundaries (TSMB), i.e. statistical thresholds for significance which are adapted depending on the so far reached sample size. Effect estimates supported by only few small trials are thus handled stricter than those supported by large samples. Further details regarding the applied method to calculate TSMB have been reported elsewhere (17). TSA will be performed with TSA 0.9 (Copenhagen Trial Unit, Copenhagen, Denmark) (16).

Our findings will be graded accordingly using the GRADE approach using Grade Profiler 3.6 (18).

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