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Soft tissue augmentation procedures for natural teeth and dental implants: an overview of systematic reviews (Protocol)

Kuswandani SO, Buti J, Rotundo R, Hutomo DI, Tan HJ, D'Aiuto F

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[Overview of Reviews Protocol]

Soft tissue augmentation procedures for natural teeth and dental implants: an overview of systematic reviews

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (overview). The objectives are as follows:

To synthesise the evidence from Cochrane and non-Cochrane systematic reviews of randomised controlled trials on the comparative clinical effectiveness, aesthetic, and patient-reported outcomes of soft tissue augmentation procedures with or without the use of soft tissue substitutes around teeth, dental implants, or both.

BACKGROUND

Description of the condition

Oral soft tissue deficiencies can occur in natural teeth, around dental implants, or both. Gingival recession is the most common oral soft tissue deficiency around teeth. It is defined as the apical shift of the free gingiva when measured against the dental cementoenamel junction.

Gingival recessions are commonly identified in adults, and their incidence increase with age. Epidemiological evidence suggested that 92% of the US population present with some gingival recessions of which 71% are linked to teeth in the aesthetic zones (i.e. upper front teeth). Age, ethnicity, tooth type and position, as well as type of dental treatment received have been identified as potential risk indicators of gingival recession (Romandini 2020). Similar findings and prevalence estimates were confirmed in a cohort of young adults in the UK with each participant presenting at least one tooth with gingival recession (Seong 2018). Periodontal phenotype, keratinised tissue width, gingival thickness, and bone morphotype have also been associated with the occurrence of gingival recession (Jepsen 2018). In particular, a lack of keratinised gingival tissue width even without evident dental root exposure in natural teeth may predispose to future gingival recession (Agudio 2008).

When discussing soft tissue deficiencies around dental implants, there are inconsistencies due to lack of agreement among clinicians about a widely accepted definition. As dental implants do not have a standard referral level for the 'normal' position of the mid-buccal mucosa, there is currently no agreed classification of mucosal recessions around dental implants. Using the mucosal margin at the time of connecting the final crown on the dental implant or the exposure of the metal portion of the implant or abutment have been suggested as reference points (Mazzotti 2018).

Possible risk indicators of mucosal recession around dental implants include traumatic tooth loss, periodontitis, and systemic diseases, such as ectodermal dysplasia or osteogenesis imperfecta affecting a site prior to placement of a dental implant (Hammerle 2018). Loss/lack of buccal bone, reduced papilla height, reduced keratinised tissue width, pathological tooth migration, and life-long skeletal changes have been linked to mucosal deficiencies after dental implant placement. Inconclusive evidence exists on the role of keratinised mucosa width and thickness (less than 2 mm) in predicting inflammation and loss of soft and hard tissues around dental implants (Kabir 2021; Kungsadalpibob 2020; Lim 2019).

It is noteworthy to report that oral soft tissue deficiencies could impact on individuals' quality of life. Dentine hypersensitivity, discomfort, and, sometimes, pain are common occurrences linked to gingival recession and impacting onto oral health-related quality of life even if most individuals might be unaware of gingival recession (Yilmaz 2020). Further, unsatisfactory aesthetics of the smile may cause self-esteem limitations and unbalanced social life, and this is particularly true when looking at dental implants in the aesthetic zones.

Lastly oral soft tissues deficiencies around teeth and dental implants represent an important economic burden for society with an estimated 149.52 billion Euros loss in Europe and 122.65 billion Euros in the USA due to dental and peri-implants complications (Botelho 2021).

Description of the interventions

Soft tissue augmentations are procedures performed around teeth or dental implants to recreate lost or reduced mucogingival tissues and to restore aesthetics and functions (Chambrone 2015a). Soft tissue augmentation procedures usually involve adding autologous grafts or soft tissue substitute materials to the gingival/mucosal defect (Lam 2017). Most common soft tissue augmentations include free gingival graft and coronally advanced flap alone or in combination with connective tissue graft (Griffin 2006; Ramachandra 2014). Consistent evidence suggests that autologous grafts are still the gold standard approach for soft tissue augmentation procedures performed around natural teeth and dental implants (Buti 2013; Tavelli 2021).

Since the early-2010s different soft tissue substitutes have been developed to reduce morbidity from soft tissue augmentation procedures. Biocompatible scaffolds have been proposed as easy-to-use devices that are well-integrated into the surrounding tissues (Langer 2004; O'Brien 2011). According to the source of tissue, substitutes could be defined as allogenic, xenogeneic, autologous, alloplastic, and tissue-engineered materials (Lam 2017).

- Allogenic materials, or human-based tissue derivatives, have been widely used for soft tissue augmentation procedures; for example, an acellular dermal matrix (Jhaveri 2010).
- Xenogeneic materials, or animal-based tissue derivatives, come from collagen matrix derived from animal dermis (Ghaanati 2011; Lam 2017).
- Platelet-rich concentrated growth factors have become alternative soft tissue substitute to autologous materials (Moraschini 2016).
- Three-dimensional printed scaffolds (Obregon 2015; Rasperini 2015).
- Living cells construct have been proposed as alternative tissue-engineered materials (McGuire 2008; McGuire 2011).

How the intervention might work

Autologous soft tissue graft represents the gold standard procedure with the aim of augmenting the oral soft tissues and compared to several soft tissue substitutes when performing mucogingival surgical procedures. These tissues, harvested from the roof of the mouth and transposed onto exposed root surfaces, predictably increase gum thickness and quality. However, morbidity, postoperative complications, and limitation on size and thickness of donor sites represent some of the limitations of autologous grafts, hence the need to identify alternative soft tissue substitutes (Chambrone 2015b; Graziani 2014; Tonetti 2014).

Evidence suggests that the types and qualities of materials used to generate soft tissue substitutes have increased (Gelin 2024; Rahimnejad 2024). This could result in clinicians having greater exposure to these substitutes that mimic the autologous tissues, but with the advantage of large availability, no donor site wound, and positive patient-reported outcomes.

The evidence supporting the use of soft tissue substitutes has been conflicting with some inferior results reported when comparing soft tissue substitutes to autologous grafts (Bertl 2017). Other

studies have highlighted the potential for better wound healing and angiogenesis of several soft tissue substitutes, proposing them as a valid alternative to autologous tissues (Cardaropoli 2009; Hammerle 2014; Stähli 2020).

Why it is important to do this overview

Several systematic reviews of randomised controlled trials reporting on the clinical outcomes of soft tissue augmentation procedures have been published, raising the question of what a clinician should use when performing soft tissue augmentation procedures in terms of soft tissue substitutes as an alternative to autologous graft-based/soft tissue substitute-free techniques around teeth and implants. Besides, the vast heterogeneity of studies reporting on keratinised tissue width and soft tissue thickness changes concerning inclusion criteria, measurement methods, and implemented surgical procedures warrants a review synthesis with further quantitative analysis of published evidence.

An initial screening of the available evidence suggests that both Cochrane and non-Cochrane systematic reviews have been published evaluating different aspects/indications of soft tissue augmentation procedures.

OBJECTIVES

To synthesise the evidence from Cochrane and non-Cochrane systematic reviews of randomised controlled trials on the comparative clinical effectiveness, aesthetic, and patient-reported outcomes of soft tissue augmentation procedures with or without the use of soft tissue substitutes around teeth, dental implants, or both.

METHODS

Authors of potentially eligible studies/reviews will not be involved in eligibility decisions about, extracting data from, carrying out the risk of bias assessment for, or performing GRADE assessments of studies they are involved in (JB and RR).

Criteria for considering reviews for inclusion

Types of reviews and studies

The overview will include all Cochrane systematic reviews and selected non-Cochrane systematic reviews, using the following criteria.

- Including all randomised controlled trials assessing soft tissue augmentation procedures with or without the use of soft tissue substitutes around natural teeth and dental implants.
- Studies conducted on adults (aged 18 years or older).
- Randomised controlled trials with at least six months' follow-up data.
- Include at least one of the primary outcomes of the overview.

We will include non-Cochrane systematic reviews if they fulfil the following criteria (Krnic Martinic 2019).

- Research question
- Sources, with a reproducible search strategy (naming of databases, naming of each platforms/engines, search dates, and complete search strategy)
- Inclusion and exclusion criteria
- Selection (screening) methods
- Critically appraise and report the quality/risk of bias of the included studies
- Information about data analysis and synthesis that allows the reproducibility of the results

There will be no language restrictions applied to non-Cochrane systematic reviews.

Types of participants

Adults (aged 18 years or older) with soft tissue deficiencies including insufficient keratinised tissue (less than 2 mm) or gingival recessions in need of soft tissue augmentation procedures around natural teeth or soft tissue dehiscence around dental implants.

Types of interventions

Mucogingival surgeries that include the use of soft tissue substitute material for augmentation procedures in natural teeth and around dental implants, including root coverage procedures, non-carious cervical lesion coverage procedures, and soft tissue augmentation to increase keratinised tissue in dental implants.

The comparators will be mucogingival surgeries using autologous graft for augmentation procedures in natural teeth and around dental implants.

We will consider all possible treatment comparisons dealing with soft tissue augmentation procedures around natural teeth and dental implants, including but not limited to the following.

- Autologous graft including coronally advanced flap only **or** coronally advanced flap plus connective tissue graft **or** free gingival graft **versus**:
  - another technique or methods of autologous graft
  - soft tissue substitute: xenogeneic collagen matrix
  - soft tissue substitute: acellular dermal matrix
  - growth factors: platelet-rich plasma; platelet-rich fibrin
  - tissue-engineered materials: three-dimensional scaffold; living cells construct
- Tunnelling techniques
- Additional materials or equipment (e.g. laser device)

Types of outcome measures

Primary outcomes

- Patient-reported outcome measures (PROM): change of aesthetics or quality of life (or both) using a visual analogue scale and questionnaire for oral health quality.
  - SatVAS – general satisfaction: patient satisfaction with overall result **as reported by the included reviews** (clinically, this is assessed by asking patients to express their overall satisfaction with the treatment outcomes on a 10-cm visual analogue scale, one for each of the two modalities). We will also include other assessment methods of general satisfaction.
  - EstVAS – aesthetic satisfaction: patient satisfaction with aesthetic result **as reported by the included reviews** (clinically, this is assessed by asking the patients two questions related to aesthetic outcome: what is your aesthetic concern about the recession and which method

of treatment and aesthetic outcome do you prefer?). We will also include other assessment methods of aesthetic satisfaction.
    - SensVAS – dental hypersensitivity: patient perception of root sensitivity **as reported by the included reviews** (clinically, hypersensitivity is assessed by asking patients to express the root sensitivity perception with the treatment outcomes on a 10-cm visual analogue scale, one for each of the two modalities). We will also include other assessment methods of hypersensitivity.
- Tooth/implant survival: percentage of tooth/implant survival.
- Keratinised tissue width gain: change (in millimetres) in width of keratinised tissue (distance between gingival margin and mucogingival junction).
- Soft tissue thickness gain: change (in millimetres) in thickness of soft tissues (keratinised gingiva/mucosa).

Secondary outcomes

- Clinical attachment level gain: change (in millimetres) in clinical attachment level (pocket depth and recession depth).
- Bleeding on probing: presence/absence of bleeding after probing.
- Gingival recession depth reduction: reduction (in millimetres) in gingival recession depth (between gingival margin and the basis of gingival sulcus).
- Gingival recession width reduction: reduction (in millimetres) in gingival recession width (horizontal measurement of gingival recession at the cementoenamel junction level).
- Percentage of complete root coverage: percentage of defects that obtained complete root coverage (applicable for gingival recession treatments).
- Aesthetic outcomes: change of aesthetic assessment, **evaluated by the periodontist**. This includes:
    - Root Coverage Aesthetic Score system (Cairo 2009; Cairo 2010). This system considers five variables: level of gingival margin, marginal tissue contour, soft tissue texture, mucogingival junction alignment, and gingival colour.
    - Pink or White Aesthetic Score measurement (Belser 2009; Fürhauser 2005). The minimum acceptable score is 12.
- Marginal bone loss: reduction (in millimetres) in bone loss around dental implants.
- Adverse events: we will consider the total number of participants with adverse events or total number of participants withdrawn. Examples of adverse events will include membrane or graft exposure, discomfort and pain, swelling, bleeding, dentine hypersensitivity, gingival necrosis, and seizure.

The time points to assess primary and secondary outcomes will include the baseline visit; the latest time point available up to three, six, 12, and more than 12 months' follow-up.

Search methods for identification of reviews

We will conduct searches for systematic reviews and meta-analyses. There will be no restrictions on the language or date of publication when searching the electronic databases.

The Information Specialist will search the following databases for relevant reviews.

- Cochrane Database of Systematic Reviews in the Cochrane Library
- MEDLINE Ovid (from 1946 onwards)
- Embase Ovid (from 1980 onwards)
- Epistemonikos

The search strategies for databases will be modelled on the search strategy designed for MEDLINE Ovid in Appendix 1.

We will search reference lists of included and relevant reviews.

We will exclude any reviews that have been retracted due to error or fraud.

Data collection and analysis

Selection of reviews

We will include both Cochrane and non-Cochrane systematic reviews. We will include all Cochrane systematic reviews based on their standardised protocol and confirmed quality of appraisal. Among the non-Cochrane systematic reviews, we will select those with the most recent evidence, having the most outcome data (Pollock 2017), and fulfilling the criteria for systematic reviews proposed by Krnic Martinic and colleagues (Krnic Martinic 2019).

In managing overlap of primary studies within included systematic reviews, we will calculate the corrected covered area to provide a numerical measure of the extent of primary study overlap between the systematic reviews. We will apply the corrected covered area calculation method from Pieper and colleagues (Pieper 2014). We will generate citation matrices that cross-link individual reviews (column) with all the included primary publications (row). One review author will process citation matrices and a second review author will check them for accuracy. We will calculate the corrected covered area as a measure of overlap by dividing the frequency of repeated occurrences of the index publications and reviews by the number of index publications. The reduction of the denominator by the number of index publications (row) results in a possible range of 0% to 100% for the corrected covered area for each review. The numerator constitutes the real overlap as it only counts included primary publications in more than one review and diminishes the impact of large reviews. As the interpretation of corrected covered area degree, the classification will be less than five as slight overlap, six to 10 as moderate overlap, 11 to 15 as high overlap, and greater than 15 as very high overlap (Lunny 2021).

Two overview authors will independently screen the titles and abstracts from the initial search. When an article is considered potentially eligible, we will scrutinise the full-text reports. In case of disagreement between the two overview authors, a third overview author will resolve any outstanding issues.

Data extraction and management

Two overview authors will independently extract data using a standardised and piloted data collection form. We will resolve disagreement by consensus. In case of disagreement between the two overview authors, a third overview author will consider the paper and make a majority decision.

We will extract the following data from each review and enter them into Review Manager (RevMan 2024).

- Review identification number
- Review author
- Search date
- Review inclusion and exclusion criteria
- Number of included trials and participants
- Settings included (single/multiple recessions, single centre/multicentre, country, fund-based)
- Participant characteristics including mean age, proportions of participants by gender
- All comparisons of soft tissue augmentation procedures
- Method and results of risk of bias in the included trials
- Outcomes presented and time points of outcome data
- Narrative summary of the data meta-analysis result (effect sizes and 95% confidence intervals)
- Details of heterogeneity assessment
- GRADE assessments
- Details of subgroup and sensitivity analysis available

We will extract the following data from each selected study for quantitative data synthesis, ideally from the review and (if needed) from the randomised controlled trials included in the review.

- Study design
- Settings
- Characteristics of the participants including mean age, proportions of participants by gender
- Comparisons of soft tissue augmentation procedures (materials or techniques)
- Follow-up duration
- Number of participants randomised and analysed
- Number of participants lost in follow-up time
- Number of participants who had an adverse event

We will identify and exclude any data duplication arising from repeated included trials from the analysis. We will contact a professional translator for any non-English systematic reviews.

Dealing with missing data

We will extract any extraction data that are missing from, inadequately reported in, or reported differently across systematic reviews directly from the underlying primary studies.

Statistical summaries

- The summary intervention effects, including the pooled effects (e.g. risk ratios, odds ratios, mean differences, 95% confidence intervals), and numbers of studies and participants contributing data to each pooled effect from comparisons and for the outcome relevant to this overview.
- Results of any subgroup or sensitivity analyses conducted by the authors for the overview outcome.
- Information required to assess and report on the certainty of the evidence for the intervention effects extracted above.

Assessment of methodological quality of included reviews

Quality of included reviews

Two overview authors who are not authors of other Cochrane reviews will appraise the quality of the reviews included in the overview using the AMSTAR 2.0 tools to assist in identifying high-quality systematic reviews (Shea 2017). We will resolve discrepancies by consensus. Where agreement cannot be reached, a third overview author will decide as a content expert.

Questions to be checked and satisfied in the analysis will include the following.

- Research question and inclusion criteria in the PICO components.
- The establishment of review methods prior to the conduct of the review and the deviations from the protocol.
- The selection of study types for inclusion.
- A comprehensive literature search strategy.
- A duplication process in performing study selection.
- A duplication process in performing data extraction.
- The list of excluded studies and justification of exclusions.
- Description of included studies.
- Risk of bias assessment.
- Reporting the sources of funding.
- The appropriate methods of statistical combination of results for meta-analysis.
- The assessment of the potential impact of risk of bias in individual studies for meta-analysis.
- Risk of bias in individual studies when interpreting the result of the reviews.
- A satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review.
- Adequate investigation of publication bias (small-study bias).
- Any potential sources of conflict of interest.

In view of the complexity of judgement needed, advice on both methodology and content might be required. Content knowledge might be required to determine if the review authors have made an adequate assessment of relevant PICO elements, and to identify potential cofounders. The individual item ratings should not be combined to create an overall score. In addition, we will consider the potential impact of an inadequate rating for each item.

A specific scheme to interpret weaknesses detected in critical and non-critical items when using the AMSTAR 2.0 tools will be adopted as follows (Shea 2017).

- High: no or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.
- Moderate: more than one non-critical weakness: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.
- Low: one critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.
- Critically low: more than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

Certainty of the evidence in the included reviews

We will assess the certainty of the evidence using GRADE, as outlined in the *GRADE Handbook* (Schünemann 2013). When available, we will use the GRADE assessments from the included Cochrane systematic reviews. When these are not available, at least two overview authors will independently examine the individual primary studies and assess the certainty of the evidence using GRADE to review pooled summary statistics and risk of bias of included trials.

The GRADE system assesses the following features for the evidence found for selected outcomes.

- Risk of bias: internal validity of the evidence.
- Inconsistency: heterogeneity or variability in the estimates of effect across studies.
- Indirectness: degree of differences between population, intervention, and outcome of interest.
- Imprecision (random error): the extent to which confidence in the effect estimate is adequate to support a particular decision.
- Risk of publication bias: degree of selective publication of studies.

The GRADE system rates the certainty of the evidence as the following.

- High: further research is very unlikely to change confidence in the estimate of the effect.
- Moderate: further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
- Low: further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
- Very low: any estimate of effect is very uncertain.

Risk of bias in included studies within reviews

We will not reassess the risk of bias of included studies, but instead will report the risk of bias according to the review authors' assessments. Where two or more Cochrane reviews include the same individual studies, we will examine these, and any variation in study risk of bias. This information will be collected during the data extraction process.

Data synthesis

Measures of treatment effect

We will extract both continuous and dichotomous data from each systematic review. For continuous data, we will calculate the mean difference with 95% confidence intervals for studies that use the same assessment scales. In studies reporting different assessment scales, we will calculate the standardised mean difference with 95% confidence intervals. For dichotomous data, we will report the odds ratio with 95% confidence intervals.

Data presentation and analysis

This overview will provide a detailed summary of evidence on different soft tissue substitute materials used in association with other surgical approaches around natural teeth and dental implants. We will report all eligible comparisons grouped by intervention type. We will use tabular formats and narrative techniques to present evidence summaries alongside the GRADE assessment for each comparison (Guyatt 2011). Where possible, we will report results from meta-analysis (including results of available subgroup analysis), along with details of the effects model and measures of statistical heterogeneity (i.e. Chi^2 tests and relevant P values, and I^2 statistics). Where meta-analysis is not available, we will report study-level effects. We will also report outcomes of subgroup and sensitivity analyses.

We will report the certainty of evidence for each eligible outcome and comparison from each included Cochrane and non-Cochrane review in an 'Overview of reviews' table designed to reflect the summary of findings tables in Cochrane reviews. We will present narrative summaries with the corresponding tables. The table will consist of outcome, intervention and comparison, contributing reviews, relative effects, number of participants, certainty of the evidence (GRADE), and comments. If possible, we will map the included reviews to specific taxonomies of interventions and describe the effectiveness of each intervention (Higgins 2023; Ryan 2014).

Subgroup analysis and investigation of heterogeneity

We will assess the presence of statistical heterogeneity in meta-analyses using the I^2 statistic, 95% confidence intervals, and Tau^2 measure (Schroll 2011).

When needed, we may apply subgroup analyses based on the variation of intervention, including the following.

- Group comparisons between different soft tissue substitutes: allogenic, xenogeneic, growth factors, three-dimensional printing allograft, and living cell construct.
- Natural teeth versus dental implants.
- Duration of follow-up: six to 12 months; greater than 12 months to five years; greater than five years.
- Risk of bias of the primary studies within the reviews: low, medium, high risk of bias.
- Measurement method: assessment by different periodontal probe.

We plan to conduct subgroup analysis for the following outcomes.

- **Primary outcomes:** patient-reported outcomes measures (type of satisfaction: general, aesthetic, or sensitivity; follow-up length time (years)); tooth/implant survival (tooth/implant; survival time (years)); keratinised tissue width gain (follow-up length time (years)); soft tissue thickness gain (follow-up length time (years)).
- **Secondary outcomes:** aesthetic outcomes (Root Coverage Aesthetic Score system; Pink or White Aesthetic Score measurement); adverse event outcomes (types of adverse event).

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The following people conducted the editorial process for this article.

- **Sign-off Editor** (final editorial decision): Toby Lasserson, Acting Editor-in-Chief, Cochrane Library
- **Sign-off Editor** (first editorial decision): Anne-Marie Glenny, The University of Manchester
- **Managing Editor** (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the article): Marwah Anas El-Wegoud, Cochrane Central Editorial Service
- **Editorial Assistant** (conducted editorial policy checks and supported editorial team): Leticia Rodrigues, Cochrane Central Editorial Service
- **Copy Editor** (copy editing and production): Anne Lawson, Cochrane Central Production Service
- **Peer-reviewers** (provided comments and recommended an editorial decision): Professor Doctor Karim Fawzy El-Sayed, Cairo University, Egypt and Christian-Albrechts University of Kiel, Germany (**clinical review**); Doctor Cristina Valles. Universitat Internacional de Catalunya, Barcelona, Spain (**clinical review**); Jennifer Hilgart, Cochrane (**methods review**); Jo Platt, Central Editorial Information Specialist (**search review**); Brian Duncan (**consumer review**).

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APPENDICES

Appendix 1. MEDLINE Ovid search strategy

0338 Soft tissue augmentation procedures for natural teeth and dental implants: an overview of systematic reviews and network meta-analysis

Proposed search strategy for MEDLINE Ovid

1. Dental implants/
2. Dental implantation/
3. Alveolar process/
4. Alveolar bone loss/
5. Gingival recession/
6. (keratin$ adj2 (mucosa$ or tissue$ or width or thick$ or gingiva$)).ti,ab,kw.
7. ((dental or oral) adj3 implant$).ti,ab,kw.
8. ((gingiva$ or gum$) adj5 (recess$ or reced$ or atroph$ or defect$ or deficienc$ or attach$)).ti,ab,kw.
9. (recession adj5 defect$).ti,ab,kw.

10. (root$ adj4 (expos$ or denud$)).ti,ab,kw.
11. "soft tissue deficienc$".ti,ab,kw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. Vestibuloplasty/
14. ((alveolar or mandib$ or maxill$) adj3 (augment$ or support$)).ti,ab,kw.
15. Tissue scaffolds/
16. Tissue conditioning, dental/
17. exp Surgical flaps/
18. (tissue adj3 (substitut$ or augment$ or graft$)).ti,ab,kw.
19. ((autologous or gingiva$ or "connective tissue" or "soft tissue" or "dermal matrix" or gum or mucogingival or muco-gingival) adj3 (graft $ or transplant$)).ti,ab,kw.
20. (("coronally advanced" or "apically positioned" or "apically repositioned" or "laterally positioned") adj2 flap$).ti,ab,kw.
21. MARF.ti,ab.
22. Transplantation, Homologous/
23. (allogeneic or allograft$ or homograft$ or "homologous transplant$" or "autologous material").ti,ab,kw.
24. (xenogen$ or autologous or alloplastic or "tissue engineer$").ti,ab,kw.
25. Acellular dermis/
26. Collagen/
27. (dermal adj5 (graft$ or transplant$ or tissue$ or matrix)).ti,ab,kw.
28. collagen.ti,ab,kw.
29. "enamel matrix protein".ti,ab,kw.
30. Platelet-rich plasma/
31. exp Fibrin/
32. (platelet$ adj5 (plasma$ or fibrin$ or concentrat$ or "growth factor$")).ti,ab,kw.
33. (PRP or L-PRP or PRF or L-PRF or "extracellular matrix membrane").ti,kw,ab.
34. exp Biocompatible materials/
35. Keratins/
36. Connective tissue/
37. Gingivoplasty/
38. gingivoplast$.ti,ab,kw.
39. ((gingiva$ or periodont$ or gum$ or mucogingiva$) adj5 (surgery or surgical$ or transplant$)).ti,ab,kw.
40. Guided tissue regeneration/
41. "guided tissue regenerat$".ti,ab,kw.
42. ("living cell$" adj2 (construct$ or technolog$)).ti,ab,kw.
43. Printing, Three-Dimensional/
44. ((3D or "three D" or 3-D or three-D or "3 D" or "three dimension$" or three-dimension$ or "3 dimension$" or 3-dimension$) adj print $).ti,kw,ab.
45. scaffold$.ti,ab,kw.
46. mucograft$.ti,ab,kw.
47. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48. 12 and 47

This search retrieved 644 records when combined with the Canadian Agency for Drugs and Technology in Health validated search filter for identifying systematic reviews in MEDLINE Ovid (https://www.cadth.ca/strings-attached-cadths-database-search-filters). Cite as: Canadian Agency for Drugs and Technology in Health 2021.Strings attached: CADTH database search filters [Internet] [cited 14 September 2021]. Available from: https://www.cadth.ca/strings-attached-cadths-database-search-filters

1. (systematic review or meta-analysis).pt.
2. meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ or network meta-analysis/
3. ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf,kw.
4. ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf,kw.
5. ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf,kw.
6. (data synthes* or data extraction* or data abstraction*).ti,ab,kf,kw.
7. (handsearch* or hand search*).ti,ab,kf,kw.
8. (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf,kw.
9. (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf,kw.
10. (meta regression* or metaregression*).ti,ab,kf,kw.
11. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
12. (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.

13. (cochrane or (health adj2 technology assessment) or evidence report).jw.
14. (comparative adj3 (efficacy or effectiveness)).ti,ab,kf,kw.
15. (outcomes research or relative effectiveness).ti,ab,kf,kw.
16. ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf,kw.
17. (multi* adj3 treatment adj3 comparison*).ti,ab,kf,kw.
18. (mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf,kw.
19. umbrella review*.ti,ab,kf,kw.
20. (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kw,kf.
21. (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kw,kf.
22. (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kw,kf.
23. or/1-23

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This overview protocol is a revision after feedback and discussion with the Cochrane Oral Health team.

SK: conceptualisation, data curation, funding acquisition, investigation, methodology, project administration, resources, validation, visualisation, writing – original draft, writing – review and editing.

JB: conceptualisation, data curation, formal analysis, methodology, resources, software, visualisation, writing – original draft, writing – review and editing.

RR: conceptualisation, data curation, resources, writing – original draft.

DIH: investigation, writing – review and editing.

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DECLARATIONS OF INTEREST

SK: none.

JB: acted as an investigator of some trials of potential interest to the review and authored some potentially useful reviews. However, they had no conflicts of interest related to this protocol.

RR: acted as an investigator of some trials of potential interest to the review and authored some potentially useful reviews. However, they had no conflicts of interest related to this protocol.

DIH: none.

HJT: none.

FD: none.

Overview authors of potentially eligible studies/reviews will not be involved in eligibility decisions about, extracting data from, carrying out the risk of bias assessment for, or performing GRADE assessments of studies they are involved in (JB and RR).

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