Article

Not peer-reviewed version

Topic Modeling for Faster Literature Screening Using Transformer-Based Embeddings

Carlo Galli *, Claudio Cusano, Marco Meleti, Nikolaos Donos, Nikolaos Donos

Posted Date: 26 July 2024

doi: 10.20944/preprints202407.2198.v1

Keywords: embedding; systematic reviews; topic modeling

Article

Topic Modeling for Faster Literature Screening Using Transformer-Based Embeddings

Carlo Galli [1,*], Claudio Cusano [2], Marco Meleti [3], Nikolaos Donos [4] and Elena Calciolari [3,4]

[1] Histology and Embryology Laboratory, Department of Medicine and Surgery, University of Parma, Via Volturno 39, 43126 Parma, Italy; carlo.galli@unipr.it
[2] Department of Electrical, Computer and Biomedical Engineering, University of Pavia, Via Ferrata 1, Pavia 27100, Italy; claudio.cusano@unipv.it
[3] Dental School, Department of Medicine and Dentistry, University of Parma, 43126 Parma, Italy; marco.meleti@unipr.it; elena.calciolari@unipr.it
[4] Centre for Oral Clinical Research, Institute of Dentistry, Faculty of Medicine and Dentistry, Queen Mary University of London, London E1 2AD, UK; n.donos@qmul.ac.uk
* Correspondence: carlo.galli@unipr.it

Abstract: Systematic reviews represent a powerful instrument to summarize the existing evidence in medical literature. However, articles for a systematic review are hard to identify, and mostly require a structured search of the literature through a number of databases, using keyword-based search strategies, followed by the painstaking manual selection of pieces of evidence that are pertinent to the query. A.I. algorithms may offer solutions to reduce the workload on investigators. We applied BERTopic, a newer and much-recognized transformer-based topic-modeling algorithm, to two datasets of 6137 and 5309 articles of newly published systematic reviews in the area of peri-implantitis and bone regeneration in implant dentistry. In the two datasets, BERTopic identified 14 and 22 clusters, respectively, and it automatically created labels describing the nature of the topics for each individual cluster based on semantic interpretation of their titles. Most themes regarded the query theme, but in both conditions, BERTopic also uncovered articles related to off-themes, which composed around 30% of the dataset—with sensitivity up to 0.79 and specificities of at least 0.99. Our results suggest that adding a topic-modeling step to the screening process could potentially save working hours for researchers involved in systematic reviews of the literature.

Keywords: embedding; systematic reviews; topic modeling

1. Introduction

The advancement of technology and internet has ushered in a new era of information sharing, greatly affecting the way research is conducted at all stages [1]. With unprecedented ease, scholars and researchers have now the ability to publish a plethora of data, reviews, and opinions on various platforms that can be accessed worldwide, using new publishing models that make sharing information easy and fast. However publishing does not only serve to disseminate knowledge for furthering research but also involves complex dynamics related to career progression and securing grant funding [2,3]. As a result, an overwhelming number of publications covering diverse topics is published every day, making it challenging to efficiently identify relevant papers amidst a sea of sometimes only tangentially related literature [4]. The challenge becomes particularly critical when conducting systematic reviews.

Systematic reviews are rigorous and thorough examinations of the existing literature to answer specific research questions [5], which rely on experimental and sometimes observational studies, with the purpose of gathering all the existing evidence on a given medical condition and, usually, its therapy. To conduct a successful systematic review, researchers must consider a wide range of sources and databases to ensure comprehensive coverage of the relevant literature [5,6], and make sure to identify all the pertinent data, minimizing evidence loss. For this purpose, researchers usually rely on established library repositories to search for scientific articles [7]. These databases, e.g. Medline, are commonly searched using specific keywords that may appear in the article, e.g. in its title or abstract. Though this approach is fast and robust, it may fail to capture relevant articles if they use different wordings or synonyms [8]. Moreover, as the lexicon may be ambiguous, this approach usually yields large numbers of publications that do not match the exact focus of the query – or are even off topic -, and forces investigators to sift through the query results to handpick the papers they need [9].

Automation has significant potential to expedite and reduce the cost of systematic reviews [10]. Recent advancements in natural language processing (NLP) and machine learning have demonstrated the possibility to automate or assist several tasks within the systematic review process. Innovations in this area have led to the development of softwares like Abstractr, ASReviews, EPPI-reviewer, and RobotSearch, which utilizes convolutional neural network architectures to identify RCTs [11,12]. Large language models are promising tools to automate some aspects of systematic reviews by enhancing literature retrieval through semantic understanding and contextual analysis of search terms [13,14]. An essential component for achieving semantic understanding is embeddings - numerical representations that encode word or even sentence meaning - which are key in NLP for capturing complex relationships between words and sentences using special architectures known as transformers [15]. Embeddings based on transformer architectures have proved very effective in several NLP tasks, and many efforts have been devoted to developing better embeddings for specific tasks, also in the biomedical field, including topic modeling [16].

Topic modeling involves identifying the main theme of unlabeled documents. This approach can be valuable in understanding complex scientific literature corpora by automatically organizing and categorizing large sets of publications based on their topics [17]. One of the latest examples among the topic-modeling algorithms is BERTopic - an advanced algorithm developed by Grootendorst in 2022 - which harnesses the power of the embeddings obtained from BERT, a well-known transformer architecture [18]. BERTopic can segment a dataset of text documents – an operation commonly known as clustering – by their semantic content and extract a series of representative keywords, which BERTopic then concatenates to create a topic label for each cluster.

The main aim of the present paper is to explore how BERTopic can be applied effectively on datasets of the scientific literature and identify relevant papers for systematic reviews in the dental field. This approach proves helpful in filtering out articles that are not pertinent for further assessment, thereby enhancing the speed and efficiency of the search process.

2. Materials and Methods

2.1. Datasets

Our analysis focused on two separate datasets, which had been previously used to identify articles of interest (henceforth "target articles") for two published systematic reviews in the dental field, on peri-implantitis and bone regeneration, respectively [19,20].

These two datasets were manually screened, searching for Off-topic articles (henceforth labelled OffTA). We adopted a broad definition of OffTAs, as those articles that did not focus on dentistry, e.g. penile prostheses, or breast implants. Pre-clinical studies were not considered OffTAs unless they were investigating areas that were clearly related to fields other than dentistry. So, for instance, a report on cellular behavior in an *in vitro* setting would not necessarily be considered an OffTA, but a pre-clinical investigation on a fracture model in rodent would. All the papers that investigated areas of dentistry (or applicable to dentistry) were considered On-topic articles (OnTAs), for both datasets. It may be argued that, when it comes to peri-implantitis, orthopedic implants may be closer to dental implants than e.g. orthognatic surgery (which is related to dentistry), or that, orthopedic research articles may be more relevant to bone regeneration of the alveolar ridges than many dental-related research areas, but, as the goal of our investigation was to filter out papers from the dataset, to make systematic reviews faster, we worked under the assumption that it would be safer to discard articles

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

that focused on different clinical areas than dentistry, and that would not increase the risk of losing important pieces of evidence for both datasets.

The first dataset included 6137 articles on the treatment of peri-implantitis and was generated through a state of the art and well-detailed keyword-based search across several databases, including Medline and Embase [20]. In that systematic review, the investigators eventually identified 24 target articles that answered the following Focused Questions (FQ):

FQ1 *In patients with peri-implantitis, what is the efficacy of different bone reconstructive therapies compared to access flap surgery (AFS) in terms of pocket reduction and change in bleeding and suppuration on probing (BOP and SOP), at a minimum of 12 months of follow-up?*

FQ2 *In patients with peri-implantitis, what is the long-term (≥12 months) performance of reconstructive therapies in terms of pocket reduction and change in BOP/SOP?*

Upon inspection, this dataset resulted composed of 3810 OnTAs (i.e. dentistry-related), and 2327 OffTAs (38%).

The second database had been used as a basis for another published systematic review by Calciolari et al. on bone augmentation techniques [19]. The dataset used for this work comprised 5309 articles obtained through a systematic literature search across several databases to address the following FQs:

FQ1: *In patients receiving GBR simultaneous to implant placement, what is the impact of biomaterials (membranes, grafts, bioactive factors) on the stability of peri-implant bone levels as assessed through 2D or 3D radiographs in RCTs/CCTs with ≥ 12 months of follow-up?*

FQ2: *In patients receiving GBR simultaneous to implant placement, what is the impact of biomaterials (membranes, grafts, bioactive factors) on bone defect dimension (width and/or height) changes as evaluated at re-assessment procedures performed at ≥4 months post GBR in RCTs/CCTs?*

Upon inspection, this dataset appeared to include only 814 OffTAs, or 15% of the total.

2.2. Purpose of the Study

The purpose of the study was to investigate whether running BERTopic, a topic-modeling algorithm, on these two datasets to segment them into topic clusters could make subsequent screening faster, by identifying groups of articles constituted only (or prevalently) of OffTAs – henceforth designated as Off-topic Groups or OffTGs – that could be safely discarded to narrow down the corpus.

2.3. Data Analysis

The data were analyzed using Google Colab Pro notebook powered by Python 3.10.12 [21] and running on T4 GPUs [22].

The analysis of the publications was conducted on their titles, based on the assumption that titles are a summary of the content of a paper, and are thus representative of their topic [23,24]. The datasets did not need to undergo any preprocessing, besides removing entries when titles were missing. Unlike previous publications [25], we did not deem necessary to lowercase the titles, nor to remove stopwords, to rely on BERTopic's capability to produce contextual embeddings [26].

Embeddings in NLP are dense vectors that represent the semantics of words in a multidimensional space [27]. Unlike older algorithms [28], BERT (Bidirectional Encoder Representations from Transformers) understands the context and creates unique word embeddings based on their usage in different contexts [15,29]. BERTopic operates through several stages, including transformer embedding models, dimensionality reduction, clustering, and cluster tagging using cTF-IDF [18]. For our study, we chose the Huggingface's 'all-mpnet-base-v2' model. Embeddings from this model are too large for efficient clustering and must be thus reduced. As several dimensionality reduction algorithms are available, we used UMAP (Uniform Manifold Approximation and Projection), which has been shown to be very effective in preserving the topological structure of data [30]. We empirically decided to reduce all-mpnet-base-v2's 768-dimension embeddings to 5-dimension embeddings. Reduced embeddings were then clustered with HDBSCAN (Hierarchical Density-Based Spatial Clustering of Applications with Noise) [31] and cTf-

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

Idf was applied to extract topic keywords in each cluster. Unlike Tf-Idf [32], cTf-Idf adjusts the weight based on the term frequency within a cluster of documents rather than within an individual document [33].

More specifically, we decided to use the following set-up:

- UMAP metric: cosine distance;
- size of the neighborhood: 15;
- number of components: 5;
- HDBSCAN clustering metric: Euclidean;
- minimum cluster size: 50.

To increase the system's speed, we used the cuML GPU-based implementation of UMAP and HDBSCAN [34]. Besides BERTopic's default representation model, we adopted KeyBERT, a more recent algorithm to improve keyword extraction [35].

We also used the OpenHermes-2.5-Mistral Large Language Model [36] to generate better labels for the topics, instead of just a sequence of concatenated keywords, which is BERTopic's standard output. A large language model (LLM) is an A.I. algorithm that can generate human-like responses [37]. LLMs are typically large and require vast computer resources, thus reduced versions have been elaborated [38], which are commonly referred to as quantized LLMs [39]. We opted for the OpenHermes-2.5-Mistral-7B-GGUF/openhermes-2.5-mistral-7b.Q4_K_M.gguf quantization, available for download on Huggingface.com.

LLMs need a prompt from the users [40] to generate a response, and we set the following prompt:

prompt = „„„ Q:
I have a topic that contains the following documents:
[DOCUMENTS]
The topic is described by the following keywords: '[KEYWORDS]'.
Based on the above information, can you give a short label of the topic of at most 5 words?
A:
"""

We used BERTopic's inbuilt functions, and the matplotlib [41] and seaborn libraries [42] for data visualization. The Datamapplot library [43] was used for effective cluster visualization. For specificity, sensitivity, and F1 assessment, we considered OffTAs as positive, and OnTAs as negative. OffTAs clustered within a OffTG were considered true positive, while OnTAs clustered in an OffTG were considered false positives.

3. Results and Discussion

3.1. Peri-Implantitis Dataset Analysis

Running BERTopic on a Colab notebook, after loading the necessary libraries and packages, required few seconds for such a small dataset. Although BERTopic proved to be capable of easily identifying several topics based on the titles in the dataset, the actual number of topics depended on the parameters of the algorithm. The four main steps that operators can control in BERTopic are:

1) Creating the embeddings
2) Reducing the embeddings' dimensions
3) Clustering the embeddings
4) Labelling the embeddings.

To create sentence embeddings from the titles we decided to use the all-mpnet-base-v2 model, which has been pre-trained on a large dataset and has proved to be effective also on academic titles [44]**.** It is relatively slower when compared to smaller models, but this did not significantly affect the computation time with little more than 6000 titles.

To improve effective clustering, we reduced the dimensions of our initial embeddings, using UMAP. This algorithm allows for a thorough customization of its parameters, including the granularity of the topological structure that it aims to preserve during dimensionality reduction, through the "number of neighbors" parameter. The clustering algorithm we chose, HDBSCAN, offers

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

the great advantage of not requiring operators to pre-determine the number of clusters (e.g. unlike K-means algorithms), although, as a result, it tends to cluster unclear documents in a null group, which is identified by the -1 label. HDBSCAN can be customized through several parameters too, including the minimum acceptable size for a cluster. The last step consists in finding a label for each cluster, which corresponds to its topic. To do that, we have chosen two representation models. A large language model, to create human-like labels, and KeyBERT, to generate keywords that are characteristic to the topic. Figure 1 shows that, by reducing the minimum size of the clusters, BERTopic was able to find more topics in our dataset, which is intuitive, because there might be niche topics, constituted by only a handful of articles, which are lost if the size threshold is too high. At the same time, changing the sensitivity of UMAP through its number of neighbors parameter altered the slope of the curve. The choice of the best settings is an arbitrary decision, which depends on the purpose of the investigators; in our case, we wanted to have enough granularity to isolate unrelated topics, while keeping the number of topics small enough to be easily manageable and several orders of magnitude smaller than the dataset itself, to make it a convenient step in the workflow. For that reason, we empirically determined the optimal number of neighbors to be 15, and the minimum cluster size to be 50. These settings generated 14 topics (Table 1). Table 1 lists the topics identified by the algorithm, from the biggest one to the smallest one. The topic list includes the '-1' null topic, where all the unclassified papers are supposed be allocated.

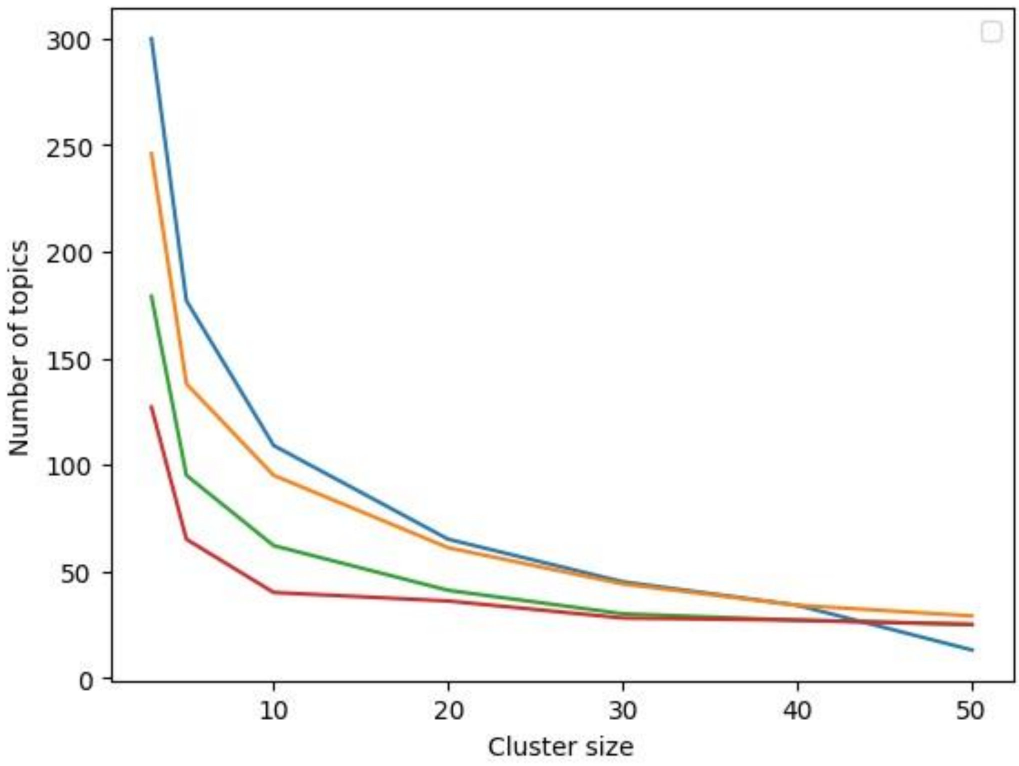

Figure 1. Line plot showing the relation between the minimum cluster size setting for HDBSCAN and the number of topics identified by BERTopic in the peri-implantitis dataset, based on the number of neighbors setting in the UMAP dimension reduction algorithm. Red line: n_neighbors=10; Blue line: n_neighbors=15; Orange line: n_neighbors=50; Green line: n_neighbors=100.

Table 1. contains the list of topics identified by BERTopic, in order of size, for the peri-implantitis dataset. Non-dental topics are indicated in bold.

Topic	Count	Name	KeyBERT	LLM
-1	357	-1_treatment_hydroxyapatite_bone_implant	['peri implantitis', 'hydroxyapatite coated', 'coated	Treating Implant Infections

0	3733	0_implant_implants_peri_bone	implants', 'dental implant', 'dental implants', 'spinal implant', 'peri implant', 'hydroxyapatite', 'implantitis', 'implant'] ['peri implantitis', 'implant bone', 'dental implant', 'peri implant', 'dental implants', 'implant placement', 'implants placed', 'bone regeneration', 'implant', 'implantitis']	Peri-Implant Bone Study
1	**587**	**1_valve_coronary_stent_patients**	**['coronary stent', 'stent implantation', 'eluting stents', 'eluting stent', 'stents', 'artery bypass', 'stent', 'coronary artery', 'patients coronary', 'stenting']**	**Valves and Stents in Coronary Arteries**
2	**232**	**2_cataract_intraocular_cataract surgery_lens**	**['inflammation cataract', 'lens implantation', 'incision cataract', 'intraocular lens', 'following cataract', 'extracapsular cataract', 'intraocular lenses', 'postoperative inflammation', 'cataract extraction', 'cataract surgery']**	**Intraocular Lens Inflammation**
3	**192**	**3_breast_breast reconstruction_reconstruction_breast implants**	**['breast reconstruction', 'reconstruction breast', 'mammary implants', 'breast implant', 'implant breast', 'breast augmentation', 'prosthetic breast', 'breast prostheses', 'breast implants', 'breast surgery']**	**Breast Reconstruction & Implants**
4	**174**	**4_stimulation_parkinson_parkinson disease_brain**	**['stimulation parkinson', 'subthalamic stimulation', 'nucleus stimulation', 'nucleus**	**Parkinson's Disease and Deep Brain Stimulation**

			parkinson', 'brain stimulation', 'implants parkinson', 'nerve stimulation', 'stimulation subthalamic', 'neuromodulation', 'parkinson disease']	
5	144	5_sinus_floor_sinus floor_elevation	['sinus floor', 'sinus elevation', 'osteotome sinus', 'sinus augmentation', 'sinus surgery', 'maxillary sinus', 'sinus implants', 'sinus lift', 'transcrestal sinus', 'eluting sinus']	Sinus Floor Elevation
6	137	6_laser_therapy_photodynamic_photodynamic therapy	['implantitis laser', 'peri implantitis', 'implantitis randomized', 'peri implant', 'laser therapy', 'implantitis', 'laser treatment', 'implant diseases', 'laser peri', 'photodynamic therapy']	Photodynamic Therapy for Peri-implantitis Treatment
7	132	7_overdentures_mandibular_mandibular overdentures_retained	['implant overdentures', 'mandibular overdentures', 'mandibular overdenture', 'implants mandibular', 'mandibular implant', 'maxillary overdentures', 'retained overdentures', 'overdentures retained', 'supported mandibular', 'overdentures supported']	Implant-retained Mandibular Overdentures
8	**127**	**8_orbital_porous_polyethylene_porous polyethylene**	**['implants orbital', 'orbital implant', 'orbital implants', 'hydroxyapatite orbital', 'polyethylene implants', 'polyethylene implant', 'implant**	**Orbital Reconstruction Implants**

			repair', 'treatment orbital', 'implant enucleation', 'orbital fractures']	
9	**96**	**9_cochlear_cochlear implantation_hearing_implantation**	**['cochlear implantation', 'cochlear implants', 'cochlear implant', 'implants cochlear', 'undergoing cochlear', 'unilateral cochlear', 'pediatric cochlear', 'following cochlear', 'hearing implants', 'outcomes cochlear']**	**Cochlear Implantation**
10	**89**	**10_fusion_cervical_lumbar_disc**	**['cervical disc', 'cervical discectomy', 'disc arthroplasty', 'discectomy fusion', 'lumbar fusion', 'cervical spine', 'spinal fusion', 'disc disease', 'anterior cervical', 'degenerative lumbar']**	**Cervical Fusion and Disc Disease**
11	**76**	**11_endometriosis_endometrial_borderline_endometrium**	**['tumors ovary', 'ovarian serous', 'ovary clinicopathologic', 'borderline ovarian', 'serous tumors', 'endometriosis', 'borderline tumors', 'human endometrium', 'ovarian', 'endometrium']**	**Serous Borderline Ovary Tumors.**
12	61	12_zirconia_abutments_clinical_single	['zirconia implants', 'zirconia dental', 'veneered zirconia', 'zirconia abutments', 'tooth implant', 'implant reconstructions', 'dental implants', 'zirconia oral', 'oral implants', 'implant abutments']	Zirconia Implants and Abutments

Quite remarkably, however, both KeyBERT and the LLM convened that these non-classified (-1 cluster) articles were anyway mostly centered on implants (and implant infections) and assigned them the title "Treating Implant Infections". This null topic cluster was quite small (n=357), and BERTopic managed to identify several further topics that were, unsurprisingly, related to peri-implantitis (e.g. topic #0 which included the bulk of the papers (n=3733) or topic #6), but also more broadly related to implant dentistry (e.g. topics #5, #7, and #12).

However, this dataset also included at least 8 completely unrelated OffTGs, some of them quite conspicuous in size, such as the following:

#1 Valves and Stents in Coronary Arteries (n=587), e.g. "Carotid-subclavian bypass grafting with polytetrafluoroethylene grafts for symptomatic subclavian artery stenosis or occlusion: a 20-year experience" [45];

#2 Intraocular Lens Inflammation (n=232), e.g. "Double-masked, placebo-controlled evaluation of loteprednol etabonate 0.5 for postoperative inflammation" [46];

#5 Parkinson's Disease and Deep Brain Stimulation (n= 174), e.g. "Three-dimensional space fluid-attenuated inversion recovery at t to improve subthalamic nucleus lead placement for deep brain stimulation in Parkinson's disease: from preclinical to clinical studies" [47];

#16 Cochlear Implantation (n=96), e.g. "Online support group users' perceptions and experiences of bone-anchored hearing aids (bahas): a qualitative study" [48].

A careful observation of the topic list suggests that more topics could be considered unrelated to the query, albeit dental-related. Some of them are small niche topics, such as #12 Zirconia Implants and Abutments (n=61), some are larger, such as topic #5 Sinus Floor Elevation (n=144); although it is thematically related to implants, nothing in its keyword descriptors mentions peri-implant disease:

['sinus floor', 'sinus elevation', 'osteotome sinus', 'sinus augmentation', 'sinus surgery', 'maxillary sinus', 'sinus implants', 'sinus lift', 'transcrestal sinus', 'eluting sinus']

Clearly, and similarly to identifying OffTAs, choosing OffTGs to discard based on their descriptors is arbitrary and there is a degree of risk in discarding dentistry- or implant-related topics. We assumed that a cautious attitude would be to retain them, and we thus decided to discard only those topics that were unrelated to dentistry as a whole, to avoid risking losing relevant articles.

To get a better grasp of how the titles of the dataset were semantically distributed, we reduced the embedding dimensionality that we used for topic modeling from 5 down to 2 dimensions, so that each title could be represented as a data point in a scatter plot (Figure 2). Closer points correspond to articles whose titles have closer meaning, and therefore topic, while farther points represent articles that belong to less closely related topics, including frank OffTAs. As it can be easily noticed, the conceptual space for this dataset of scientific publications is not homogeneous, but there are several areas of higher density, which constitute the individual topics, and some topics appear isolated. Unsurprisingly, OffTAs tend to be distributed peripherally, as a satellite constellation of articles with looser association to the core of the dataset, which appears in the middle of the plot, and includes most of the dental-related articles (Figure 2).

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

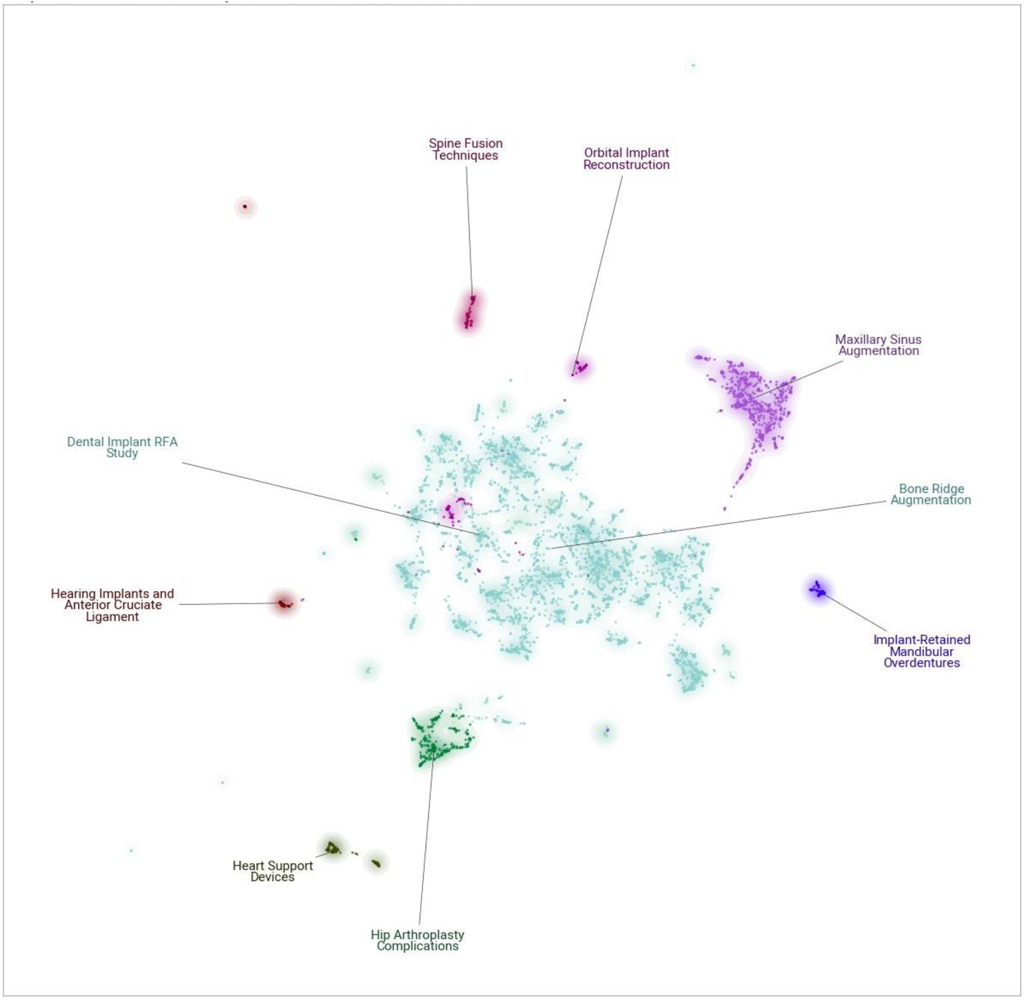

Figure 2. Scatterplot of the semantic distribution of a dataset of titles of scientific articles selected from different biomedical databases using a keyword-based search for peri-implantitis. Titles are not homogeneously distributed, but rather form clusters that tend to correspond to topics. Every topic is marked by a different color.

Even if we just consider the topics highlighted in Table 1 and that are grossly unrelated to the purpose of the systematic review (i.e. unrelated to dentistry in general), they alone account for about 30% of the papers in the dataset (or 1856 papers out of the 6137 titles that had to be manually screened at the time the systematic review was performed).

As this dataset had already been published, we also already knew which articles had been selected for the review. As Table 2 shows, the target articles that corresponded to the query were not contained in any of the OffTGs. OffTGs (and the OffTAs contained in them) removal during screening would thus not have negatively affected the review.

Table 2. contains the list of the target articles identified in Donos et al. systematic review on peri-implantitis (Donos et al., 2023). No article was clustered in any of the unrelated topic groups.

Authors	Title	Topic	Reference
Andersen, Heidi, Aass, Anne Merete and Wohlfahrt, Johan Caspar	Porous titanium granules in the treatment of peri-implant osseous defects-a 7-year follow-up study	#0 Peri-Implant Bone Study	[49]
Jepsen, K., Jepsen, S., Laine, M. L., Anssari Moin, D.,	Reconstruction of Peri-implant Osseous Defects: A	#0 Peri-Implant Bone Study	[50]

 doi:10.20944/preprints202407.2198.v1

Pilloni, A., Zeza, B., Sanz, M., Ortiz-Vigon, A., Roos-Jansaker, A. M. and Renvert, S.	Multicenter Randomized Trial		
Wohlfahrt, Johan Caspar, Lyngstadaas, Stale Petter, Ronold, Hans Jacob, Saxegaard, Erik, Ellingsen, Jan Eirik, Karlsson, Stig and Aass, Anne Merete	Porous titanium granules in the surgical treatment of peri-implant osseous defects: a randomized clinical trial	#0 Peri-Implant Bone Study	[51]
Emanuel, Noam, Machtei, Eli E., Reichart, Malka and Shapira, Lior	D-PLEX500: a local biodegradable prolonged release doxycycline-formulated bone graft for the treatment for peri-implantitis. A randomized controlled clinical study	#0 Peri-Implant Bone Study	[52]
Renvert, Stefan, Giovannoli, Jean-Louis, Roos-Jansaker, Ann-Marie and Rinke, Sven	Surgical treatment of peri-implantitis with or without a deproteinized bovine bone mineral and a native bilayer collagen membrane: A randomized clinical trial	#0 Peri-Implant Bone Study	[53]
Isehed, C., Holmlund, A., Renvert, S., Svenson, B., Johansson, I. and Lundberg, P.	Effectiveness of enamel matrix derivative on the clinical and microbiological outcomes following surgical regenerative treatment of peri-implantitis. A randomized controlled trial	#0 Peri-Implant Bone Study	[54]
Isehed, C., Svenson, B., Lundberg, P. and Holmlund, A.	Surgical treatment of peri-implantitis using enamel matrix derivative, an RCT: 3- and 5-year follow-up	#0 Peri-Implant Bone Study	[55]
Renvert, Stefan, Roos-Jansaker, Ann-Marie and Persson, Gosta Rutger	Surgical treatment of peri-implantitis lesions with or without the use of a bone substitute-a randomized clinical trial	#0 Peri-Implant Bone Study	[56]
Nct	Peri-implantitis - Reconstructive Surgical Therapy	#0 Peri-Implant Bone Study	[57]
Froum, Stuart J., Froum, Scott H. and Rosen, Paul S.	A Regenerative Approach to the Successful Treatment of Peri-implantitis: A Consecutive Series of 170 Implants in 100 Patients with 2- to 10-Year Follow-up	#0 Peri-Implant Bone Study	[58]
Gonzalez Regueiro, Iria, Martinez Rodriguez, Natalia, Barona Dorado, Cristina, Sanz-Sanchez, Ignacio,	Surgical approach combining implantoplasty and reconstructive therapy with locally delivered antibiotic in	#0 Peri-Implant Bone Study	[59]

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

Montero, Eduardo, Ata-Ali, Javier, Duarte, Fernando and Martinez-Gonzalez, Jose Maria	the treatment of peri-implantitis: A prospective clinical case series		
Isler, S.C., Soysal, F., Ceyhanli, T., Bakirarar, B. and Unsal, B.	Regenerative surgical treatment of peri-implantitis using either a collagen membrane or concentrated growth factor: A 12-month randomized clinical trial	#0 Peri-Implant Bone Study	[60]
La Monaca, Gerardo, Pranno, Nicola, Annibali, Susanna, Cristalli, Maria Paola and Polimeni, Antonella	Clinical and radiographic outcomes of a surgical reconstructive approach in the treatment of peri-implantitis lesions: A 5-year prospective case series	#0 Peri-Implant Bone Study	[61]
Mercado, Faustino, Hamlet, Stephen and Ivanovski, Saso	Regenerative surgical therapy for peri-implantitis using deproteinized bovine bone mineral with 10% collagen, enamel matrix derivative and Doxycycline-A prospective 3-year cohort study	#0 Peri-Implant Bone Study	[62]
Polymeri, Angeliki, Anssari-Moin, David, van der Horst, Joyce, Wismeijer, Daniel, Laine, Marja L. and Loos, Bruno G.	Surgical treatment of peri-implantitis defects with two different xenograft granules: A randomized clinical pilot study	#0 Peri-Implant Bone Study	[63]
Roccuzzo, Mario, Gaudioso, Luigi, Lungo, Marco and Dalmasso, Paola	Surgical therapy of single peri-implantitis intrabony defects, by means of deproteinized bovine bone mineral with 10% collagen	#0 Peri-Implant Bone Study	[64]
Roccuzzo, Mario, Mirra, Davide, Pittoni, Dario, Ramieri, Guglielmo and Roccuzzo, Andrea	Reconstructive treatment of peri-implantitis infrabony defects of various configurations: 5-year survival and success	#0 Peri-Implant Bone Study	[65]
Isrctn	Reconstructive surgical therapy of peri-implantitis bone defects	#0 Peri-Implant Bone Study	[66]
Aghazadeh, A., Rutger Persson, G. and Renvert, S.	A single-centre randomized controlled clinical trial on the adjunct treatment of intra-bony defects with autogenous bone or a xenograft: results after 12 months	#0 Peri-Implant Bone Study	[67]
Aghazadeh, A., Persson, R.G. and Renvert, S.	Impact of bone defect morphology on the outcome	#0 Peri-Implant Bone Study	[68]

	of reconstructive treatment of peri-implantitis		
Nct	Evaluation of Photodynamic Therapy in Treatment of Peri-implantitis	#6 Photodynamic Therapy for Peri-implantitis Treatment	[69]
Roos-Jansaker, Ann-Marie, Renvert, Helena, Lindahl, Christel and Renvert, Stefan	Submerged healing following surgical treatment of peri-implantitis: a case series	#0 Peri-Implant Bone Study	[70]
Roos-Jansaker, Ann-Marie, Lindahl, Christel, Persson, G. Rutger and Renvert, Stefan	Long-term stability of surgical bone regenerative procedures of peri-implantitis lesions in a prospective case-control study over 3 years	#0 Peri-Implant Bone Study	[71]
Roos-Jansaker, Ann-Marie, Persson, Gosta Rutger, Lindahl, Christel and Renvert, Stefan	Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up	#0 Peri-Implant Bone Study	[72]

If we consider where the target articles were allocated (Figure 3), it is apparent that most of them ended up in the #0 group (n=23), followed by group #6 Photodynamic Therapy for Peri-implantitis Treatment (n=1).

This supports the idea that BERTopic working on all-mpnet-base-v2 embeddings is robust enough to discriminate not only OffTGs from dental-related topics, but, within dental topics, what the peri-implantitis topics are.

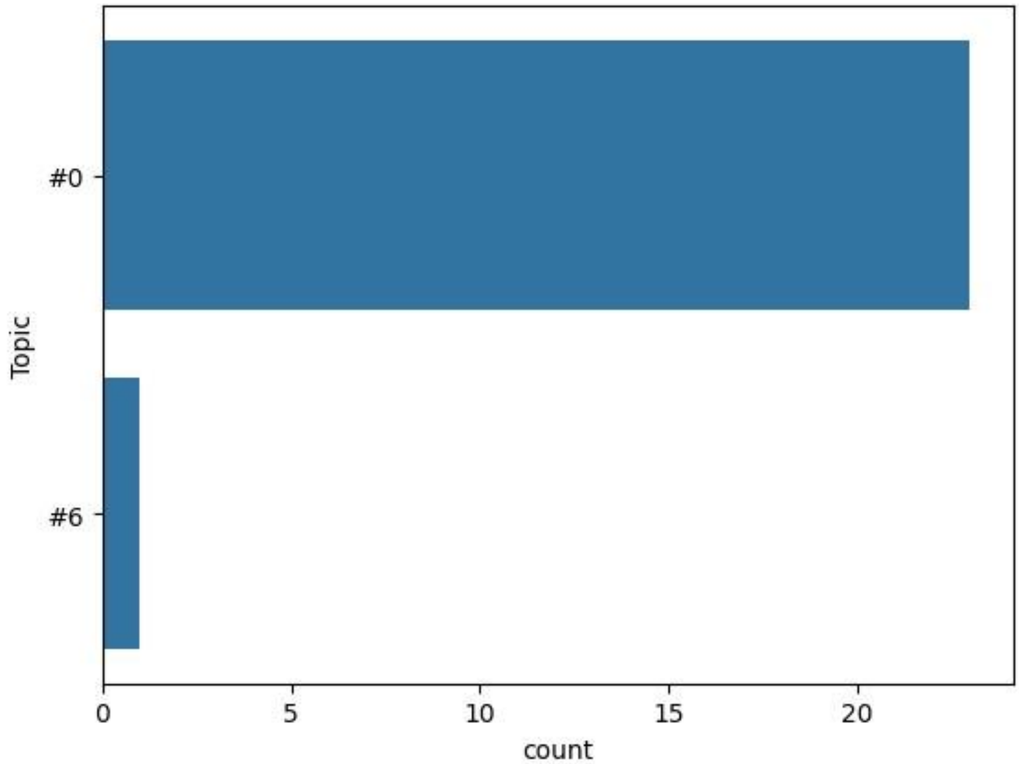

Figure 3. Barchart representing the allocation of the target articles in the peri-implantitis dataset by BERTopic.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

We then further analyzed the dataset, and found that 6 OnTAs had been misclassified into OffTGs, and more precisely in topic #8 Porous Polyethylene Orbital Reconstruction; the first misclassified paper was about orthognatic surgery, and so not directly related to implants:

- "Long-term evaluation of the use of coralline hydroxyapatite in orthognathic surgery" [73]

The remaining five papers focused on craniofacial surgery, and thus understandably closer to orbital surgery than to dental -related topics:

- "Timing of cranial reconstruction after cranioplasty infections: are we ready for a re-thinking? A comparative analysis of delayed versus immediate cranioplasty after debridement in a series of 48 patients" [74]
- "HTR® polymer facial implants: A five-year clinical experience" [75]
- "Gore-Tex chin implants: a review of 324 cases" [76]
- "The application of alloplastic materials for augmentation in cosmetic facial surgery" [77]
- "Japanese National Questionnaire Survey in 2018 on Complications Related to Cranial Implants in Neurosurgery" [78]

In this case, therefore, it can be argued that BERTopic did not really misclassify these papers and discarding them would not have jeopardized the systematic review. Upon inspection, we also found 469 OffTAs (i.e. unrelated to dentistry) that had not been clustered in the OffTGs but had been allocated to dental topics. This classification thus yields a Specificity=0.99, a Sensitivity=0.79, and F1 score= 0.88.

3.2. Bone Augmentation Dataset Analysis

We again applied BERTopic on the titles of the articles of the second dataset and tuned the clustering parameters as previously described to get an approachable number of topics. As Figure 4 shows, generally speaking, decreasing the minimum size of the acceptable clusters in the HDBSCAN algorithm again increased the number of topics identified by BERTopic.

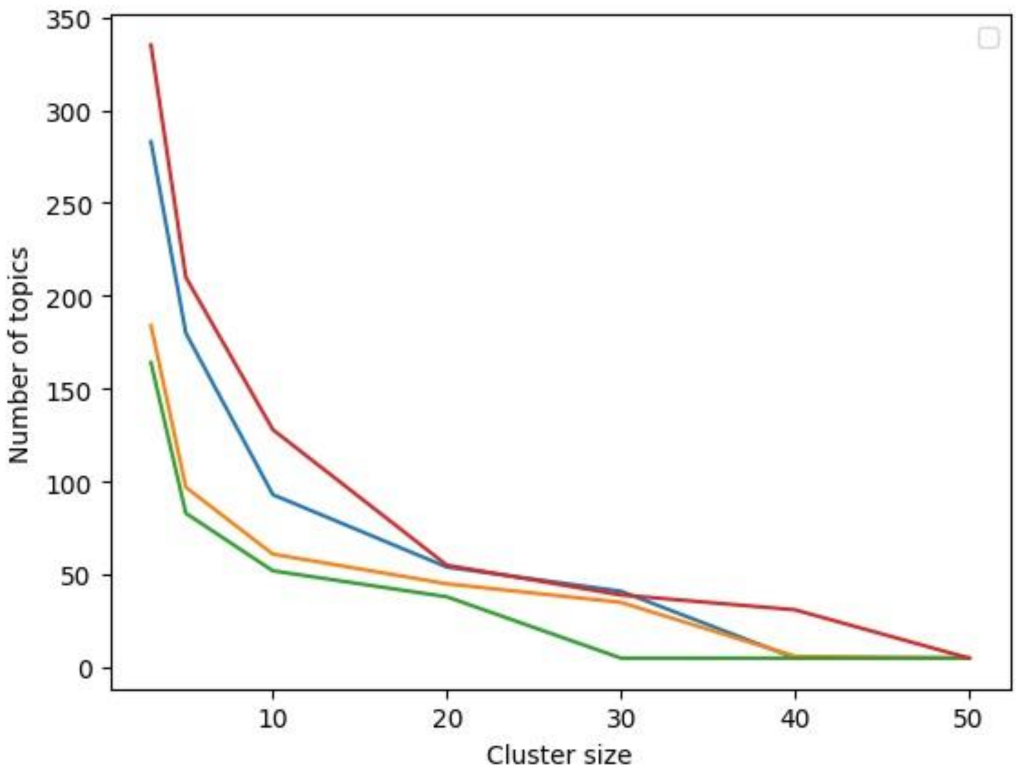

Figure 4. Lineplot showing the relation between the minimum cluster size setting for HDBSCAN and the number of topics identified by BERTopic in the bone regeneration dataset, based on the number of neighbors setting in the UMAP dimension reduction algorithm. Red line: n_neighbors=10; Blue line: n_neighbors=15; Orange line: n_neighbors=50; Green line: n_neighbors=100.

At the same time, changing the parameters of the UMAP algorithm allows BERTopic to better recognize local features in the distribution of the data points. We maintained the same parameters as for the first dataset, which yielded 22 topics. Table 3 lists the topics identified in this dataset.

Table 3. contains the list of topics identified by BERTopic, in order of size, for the bone augmentation dataset. Non-dental topics are indicated in bold.

Topic	Count	Name	KeyBERT	LLM
-1	1515	-1_bone_implant_implants_dental	['bone augmentation', 'implant placement', 'implants placed', 'dental implant', 'bone regeneration', 'dental implants', 'implant', 'peri implant', 'implants', 'osseointegration']	Dental Implants Studies
0	727	0_implants_implant_immediate_year	['dental implant', 'dental implants', 'single implants', 'implant placement', 'implants placed', 'edentulous maxilla', 'implant stability', 'edentulous patients', 'implants year', 'posterior mandible']	Dental Implants in Edentulous Patients
1	692	1_sinus_maxillary sinus_sinus floor_floor	['sinus grafting', 'sinus augmentation', 'sinus floor', 'osteotome sinus', 'maxillary sinus', 'sinus elevation', 'sinus lift', 'sinus membrane', 'bone graft', 'lateral sinus']	Sinus Floor Elevation
2	**296**	**2_hip_arthroplasty_total_femoral**	**['hip arthroplasty', 'hip replacement', 'revision hip', 'total hip', 'femoral stem', 'femoral stems', 'acetabular revision', 'arthroplasty using', 'knee arthroplasty', 'bone grafting']**	**Hip Arthroplasty**
3	265	3_alveolar_alveolar ridge_ridge_preservation	['alveolar ridge', 'alveolar ridges', 'alveolar bone', 'placement alveolar', 'study alveolar', 'trial alveolar', 'vertical alveolar', 'following alveolar', 'alveolar	Alveolar Ridge Augmentation Techniques

			distraction', 'alveolar cleft']	
4	225	4_titanium_titanium implants_surface_implants	['titanium dental', 'titanium implant', 'titanium implants', 'osseointegration titanium', 'implant surfaces', 'etched titanium', 'titanium surfaces', 'titanium surface', 'dental implants', 'porous titanium']	Titanium Implants Surface Acid-Etching Osse
5	167	5_ridge_ridge augmentation_ridge preservation_preservation	['bone allograft', 'tooth extraction', 'ridge preservation', 'autogenous bone', 'dried bone', 'ridge augmentation', 'bone mineral', 'molar extraction', 'tooth', 'bovine bone']	Ridge Preservation Bone Allograft
6	147	6_bone_guided_regeneration_guided bone	['implants regenerated', 'bone regeneration', 'bone grafting', 'dental implants', 'dental implant', 'bone grafts', 'implants using', 'bone augmentation', 'bone graft', 'immediate implant']	Bone Grafting for Dental Implants
7	146	7_buccal_tissue_soft_soft tissue	['mucosa implants', 'implant mucosa', 'tissue augmentation', 'dental implants', 'implant soft', 'buccal dehiscence', 'buccal soft', 'immediate implant', 'implant placement', 'dermal graft']	Soft Tissue Augmentation for Dental Implants
8	140	8_peri_peri implantitis_implantitis_peri implant	['peri implantitis', 'peri implant', 'implantitis randomized', 'implantitis prospective', 'implantitis using', 'implantitis systematic', 'implantitis defects', 'implantitis lesions',	Peri-Implantitis Treatment

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

			'implantitis impact', 'implant health']	
9	138	9_sockets_extraction_socket_extraction sockets	['socket implant', 'grafted sockets', 'extraction socket', 'sockets clinical', 'socket augmentation', 'healing extraction', 'implant placement', 'socket preservation', 'extraction sockets', 'implants placed']	Implants in Fresh Extraction Sockets
10	**117**	**10_assist_ventricular_heart_ventricular assist**	**['ventricular assist', 'biventricular assist', 'circulatory support', 'heart transplantation', 'cardiogenic shock', 'life support', 'heart transplant', 'bridge heart', 'left ventricular', 'extracorporeal']**	**Ventricular Assist Devices**
11	102	11_platelet_platelet rich_rich_rich fibrin	['implants platelet', 'fibrin socket', 'implant stability', 'using platelet', 'platelet gel', 'fibrin membrane', 'use platelet', 'effects platelet', 'influence platelet', 'bone healing']	Platelet-Rich Fibrin Effects on Dental Implants
12	**93**	**12_fusion_lumbar_cervical_interbody**	**['cervical fusion', 'cervical discectomy', 'cervical disc', 'lumbar fusion', 'disc arthroplasty', 'discectomy fusion', 'fusion lumbar', 'spine fusion', 'spine surgery', 'cervical spine']**	**Cervical and Lumbar Fusion Studies**
13	89	13_bone morphogenetic_morphogenetic_protein_morphogenetic protein	['bone morphogenetic', 'recombinant bone', 'bone regeneration', 'osteogenesis', 'bone formation', 'osteoconductive bulking', 'morphogenetic protein', 'protein bone', 'morphogenetic proteins',	Bone Regeneration Recombinant Human BMP

 doi:10.20944/preprints202407.2198.v1

			'osseointegration dental']	
14	81	14_hydroxyapatite_hydroxyapatite coated_coated_implants	['hydroxyapatite implants', 'hydroxyapatite implant', 'hydroxyapatite coated', 'hydroxyapatite coating', 'treated hydroxyapatite', 'nanocrystalline hydroxyapatite', 'nano hydroxyapatite', 'ceramic hydroxyapatite', 'threaded hydroxyapatite', 'supported hydroxyapatite']	Hydroxyapatite-coated Dental Implants Studies
15	73	15_periodontal_defects_intrabony_treatment	['periodontal intrabony', 'intrabony periodontal', 'periodontal therapy', 'treatment periodontal', 'periodontal defects', 'periodontal infrabony', 'human periodontal', 'periodontal', 'enamel matrix', 'intrabony defects']	Periodontal defect treatment
16	71	16_membranes_guided bone_guided_membrane	['bone regeneration', 'linked collagen', 'membrane collagen', 'regeneration dental', 'collagen membrane', 'collagen membranes', 'guided tissue', 'guided bone', 'collagen', 'resorbable membranes']	Collagen Membranes for Guided Bone Regeneration
17	64	17_overdentures_retained_mandibular_mandibular overdentures	['implant overdentures', 'mandibular overdentures', 'mandibular overdenture', 'implants mandibular', 'mandibular implant', 'retained	Implant-retained Mandibular Overdentures

 doi:10.20944/preprints202407.2198.v1

			overdentures', 'maxillary overdentures', 'overdentures retained', 'retained mandibular', 'retained overdenture']	
18	57	18_antibiotic_antibiotics_implant_infection	['implant infections', 'antibiotic prophylaxis', 'prophylactic antibiotic', 'infection dental', 'antibiotics clinical', 'antibiotic regimens', 'antimicrobial', 'preoperative antibiotics', 'dental implant', 'dental implants']	Antibiotic Prophylaxis for Dental Implants
19	**54**	**19_hearing_anchored hearing_bone anchored_anchored**	**['cochlear implants', 'cochlear implantation', 'cochlear implant', 'hearing implant', 'hearing implants', 'implant bone', 'anchored hearing', 'auditory osseointegrated', 'hearing aids', 'pediatric cochlear']**	**Bone Anchored Hearing Implant**
20	**50**	**20_orbital_retinal_lens_intraocular**	**['orbital implant', 'orbital implants', 'retinal prosthesis', 'infancy orbital', 'retinal detachment', 'inferior orbital', 'acrylic intraocular', 'study retinal', 'intravitreal', 'intraocular lens']**	**Orbital & Retinal Implants**

The topics were visually inspected and, based on their LLM description and their keyword descriptors, we assessed that most topics were, as expected, related to bone regeneration (e.g. topic #3 Alveolar Ridge Augmentation Techniques), ridge preservation (e.g. topic #5 Ridge Preservation Bone Allograft) or otherwise implant-related (e.g. topic #9 Implants in Fresh Extraction Sockets).

However, a careful inspection of the dataset also revealed 5 OffTGs that appeared completely unrelated to the dental field and that altogether totaled 610 OffTAs (Table 3, bold). These topics included:

#2 Hip Arthroplasty (n=296), e.g. "Timing of tibial tubercle osteotomy in two-stage revision of infected total knee arthroplasty does not affect union and reinfection rate. A systematic review" [79]

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

#12 Cervical and Lumbar Fusion Studies (n=93), e.g. "A Long-Term Follow-up, Multicenter, Comparative Study of the Radiologic, and Clinical Results between a CaO-SiO2-P2O5-B2O3Bioactive Glass Ceramics (BGS-7) Intervertebral Spacer and Titanium Cage in 1-Level Posterior Lumbar Interbody Fusion" [80]

#10 Ventricular Assist Devices (n=117), e.g. "Heart transplantation of patients with ventricular assist devices: impact of normothermic ex-vivo preservation using organ care system compared with cold storage" [81]

The dataset also contained 1 topic that, albeit related to dentistry, was not centered on implant dentistry or bone regeneration, i.e. topic #15 Periodontal defect treatment, and that could thus be potentially discarded, but was retained following a conservative attitude, as explained above.

When we plotted the dimensionally reduced embeddings for these 5 selected OffTGs, these were again mostly located at the periphery of the scatter plot (Figure 5), at some semantic distance from the bulk of the data points. Taken together, the bone augmentation dataset comprised a smaller proportion of OffTAs than the peri-implantitis dataset, because our analysis identified only 11% of papers that could be safely excluded from further consideration (632 OffTAs out of 5309 articles).

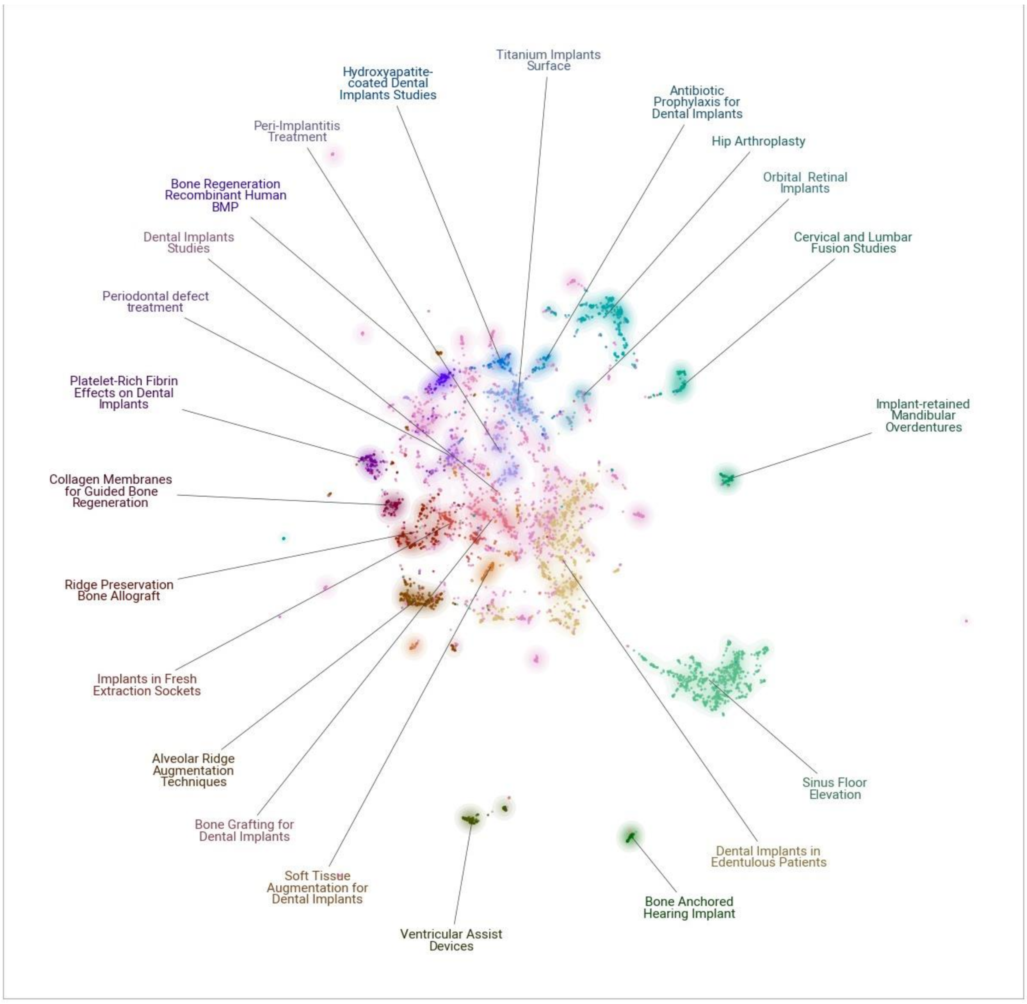

Figure 5. Scatterplot of the semantic distribution of a dataset of titles of scientific articles selected from different biomedical databases using a keyword-based search for bone augmentation. Every topic is marked by a different color.

We then assessed the allocation of the 36 target articles that were identified by the manual screening in the systematic review. No target article had been allocated to any of the OffTGs, so that their removal from the dataset prior to the manual screening would not have negatively affected the outcome of the review (Table 4).

 doi:10.20944/preprints202407.2198.v1

Table 4. contains the list of the target articles identified in Donos et al. systematic review on bone regeneration [19]. No article was clustered in any of the OffTGs.

Authors	Title	Topic	Reference
Naenni, N., Stucki, L., Hüsler, J., Schneider, D., Hämmerle, C.H., Jung, R.E. and Thoma, D.S.,	Implants sites with concomitant bone regeneration using a resorbable or non-resorbable membrane result in stable marginal bone levels and similar profilometric outcomes over 5 years.	#16 Collagen Membranes for Guided Bone Regeneration	[82]
Basler, T., Naenni, N., Schneider, D., Hämmerle, C.H., Jung, R.E. and Thoma, D.S	Randomized controlled clinical study assessing two membranes for guided bone regeneration of peri-implant bone defects: 3-year results.	#16 Collagen Membranes for Guided Bone Regeneration	[83]
Mau, J.L., Grodin, E., Lin, J.J., Chen, M.C.J., Ho, C.H. and Cochran, D.,	A comparative, randomized, prospective, two-center clinical study to evaluate the clinical and esthetic outcomes of two different bone grafting techniques in early implant placement.	#6 'Bone Grafting for Dental Implants	[84]
Annen, B.M., Ramel, C.F., Hammerle, C.H.F. and Jung, R.E.,	Use of a new cross-linked collagen membrane for the treatment of peri-implant dehiscence defects: a randomised controlled double-blinded clinical trial.	#16 Collagen Membranes for Guided Bone Regeneration	[85]
Naenni, N., Schneider, D., Jung, R.E., Hüsler, J., Hämmerle, C.H. and Thoma, D.S.,	Randomized clinical study assessing two membranes for guided bone regeneration of peri-implant bone defects: clinical and histological outcomes at 6 months.	#16 Collagen Membranes for Guided Bone Regeneration	[86]
Lee, J.H., Lee, J.S., Baek, W.S., Lim, H.C., Cha, J.K., Choi, S.H. and Jung, U.W.	Assessment of dehydrothermally cross-linked collagen membrane for guided bone regeneration around peri-implant dehiscence defects: a randomized single-blinded clinical trial.	#16 Collagen Membranes for Guided Bone Regeneration	[87]
Lee, J.H., Park, S.H., Kim, D.H. and Jung, U.W.	Assessment of clinical and radiographic outcomes of guided bone regeneration with dehydrothermally cross-linked collagen membrane around peri-implant dehiscence defects: Results from a 3-year randomized clinical trial.	#16 Collagen Membranes for Guided Bone Regeneration	[88]

 doi:10.20944/preprints202407.2198.v1

Becker, J., Al-Nawas, B., Klein, M.O., Schliephake, H., Terheyden, H. and Schwarz, F.,	Use of a new cross-linked collagen membrane for the treatment of dehiscence-type defects at titanium implants: a prospective, randomized-controlled double-blinded clinical multicenter study.	-1 Dental Implants Studies	[89]
Schwarz, F., Schmucker, A. and Becker,	Long-term outcomes of simultaneous guided bone regeneration using native and cross-linked collagen membranes after 8 years.	#16 Collagen Membranes for Guided Bone Regeneration	[90]
Schwarz, F., Hegewald, A., Sahm, N. and Becker, J.	Long-term follow-up of simultaneous guided bone regeneration using native and cross-linked collagen membranes over 6 years.	#16 Collagen Membranes for Guided Bone Regeneration	[91]
Schwarz, F., Sahm, N. and Becker, J.	Impact of the outcome of guided bone regeneration in dehiscence-type defects on the long-term stability of peri-implant health: clinical observations at 4 years.	#6 Bone Grafting for Dental Implants	[92]
Benic, G.I., Eisner, B.M., Jung, R.E., Basler, T., Schneider, D. and Hämmerle, C.H.,	Hard tissue changes after guided bone regeneration of peri-implant defects comparing block versus particulate bone substitutes: 6-month results of a randomized controlled clinical trial.	#6 Bone Grafting for Dental Implants	[93]
Carpio, L., Loza, J., Lynch, S. and Genco, R.	Guided bone regeneration around endosseous implants with anorganic bovine bone mineral. A randomized controlled trial comparing bioabsorbable versus non-resorbable barriers.	#6 Bone Grafting for Dental Implants	[94]
Deesricharoenkiat, N., Jasilynn, P., Chuenchompoonut, V., Mattheos, N. and Thunyakitpisal, P.	The effect of acemannan in implant placement with simultaneous guided bone regeneration in the aesthetic zone: A randomized controlled trial.	#6 Bone Grafting for Dental Implants	[95]
Jung, R.E., Glauser, R., Schärer, P., Hämmerle, C.H., Sailer, H.F. and Weber, F.E.,	Effect of rhBMP-2 on guided bone regeneration in humans: A randomized, controlled clinical and histomorphometric study.	-1 Dental Implants Studies	[96]
Jung, R.E., Windisch, S.I., Eggenschwiler, A.M.,	A randomized-controlled clinical trial evaluating clinical and radiological	#6 Bone Grafting for Dental Implants	[97]

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

Thoma, D.S., Weber, F.E. and Hämmerle, C.H.	outcomes after 3 and 5 years of dental implants placed in bone regenerated by means of GBR techniques with or without the addition of BMP-2.		
Jung, R.E., Kovacs, M.N., Thoma, D.S. and Hämmerle, C.H.	Informative title: guided bone regeneration with and without rhBMP-2: 17-year results of a randomized controlled clinical trial.	#13 Bone Regeneration Recombinant Human BMP	[98]
Jung, R.E., Hälg, G.A., Thoma, D.S. and Hämmerle, C.H.	A randomized, controlled clinical trial to evaluate a new membrane for guided bone regeneration around dental implants.	#16 Collagen Membranes for Guided Bone Regeneration	[99]
Ramel, C.F., Wismeijer, D.A., F Hämmerle, C.H. and Jung, R.E.	A randomized, controlled clinical evaluation of a synthetic gel membrane for guided bone regeneration around dental implants: clinical and radiologic 1-and 3-year results.	#16 Collagen Membranes for Guided Bone Regeneration	[100]
Jung, R.E., Benic, G.I., Scherrer, D. and Hämmerle, C.H.	Cone beam computed tomography evaluation of regenerated buccal bone 5 years after simultaneous implant placement and guided bone regeneration procedures–a randomized, controlled clinical trial.	#7 Soft Tissue Augmentation for Dental Implants.	[101]
Jung, R.E., Mihatovic, I., Cordaro, L., Windisch, P., Friedmann, A., Blanco Carrion, J., Sanz Sanchez, I., Hallman, M., Quirynen, M. and Hammerle, C.H.	Comparison of a polyethylene glycol membrane and a collagen membrane for the treatment of bone dehiscence defects at bone level implants—A prospective, randomized, controlled, multicenter clinical trial.	#16 Collagen Membranes for Guided Bone Regeneration	[102]
Benic, G.I., Bienz, S.P., Song, Y.W., Cha, J.K., Hämmerle, C.H., Jung, U.W. and Jung, R.E.	Randomized controlled clinical trial comparing guided bone regeneration of peri-implant defects with soft-type block versus particulate bone substitutes: six-month results of hard-tissue changes.	-1 Dental Implant Studies	[103]
Lee, D.W., Kim, K.T., Joo, Y.S., Yoo, M.K., Yu, J.A. and Ryu, J.J.	The role of two different collagen membranes for dehiscence defect around implants in humans.	-1 Dental Implant Studies	[104]

 doi:10.20944/preprints202407.2198.v1

Mattout, P., Nowzari, H. and Mattout, C.,	Clinical evaluation of guided bone regeneration at exposed parts of Brånemark dental implants with and without bone allograft.	#6 Bone Grafting for Dental Implants	[105]
Merli, M., Moscatelli, M., Mariotti, G., Pagliaro, U., Raffaelli, E. and Nieri, M.	Comparing membranes and bone substitutes in a one-stage procedure for horizontal bone augmentation. A double-blind randomised controlled trial	-1 Dental Implant Studies	[106]
Merli, M., Moscatelli, M., Mariotti, G., Pagliaro, U., Raffaelli, E. and Nieri, M.	Comparing membranes and bone substitutes in a one-stage procedure for horizontal bone augmentation. Three-year post-loading results of a double-blind randomised controlled trial.	-1 Dental Implant Studies	[107]
Park, S.H., Lee, K.W., Oh, T.J., Misch, C.E., Shotwell, J. and Wang, H.L.	Effect of absorbable membranes on sandwich bone augmentation.	#16 Collagen Membranes for Guided Bone Regeneration	[108]
Schneider, D., Weber, F.E., Grunder, U., Andreoni, C., Burkhardt, R. and Jung, R.E.	A randomized controlled clinical multicenter trial comparing the clinical and histological performance of a new, modified polylactide-co-glycolide acid membrane to an expanded polytetrafluorethylene membrane in guided bone regeneration procedures.	#16 Collagen Membranes for Guided Bone Regeneration	[109]
Temmerman, A., Cortellini, S., Van Dessel, J., De Greef, A., Jacobs, R., Dhondt, R., Teughels, W. and Quirynen, M.	Bovine-derived xenograft in combination with autogenous bone chips versus xenograft alone for the augmentation of bony dehiscences around oral implants: A randomized, controlled, split-mouth clinical trial.	-1 Dental Implant Studies	[110]
Simion, M., Misitano, U., Gionso, L. and Salvato, A.	Treatment of dehiscences and fenestrations around dental implants using resorbable and nonresorbable membranes associated with bone autografts: a comparative clinical study.	#16 Collagen Membranes for Guided Bone Regeneration	[111]
Urban, I.A., Wessing, B., Alández, N., Meloni, S., González-Martin, O., Polizzi, G., Sanz-Sanchez, I., Montero, E. and Zechner, W.	A multicenter randomized controlled trial using a novel collagen membrane for guided bone regeneration at dehisced single implant sites: Outcome at prosthetic delivery and at 1-year follow?up.	#16 Collagen Membranes for Guided Bone Regeneration	[112]
Wessing, B., Urban, I., Montero, E., Zechner, W., Hof, M., Alandez Chamorro, J., Alandez Martin, N., Polizzi, G., Meloni, S. and Sanz, M.	A multicenter randomized controlled clinical trial using a new resorbable non-cross-linked collagen membrane for guided bone regeneration at dehisced single implant sites: interim results of a bone augmentation procedure.	#16 Collagen Membranes for Guided Bone Regeneration	[113]

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 26 July 2024 doi:10.20944/preprints202407.2198.v1

Van Assche, N., Michels, S., Naert, I. and Quirynen, M.	Randomized controlled trial to compare two bone substitutes in the treatment of bony dehiscences.	#6 Bone Grafting for Dental Implants	[114]
Veis, A.A., Tsirlis, A.T. and Parisis, N.A.	Effect of autogenous harvest site location on the outcome of ridge augmentation for implant dehiscences.	-1 Dental Implant Studies	[115]
Wen, S.C., Fu, J.H. and Wang, H.L.	Effect of Deproteinized Bovine Bone Mineral at Implant Dehiscence Defects Grafted by the Sandwich Bone Augmentation Technique.	-1 Dental Implant Studies	[116]
Tsai, Y.L., Tsao, J.P., Wang, C.L., Grodin, E., Lin, J.J., Chen, C.J., Ho, C.H., Cochran, D. and Mau, J.L.P.	Stability of contour augmentation of implant-supported single crowns in the esthetic zone: One-year cone-beam computed tomography results of a comparative, randomized, prospective, two-center clinical study using two different bone grafting techniques in early implant placement.	#0 Dental Implants in Edentulous Patients	[117]

Interestingly, most target papers belonged to either group #16 Collagen Membranes for Guided Bone Regeneration (16 papers out of 36 target articles), group #6 Bone Grafting for Dental Implants (8 target articles) or group -1 (9 target articles) (Figure 6). This should actually give readers some pause, as, out of 5309 articles, 45% of the target articles were found in topic #16, which comprises only 71 papers, and all the 36 articles were contained in 6 topic groups, which contained 2695 articles (noticeably, topic -1 alone contained 1515 papers).

We then manually screened the corpus again and found that no (dental) OnTA had been clustered in the OffTGs, yielding a classification Specificity=1. Upon inspection, we also found 204 OffTAs (i.e. unrelated to dentistry) that had not been clustered in the OffTGs. The Recall (or Sensitivity) for this task is thus 0.74, and the F1 score for this classification task is 0.85, in line with the results for the first dataset. This indicates that a few more papers could have been filtered out from the dataset, but it also confirms that no real dental paper (i.e. a potential target article for a systematic review) was inadvertently lost due to misclassification.

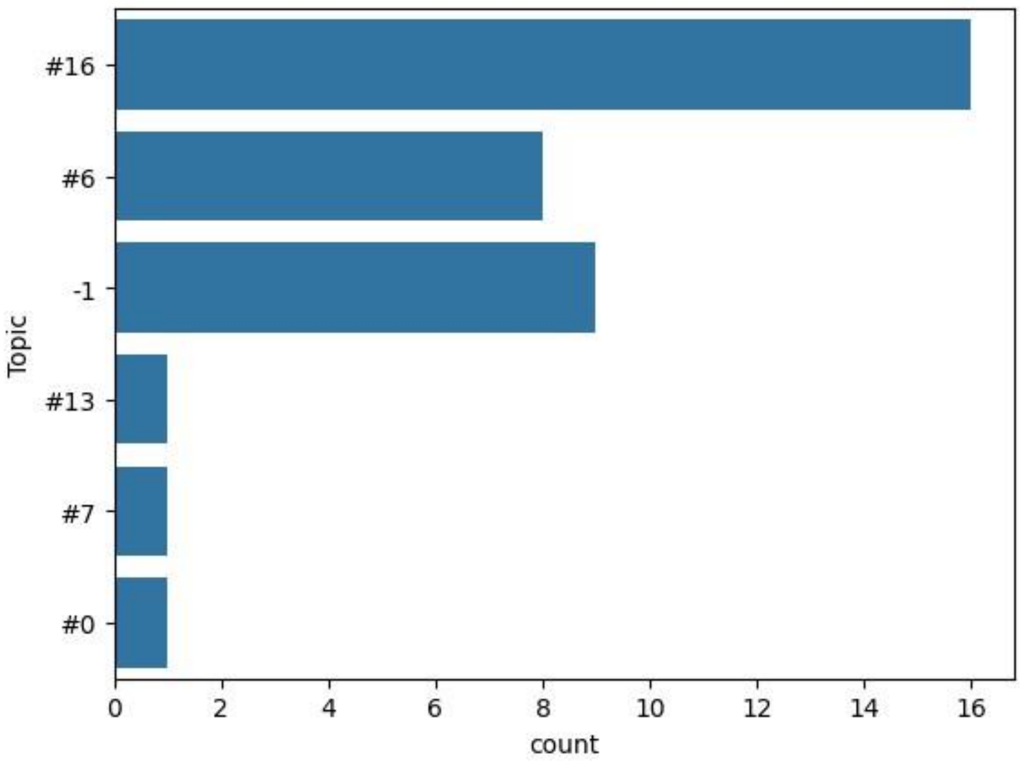

Figure 6. Barchart representing the allocation of the target articles in the bone regeneration dataset by BERTopic.

Overall, high performing topic-modeling algorithms, such as BERTopic, open up the possibility to segment whole datasets into clusters labelled by their topic. Some of these topics are clearly unrelated to the matter at hand and can be potentially, and based on our data, safely removed and excluded from further screening, saving a variable amount of time to investigators. The first dataset, on peri-implantitis, was more heterogeneous and 8 OffTGs were identified, which contained about 30% of the total number of papers in the dataset. It can be assumed that their exclusion would have significantly impacted the total manual screening time. The second dataset, on bone regeneration, was cleaner, and the 5 frank OffTGs that BERTopic identified were smaller. It can be therefore assumed that cleaner, more focused datasets will benefit from this semantic filtering less than broader and more heterogeneous datasets. At the same time, it can also be hypothesized that the availability of these protocols of semantic filtering could affect the way keyword-based searches are conducted, relaxing the need for more stringent queries, and allowing for broader and more heterogeneous datasets, which can be filtered using semantic-based algorithms before manual screening.

Our brief analysis also suggests that some topics might even be positively selected to conduct a more restricted and focused screening, with some caveats. In our situation, it was easy to retrospectively identify the topics where the target articles were contained but doing that with a new dataset would not be as straightforward, because many topics would be about closely related areas, and excluding them would be risky. As an example of this, considering an hypothetical adoption of BERTopic in the pre-screening phase of thed bone regeneration dataset for a systematic review, topic #16 Collagen Membranes for Guided Bone Regeneration could have been an easy pick for further assessment, but at this stage there would have been no rationale to safely exclude e.g. the quite large (n=692) #1 Sinus Floor Elevation group by just looking at its LLM descriptor or its keywords.

4. Conclusions

Our analysis focused on two separate datasets, and relied on BERTopic, a popular topic-modeling algorithm, to identify sets of articles to discard from datasets of the biomedical literature prior to manual screening, to make evidence identification for systematic reviews faster. Taken together, our data show that encoding article titles with the all-mpnet-base-v2 model and then running BERTopic on them is an inexpensive, user-friendly, and quick way to cluster articles into topics and have an effective overview of the dataset's semantic structure. This procedure has a degree of granularity sufficient to identify groups of articles that can be safely removed from the dataset before it is processed by the investigators during the reliable - but slow and labor intensive - step of manual inspection. The number of topics in the dataset that are unrelated to the query varies according to the query itself, the keywords used to conduct it, and the database used to create the dataset, but, in one of the two datasets we used, we were able to filter out more than 1800 articles, or 30% of the dataset. Furthermore, we also observed that the target articles that had been actually identified for the systematic reviews tended to be found in few clusters, opening the possibility that semantic search can not only help investigators identify unrelated articles to discard, but also select a subset of the initial dataset to focus manual inspection on, with faster processing.

Author Contributions: Conceptualization, C.G. and E.C.; methodology, C.C.; software, C.C. and C.G.; formal analysis, C.C. and C.G.; resources, E.C. and N.D.; data curation, M.M.; writing—original draft preparation, C.G. and M.M.; writing—review and editing, N.D. and E.C.; supervision, E.C.; All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Data are available upon request.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Reips, U.-D.; Barak, A. *How Internet-Mediated Research Changes Science*; University Press, 2008; ISBN 0521694647.
2. Hyland, K. Academic Publishing: Issues and Challenges in the Construction of Knowledge. **2016**.
3. Lee, I. Publish or Perish: The Myth and Reality of Academic Publishing. *Language teaching* **2014**, *47*, 250–261.
4. Landhuis, E. Scientific Literature: Information Overload. *Nature* **2016**, *535*, 457–458.
5. Dickersin, K.; Scherer, R.; Lefebvre, C. Systematic Reviews: Identifying Relevant Studies for Systematic Reviews. *Bmj* **1994**, *309*, 1286–1291.
6. Bramer, W.M.; Rethlefsen, M.L.; Kleijnen, J.; Franco, O.H. Optimal Database Combinations for Literature Searches in Systematic Reviews: A Prospective Exploratory Study. *Syst Rev* **2017**, *6*, 1–12.
7. Lu, Z. PubMed and beyond: A Survey of Web Tools for Searching Biomedical Literature. *Database* **2011**, *2011*, baq036–baq036, doi:10.1093/database/baq036.
8. Gusenbauer, M.; Haddaway, N.R. Which Academic Search Systems Are Suitable for Systematic Reviews or Meta-analyses? Evaluating Retrieval Qualities of Google Scholar, PubMed, and 26 Other Resources. *Res Synth Methods* **2020**, *11*, 181–217, doi:10.1002/jrsm.1378.
9. Grivell, L. Mining the Bibliome: Searching for a Needle in a Haystack? *EMBO Rep* **2002**, *3*, 200–203, doi:10.1093/embo-reports/kvf059.
10. Jin, Q.; Leaman, R.; Lu, Z. PubMed and beyond: Biomedical Literature Search in the Age of Artificial Intelligence. *EBioMedicine* **2024**, *100*, 104988, doi:10.1016/j.ebiom.2024.104988.
11. van de Schoot, R.; de Bruin, J.; Schram, R.; Zahedi, P.; de Boer, J.; Weijdema, F.; Kramer, B.; Huijts, M.; Hoogerwerf, M.; Ferdinands, G. ASReview: Open Source Software for Efficient and Transparent Active Learning for Systematic Reviews. *ArXiv, vol. abs/2006.12166* **2020**.
12. Khalil, H.; Ameen, D.; Zarnegar, A. Tools to Support the Automation of Systematic Reviews: A Scoping Review. *J Clin Epidemiol* **2022**, *144*, 22–42, doi:10.1016/j.jclinepi.2021.12.005.
13. Nentidis, A.; Krithara, A.; Paliouras, G.; Gasco, L.; Krallinger, M. BioASQ at CLEF2022: The Tenth Edition of the Large-Scale Biomedical Semantic Indexing and Question Answering Challenge. In; 2022; pp. 429–435.
14. Esteva, A.; Kale, A.; Paulus, R.; Hashimoto, K.; Yin, W.; Radev, D.; Socher, R. COVID-19 Information Retrieval with Deep-Learning Based Semantic Search, Question Answering, and Abstractive Summarization. *NPJ Digit Med* **2021**, *4*, 68, doi:10.1038/s41746-021-00437-0.

15. Vaswani, A.; Shazeer, N.; Parmar, N.; Uszkoreit, J.; Jones, L.; Gomez, A.N.; Kaiser, Ł.; Polosukhin, I. Attention Is All You Need. *Adv Neural Inf Process Syst* **2017**, *30*.
16. Noh, J.; Kavuluru, R. Improved Biomedical Word Embeddings in the Transformer Era. *J Biomed Inform* **2021**, *120*, 103867, doi:10.1016/j.jbi.2021.103867.
17. Likhareva, D.; Sankaran, H.; Thiyagarajan, S. Empowering Interdisciplinary Research with BERT-Based Models: An Approach Through SciBERT-CNN with Topic Modeling. *arXiv preprint arXiv:2404.13078* **2024**.
18. Grootendorst, M. BERTopic: Neural Topic Modeling with a Class-Based TF-IDF Procedure. *arXiv preprint arXiv:2203.05794* **2022**.
19. Calciolari, E.; Corbella, S.; Gkranias, N.; Viganó, M.; Sculean, A.; Donos, N. Efficacy of Biomaterials for Lateral Bone Augmentation Performed with Guided Bone Regeneration. A Network Meta-analysis. *Periodontol 2000* **2023**, *93*, 77–106.
20. Donos, N.; Calciolari, E.; Ghuman, M.; Baccini, M.; Sousa, V.; Nibali, L. The Efficacy of Bone Reconstructive Therapies in the Management of Peri-Implantitis. A Systematic Review and Meta-Analysis. *J Clin Periodontol* 2023.
21. Bassi, S. A Primer on Python for Life Science Researchers. *PLoS Comput Biol* **2007**, *3*, e199.
22. Jia, Z.; Maggioni, M.; Smith, J.; Scarpazza, D.P. Dissecting the NVidia Turing T4 GPU via Microbenchmarking. *arXiv preprint arXiv:1903.07486* **2019**.
23. Cook, D.A.; Beckman, T.J.; Bordage, G. A Systematic Review of Titles and Abstracts of Experimental Studies in Medical Education: Many Informative Elements Missing. *Med Educ* **2007**, *41*, 1074–1081.
24. Hartley, J. Planning That Title: Practices and Preferences for Titles with Colons in Academic Articles. *Libr Inf Sci Res* **2007**, *29*, 553–568.
25. Guizzardi, S.; Colangelo, M.T.; Mirandola, P.; Galli, C. Modeling New Trends in Bone Regeneration, Using the BERTopic Approach. *Regenerative Med* **2023**, *18*, 719–734.
26. Saif, H.; Fernandez, M.; He, Y.; Alani, H. On Stopwords, Filtering and Data Sparsity for Sentiment Analysis of Twitter. **2014**.
27. Gutiérrez, L.; Keith, B. A Systematic Literature Review on Word Embeddings. In Proceedings of the Trends and Applications in Software Engineering: Proceedings of the 7th International Conference on Software Process Improvement (CIMPS 2018) 7; Springer, 2019; pp. 132–141.
28. Wang, S.; Zhou, W.; Jiang, C. A Survey of Word Embeddings Based on Deep Learning. *Computing* **2020**, *102*, 717–740.
29. Liu, Q.; Kusner, M.J.; Blunsom, P. A Survey on Contextual Embeddings. *arXiv preprint arXiv:2003.07278* **2020**.
30. McInnes, L.; Healy, J.; Melville, J. Umap: Uniform Manifold Approximation and Projection for Dimension Reduction. *arXiv preprint arXiv:1802.03426* **2018**.
31. McInnes, L.; Healy, J.; Astels, S. Hdbscan: Hierarchical Density Based Clustering. *J. Open Source Softw.* **2017**, *2*, 205.
32. Qaiser, S.; Ali, R. Text Mining: Use of TF-IDF to Examine the Relevance of Words to Documents. *Int J Comput Appl* **2018**, *181*, 25–29.
33. Xu, D.D.; Wu, S.B. An Improved TFIDF Algorithm in Text Classification. *Applied Mechanics and Materials* **2014**, *651*, 2258–2261.
34. Raschka, S.; Patterson, J.; Nolet, C. Machine Learning in Python: Main Developments and Technology Trends in Data Science, Machine Learning, and Artificial Intelligence. *Information* **2020**, *11*, 193, doi:10.3390/info11040193.
35. Issa, B.; Jasser, M.B.; Chua, H.N.; Hamzah, M. A Comparative Study on Embedding Models for Keyword Extraction Using KeyBERT Method. In Proceedings of the 2023 IEEE 13th International Conference on System Engineering and Technology (ICSET); IEEE, 2023; pp. 40–45.
36. Teknium Teknium/OpenHermes-2.5-Mistral-7B Available online: https://huggingface.co/teknium/OpenHermes-2.5-Mistral-7B (accessed on 10 February 2024).
37. Thirunavukarasu, A.J.; Ting, D.S.J.; Elangovan, K.; Gutierrez, L.; Tan, T.F.; Ting, D.S.W. Large Language Models in Medicine. *Nat Med* **2023**, *29*, 1930–1940.
38. Kaddour, J.; Harris, J.; Mozes, M.; Bradley, H.; Raileanu, R.; McHardy, R. Challenges and Applications of Large Language Models. *arXiv preprint arXiv:2307.10169* **2023**.
39. Park, S.; Choi, J.; Lee, S.; Kang, U. A Comprehensive Survey of Compression Algorithms for Language Models. *arXiv preprint arXiv:2401.15347* **2024**.

40. Meskó, B. Prompt Engineering as an Important Emerging Skill for Medical Professionals: Tutorial. *J Med Internet Res* **2023**, *25*, e50638, doi:10.2196/50638.
41. Hunter, J.D. Matplotlib: A 2D Graphics Environment. *Comput Sci Eng* **2007**, *9*, doi:10.1109/MCSE.2007.55.
42. Waskom, M. Seaborn: Statistical Data Visualization. *J Open Source Softw* **2021**, *6*, doi:10.21105/joss.03021.
43. McInnes, L. DataMapPlot.
44. Galli, C.; Donos, N.; Calciolari, E. Performance of 4 Pre-Trained Sentence Transformer Models in the Semantic Query of a Systematic Review Dataset on Peri-Implantitis. *Information* **2024**, *15*, 68.
45. AbuRahma, A.F.; Robinson, P.A.; Jennings, T.G. Carotid-Subclavian Bypass Grafting with Polytetrafluoroethylene Grafts for Symptomatic Subclavian Artery Stenosis or Occlusion: A 20-Year Experience. *J Vasc Surg* **2000**, *32*, 411–419.
46. Stewart, R.; Horwitz, B.; Howes, J.; Novack, G.D.; Hart, K. Double-Masked, Placebo-Controlled Evaluation of Loteprednol Etabonate 0.5 for Postoperative Inflammation. *J Cataract Refract Surg* **1998**, *24*, 1480–1489.
47. Senova, S.; Hosomi, K.; Gurruchaga, J.-M.; Gouello, G.; Ouerchefani, N.; Beaugendre, Y.; Lepetit, H.; Lefaucheur, J.-P.; Badin, R.A.; Dauguet, J. Three-Dimensional SPACE Fluid-Attenuated Inversion Recovery at 3 T to Improve Subthalamic Nucleus Lead Placement for Deep Brain Stimulation in Parkinson's Disease: From Preclinical to Clinical Studies. *J Neurosurg* **2016**, *125*, 472–480.
48. Almugathwi, M.; Wearden, A.; Green, K.; Hill-Feltham, P.; Powell, R. Online Support Group Users' Perceptions and Experiences of Bone-Anchored Hearing Aids (BAHAs): A Qualitative Study. *Int J Audiol* **2020**, *59*, 850–858.
49. Andersen, H.; Aass, A.M.; Wohlfahrt, J.C. Porous Titanium Granules in the Treatment of Peri-Implant Osseous Defects—a 7-Year Follow-up Study. *Int J Implant Dent* **2017**, *3*, 1–7.
50. Jepsen, K.; Jepsen, S.; Laine, M.L.; Anssari Moin, D.; Pilloni, A.; Zeza, B.; Sanz, M.; Ortiz-Vigon, A.; Roos-Jansåker, A.M.; Renvert, S. Reconstruction of Peri-Implant Osseous Defects: A Multicenter Randomized Trial. *J Dent Res* **2016**, *95*, 58–66.
51. Wohlfahrt, J.C.; Lyngstadaas, S.P.; Rønold, H.J.; Saxegaard, E.; Ellingsen, J.E.; Karlsson, S.; Aass, A.M. Porous Titanium Granules in the Surgical Treatment of Peri-Implant Osseous Defects: A Randomized Clinical Trial. *International Journal of Oral & Maxillofacial Implants* **2012**, *27*.
52. Emanuel, N.; Machtei, E.E.; Reichart, M.; Shapira, L. D-PLEX500: A Local Biodegradable Prolonged Release Doxycycline-Formulated Bone Graft for the Treatment for Peri-Implantitis. A Randomized Controlled Clinical Study. *Quintessence Int (Berl)* **2020**, *51*, 546–553.
53. Renvert, S.; Giovannoli, J.; Roos-Jansåker, A.; Rinke, S. Surgical Treatment of Peri-implantitis with or without a Deproteinized Bovine Bone Mineral and a Native Bilayer Collagen Membrane: A Randomized Clinical Trial. *J Clin Periodontol* **2021**, *48*, 1312–1321.
54. Isehed, C.; Holmlund, A.; Renvert, S.; Svenson, B.; Johansson, I.; Lundberg, P. Effectiveness of Enamel Matrix Derivative on the Clinical and Microbiological Outcomes Following Surgical Regenerative Treatment of Peri-implantitis. A Randomized Controlled Trial. *J Clin Periodontol* **2016**, *43*, 863–873.
55. Isehed, C.; Svenson, B.; Lundberg, P.; Holmlund, A. Surgical Treatment of Peri-implantitis Using Enamel Matrix Derivative, an RCT: 3-and 5-year Follow-up. *J Clin Periodontol* **2018**, *45*, 744–753.
56. Renvert, S.; Roos-Jansåker, A.; Persson, G.R. Surgical Treatment of Peri-implantitis Lesions with or without the Use of a Bone Substitute—a Randomized Clinical Trial. *J Clin Periodontol* **2018**, *45*, 1266–1274.
57. Nct Peri-Implantitis - Reconstructive Surgical Therapy Available online: https://clinicaltrials.gov/show/NCT03077061 2017 (accessed on 10 April 2022).
58. Froum, S.J.; Froum, S.H.; Rosen, P.S. A Regenerative Approach to the Successful Treatment of Peri-Implantitis: A Consecutive Series of 170 Implants in 100 Patients with 2-to 10-Year Follow-Up. *International Journal of Periodontics & Restorative Dentistry* **2015**, *35*.
59. Gonzalez Regueiro, I.; Martinez Rodriguez, N.; Barona Dorado, C.; Sanz-Sánchez, I.; Montero, E.; Ata-Ali, J.; Duarte, F.; Martínez-González, J.M. Surgical Approach Combining Implantoplasty and Reconstructive Therapy with Locally Delivered Antibiotic in the Treatment of Peri-implantitis: A Prospective Clinical Case Series. *Clin Implant Dent Relat Res* **2021**, *23*, 864–873.
60. Isler, S.C.; Soysal, F.; Ceyhanlı, T.; Bakırarar, B.; Unsal, B. Regenerative Surgical Treatment of Peri-implantitis Using Either a Collagen Membrane or Concentrated Growth Factor: A 12-month Randomized Clinical Trial. *Clin Implant Dent Relat Res* **2018**, *20*, 703–712.

 doi:10.20944/preprints202407.2198.v1

61. La Monaca, G.; Pranno, N.; Annibali, S.; Cristalli, M.P.; Polimeni, A. Clinical and Radiographic Outcomes of a Surgical Reconstructive Approach in the Treatment of Peri-implantitis Lesions: A 5-year Prospective Case Series. *Clin Oral Implants Res* **2018**, *29*, 1025–1037.
62. Mercado, F.; Hamlet, S.; Ivanovski, S. Regenerative Surgical Therapy for Peri-implantitis Using Deproteinized Bovine Bone Mineral with 10% Collagen, Enamel Matrix Derivative and Doxycycline—A Prospective 3-year Cohort Study. *Clin Oral Implants Res* **2018**, *29*, 583–591.
63. Polymeri, A.; Anssari-Moin, D.; van der Horst, J.; Wismeijer, D.; Laine, M.L.; Loos, B.G. Surgical Treatment of Peri-implantitis Defects with Two Different Xenograft Granules: A Randomized Clinical Pilot Study. *Clin Oral Implants Res* **2020**, *31*, 1047–1060.
64. Roccuzzo, M.; Gaudioso, L.; Lungo, M.; Dalmasso, P. Surgical Therapy of Single Peri-implantitis Intrabony Defects, by Means of Deproteinized Bovine Bone Mineral with 10% Collagen. *J Clin Periodontol* **2016**, *43*, 311–318.
65. Roccuzzo, M.; Mirra, D.; Pittoni, D.; Ramieri, G.; Roccuzzo, A. Reconstructive Treatment of Peri-implantitis Infrabony Defects of Various Configurations: 5-year Survival and Success. *Clin Oral Implants Res* **2021**, *32*, 1209–1217.
66. Isrctn Reconstructive Surgical Therapy of Peri-Implantitis Bone Defects Available online: https://trialsearch.who.int/Tri-al2.aspx?TrialID=ISRCTN67095066 2019 (accessed on 10 April 2022).
67. Aghazadeh, A.; Rutger Persson, G.; Renvert, S. A Single-centre Randomized Controlled Clinical Trial on the Adjunct Treatment of Intra-bony Defects with Autogenous Bone or a Xenograft: Results after 12 Months. *J Clin Periodontol* **2012**, *39*, 666–673.
68. Aghazadeh, A.; Persson, R.G.; Renvert, S. Impact of Bone Defect Morphology on the Outcome of Reconstructive Treatment of Peri-Implantitis. *Int J Implant Dent* **2020**, *6*, 1–10.
69. Nct Evaluation of Photodynamic Therapy in Treatment of Peri-Implantitis Available online: https://clinicaltrials.gov/show/NCT05187663 2022 (accessed on 10 April 2022).
70. Roos-Jansåker, A.; Renvert, H.; Lindahl, C.; Renvert, S. Submerged Healing Following Surgical Treatment of Peri-implantitis: A Case Series. *J Clin Periodontol* **2007**, *34*, 723–727.
71. Roos-Jansåker, A.; Lindahl, C.; Persson, G.R.; Renvert, S. Long-term Stability of Surgical Bone Regenerative Procedures of Peri-implantitis Lesions in a Prospective Case–Control Study over 3 Years. *J Clin Periodontol* **2011**, *38*, 590–597.
72. Roos-Jansåker, A.; Persson, G.R.; Lindahl, C.; Renvert, S. Surgical Treatment of Peri-implantitis Using a Bone Substitute with or without a Resorbable Membrane: A 5-year Follow-up. *J Clin Periodontol* **2014**, *41*, 1108–1114.
73. Cottrell, D.A.; Wolford, L.M. Long-Term Evaluation of the Use of Coralline Hydroxyapatite in Orthognathic Surgery. *Journal of oral and maxillofacial surgery* **1998**, *56*, 935–941.
74. Di Rienzo, A.; Colasanti, R.; Gladi, M.; Dobran, M.; Della Costanza, M.; Capece, M.; Veccia, S.; Iacoangeli, M. Timing of Cranial Reconstruction after Cranioplasty Infections: Are We Ready for a Re-Thinking? A Comparative Analysis of Delayed versus Immediate Cranioplasty after Debridement in a Series of 48 Patients. *Neurosurg Rev* **2021**, *44*, 1523–1532.
75. Eppley, B.L.; Sadove, A.M.; Holmstrom, H.; Kahnberg, K.-E. HTR® Polymer Facial Implants: A Five-Year Clinical Experience. *Aesthetic Plast Surg* **1995**, *19*, 445–450.
76. Godin, M.; Costa, L.; Romo, T.; Truswell, W.; Wang, T.; Williams, E. Gore-Tex Chin Implants: A Review of 324 Cases. *Arch Facial Plast Surg* **2003**, *5*, 224–227.
77. Jansma, J.; Schepers, R.H.; Vissink, A. The Application of Alloplastic Materials for Augmentation in Cosmetic Facial Surgery. *Ned Tijdschr Tandheelkd* **2014**, *121*, 565–570.
78. Yasuhara, T.; Murai, S.; Mikuni, N.; Miyamoto, S.; Date, I. Japanese National Questionnaire Survey in 2018 on Complications Related to Cranial Implants in Neurosurgery. *Neurol Med Chir (Tokyo)* **2020**, *60*, 337–350.
79. Kitridis, D.; Givissis, P.; Chalidis, B. Timing of Tibial Tubercle Osteotomy in Two-Stage Revision of Infected Total Knee Arthroplasty Does Not Affect Union and Reinfection Rate. A Systematic Review. *Knee* **2020**, *27*, 1787–1794.
80. Lee, J.H.; Kim, S.K.; Kang, S.S.; Han, S.J.; Lee, C.-K.; Chang, B.-S. A Long-Term Follow-up, Multicenter, Comparative Study of the Radiologic, and Clinical Results between a CaO-SiO2-P2O5-B2O3 Bioactive Glass Ceramics (BGS-7) Intervertebral Spacer and Titanium Cage in 1-Level Posterior Lumbar Interbody Fusion. *Clin Spine Surg* **2020**, *33*, E322–E329.

81. Kaliyev, R.; Lesbekov, T.; Bekbossynov, S.; Nurmykhametova, Z.; Bekbossynova, M.; Novikova, S.; Medressova, A.; Smagulov, N.; Faizov, L.; Samalavicius, R. Heart Transplantation of Patients with Ventricular Assist Devices: Impact of Normothermic Ex-Vivo Preservation Using Organ Care System Compared with Cold Storage. *J Cardiothorac Surg* **2020**, *15*, 1–6.
82. Naenni, N.; Stucki, L.; Hüsler, J.; Schneider, D.; Hämmerle, C.H.F.; Jung, R.E.; Thoma, D.S. Implants Sites with Concomitant Bone Regeneration Using a Resorbable or Non-resorbable Membrane Result in Stable Marginal Bone Levels and Similar Profilometric Outcomes over 5 Years. *Clin Oral Implants Res* **2021**, *32*, 893–904.
83. Basler, T.; Naenni, N.; Schneider, D.; Hämmerle, C.H.F.; Jung, R.E.; Thoma, D.S. Randomized Controlled Clinical Study Assessing Two Membranes for Guided Bone Regeneration of Peri-implant Bone Defects: 3-year Results. *Clin Oral Implants Res* **2018**, *29*, 499–507.
84. Mau, J.L.; Grodin, E.; Lin, J.; Chen, M.C.; Ho, C.; Cochran, D. A Comparative, Randomized, Prospective, Two-center Clinical Study to Evaluate the Clinical and Esthetic Outcomes of Two Different Bone Grafting Techniques in Early Implant Placement. *J Periodontol* **2019**, *90*, 247–255.
85. Annen, B.M.; Ramel, C.F.; Hammerle, C.H.F.; Jung, R.E. Use of a New Cross-Linked Collagen Membrane for the Treatment of Peri-Implant Dehiscence Defects: A Randomised Controlled Double-Blinded Clinical Trial. *Eur J Oral Implantol* **2011**, *4*.
86. Naenni, N.; Schneider, D.; Jung, R.E.; Hüsler, J.; Hämmerle, C.H.F.; Thoma, D.S. Randomized Clinical Study Assessing Two Membranes for Guided Bone Regeneration of Peri-implant Bone Defects: Clinical and Histological Outcomes at 6 Months. *Clin Oral Implants Res* **2017**, *28*, 1309–1317.
87. Lee, J.-H.; Lee, J.-S.; Baek, W.-S.; Lim, H.-C.; Cha, J.-K.; Choi, S.-H.; Jung, U.-W. Assessment of Dehydrothermally Cross-linked Collagen Membrane for Guided Bone Regeneration around Peri-Implant Dehiscence Defects: A Randomized Single-Blinded Clinical Trial. *J Periodontal Implant Sci* **2015**, *45*, 229.
88. Lee, J.-H.; Park, S.-H.; Kim, D.-H.; Jung, U.-W. Assessment of Clinical and Radiographic Outcomes of Guided Bone Regeneration with Dehydrothermally Cross-Linked Collagen Membrane around Peri-Implant Dehiscence Defects: Results from a 3-Year Randomized Clinical Trial. *Oral Biology Research* **2019**, *43*, 8–16.
89. Becker, J.; Al-Nawas, B.; Klein, M.O.; Schliephake, H.; Terheyden, H.; Schwarz, F. Use of a New Cross-linked Collagen Membrane for the Treatment of Dehiscence-type Defects at Titanium Implants: A Prospective, Randomized-controlled Double-blinded Clinical Multicenter Study. *Clin Oral Implants Res* **2009**, *20*, 742–749.
90. Schwarz, F.; Schmucker, A.; Becker, J. Long-term Outcomes of Simultaneous Guided Bone Regeneration Using Native and Cross-linked Collagen Membranes after 8 Years. *Clin Oral Implants Res* **2017**, *28*, 779–784.
91. Schwarz, F.; Hegewald, A.; Sahm, N.; Becker, J. Long-term Follow-up of Simultaneous Guided Bone Regeneration Using Native and Cross-linked Collagen Membranes over 6 Years. *Clin Oral Implants Res* **2014**, *25*, 1010–1015.
92. Schwarz, F.; Sahm, N.; Becker, J. Impact of the Outcome of Guided Bone Regeneration in Dehiscence-type Defects on the Long-term Stability of Peri-implant Health: Clinical Observations at 4 Years. *Clin Oral Implants Res* **2012**, *23*, 191–196.
93. Benic, G.I.; Eisner, B.M.; Jung, R.E.; Basler, T.; Schneider, D.; Hämmerle, C.H.F. Hard Tissue Changes after Guided Bone Regeneration of Peri-implant Defects Comparing Block versus Particulate Bone Substitutes: 6-month Results of a Randomized Controlled Clinical Trial. *Clin Oral Implants Res* **2019**, *30*, 1016–1026.
94. Carpio, L.; Loza, J.; Lynch, S.; Genco, R. Guided Bone Regeneration around Endosseous Implants with Anorganic Bovine Bone Mineral. A Randomized Controlled Trial Comparing Bioabsorbable versus Non-resorbable Barriers. *J Periodontol* **2000**, *71*, 1743–1749.
95. Deesricharoenkiat, N.; Jansisyanont, P.; Chuenchompoonut, V.; Mattheos, N.; Thunyakitpisal, P. The Effect of Acemannan in Implant Placement with Simultaneous Guided Bone Regeneration in the Aesthetic Zone: A Randomized Controlled Trial. *Int J Oral Maxillofac Surg* **2022**, *51*, 535–544.
96. Jung, R.E.; Glauser, R.; Schärer, P.; Hämmerle, C.H.F.; Sailer, H.F.; Weber, F.E. Effect of RhBMP-2 on Guided Bone Regeneration in Humans: A Randomized, Controlled Clinical and Histomorphometric Study. *Clin Oral Implants Res* **2003**, *14*, 556–568.
97. Jung, R.E.; Windisch, S.I.; Eggenschwiler, A.M.; Thoma, D.S.; Weber, F.E.; Hämmerle, C.H.F. A Randomized-controlled Clinical Trial Evaluating Clinical and Radiological Outcomes after 3 and 5 Years

of Dental Implants Placed in Bone Regenerated by Means of GBR Techniques with or without the Addition of BMP-2. *Clin Oral Implants Res* **2009**, *20*, 660–666.
98. Jung, R.E.; Kovacs, M.N.; Thoma, D.S.; Hämmerle, C.H.F. Informative Title: Guided Bone Regeneration with and without RhBMP-2: 17-year Results of a Randomized Controlled Clinical Trial. *Clin Oral Implants Res* **2022**, *33*, 302–312.
99. Jung, R.E.; Hälg, G.A.; Thoma, D.S.; Hämmerle, C.H.F. A Randomized, Controlled Clinical Trial to Evaluate a New Membrane for Guided Bone Regeneration around Dental Implants. *Clin Oral Implants Res* **2009**, *20*, 162–168.
100. Ramel, C.F.; Wismeijer, D.A.; F Hämmerle, C.H.; Jung, R.E. A Randomized, Controlled Clinical Evaluation of a Synthetic Gel Membrane for Guided Bone Regeneration around Dental Implants: Clinical and Radiologic 1-and 3-Year Results. *International Journal of Oral & Maxillofacial Implants* **2012**, *27*.
101. Jung, R.E.; Benic, G.I.; Scherrer, D.; Hämmerle, C.H.F. Cone Beam Computed Tomography Evaluation of Regenerated Buccal Bone 5 Years after Simultaneous Implant Placement and Guided Bone Regeneration Procedures–a Randomized, Controlled Clinical Trial. *Clin Oral Implants Res* **2015**, *26*, 28–34.
102. Jung, R.E.; Mihatovic, I.; Cordaro, L.; Windisch, P.; Friedmann, A.; Blanco Carrion, J.; Sanz Sanchez, I.; Hallman, M.; Quirynen, M.; Hammerle, C.H.F. Comparison of a Polyethylene Glycol Membrane and a Collagen Membrane for the Treatment of Bone Dehiscence Defects at Bone Level Implants—A Prospective, Randomized, Controlled, Multicenter Clinical Trial. *Clin Oral Implants Res* **2020**, *31*, 1105–1115.
103. Benic, G.I.; Bienz, S.P.; Song, Y.W.; Cha, J.; Hämmerle, C.H.F.; Jung, U.; Jung, R.E. Randomized Controlled Clinical Trial Comparing Guided Bone Regeneration of Peri-implant Defects with Soft-type Block versus Particulate Bone Substitutes: Six-month Results of Hard-tissue Changes. *J Clin Periodontol* **2022**, *49*, 480–495.
104. Lee, D.-W.; Kim, K.-T.; Joo, Y.-S.; Yoo, M.-K.; Yu, J.-A.; Ryu, J.-J. The Role of Two Different Collagen Membranes for Dehiscence Defect around Implants in Humans. *Journal of Oral Implantology* **2015**, *41*, 445–448.
105. Mattout, P.; Nowzari, H.; Mattout, C. Clinical Evaluation of Guided Bone Regeneration at Exposed Parts of Brånemark Dental Implants with and without Bone Allograft. *Clin Oral Implants Res* **1995**, *6*, 189–195.
106. Merli, M.; Moscatelli, M.; Mariotti, G.; Pagliaro, U.; Raffaelli, E.; Nieri, M. Comparing Membranes and Bone Substitutes in a One-Stage Procedure for Horizontal Bone Augmentation. A Double-Blind Randomised Controlled Trial. *Eur J Oral Implantol* **2015**, *8*.
107. Merli, M.; Moscatelli, M.; Mariotti, G.; Pagliaro, U.; Raffaelli, E.; Nieri, M. Comparing Membranes and Bone Substitutes in a One-Stage Procedure for Horizontal Bone Augmentation. Three-Year Post-Loading Results of a Double-Blind Randomised Controlled Trial. *Eur J Oral Implantol* **2018**, *11*.
108. Park, S.; Lee, K.; Oh, T.; Misch, C.E.; Shotwell, J.; Wang, H. Effect of Absorbable Membranes on Sandwich Bone Augmentation. *Clin Oral Implants Res* **2008**, *19*, 32–41.
109. Schneider, D.; Weber, F.E.; Grunder, U.; Andreoni, C.; Burkhardt, R.; Jung, R.E. A Randomized Controlled Clinical Multicenter Trial Comparing the Clinical and Histological Performance of a New, Modified Polylactide-co-glycolide Acid Membrane to an Expanded Polytetrafluorethylene Membrane in Guided Bone Regeneration Procedures. *Clin Oral Implants Res* **2014**, *25*, 150–158.
110. Temmerman, A.; Cortellini, S.; Van Dessel, J.; De Greef, A.; Jacobs, R.; Dhondt, R.; Teughels, W.; Quirynen, M. Bovine-derived Xenograft in Combination with Autogenous Bone Chips versus Xenograft Alone for the Augmentation of Bony Dehiscences around Oral Implants: A Randomized, Controlled, Split-mouth Clinical Trial. *J Clin Periodontol* **2020**, *47*, 110–119.
111. Simion, M.; Misitano, U.; Gionso, L.; Salvato, A. Treatment of Dehiscences and Fenestrations around Dental Implants Using Resorbable and Nonresorbable Membranes Associated with Bone Autografts: A Comparative Clinical Study. *International Journal of Oral & Maxillofacial Implants* **1997**, *12*.
112. Urban, I.A.; Wessing, B.; Alández, N.; Meloni, S.; González-Martin, O.; Polizzi, G.; Sanz-Sanchez, I.; Montero, E.; Zechner, W. A Multicenter Randomized Controlled Trial Using a Novel Collagen Membrane for Guided Bone Regeneration at Dehisced Single Implant Sites: Outcome at Prosthetic Delivery and at 1-year Follow-up. *Clin Oral Implants Res* **2019**, *30*, 487–497.
113. Wessing, B.; Urban, I.; Montero, E.; Zechner, W.; Hof, M.; Alandez Chamorro, J.; Alandez Martin, N.; Polizzi, G.; Meloni, S.; Sanz, M. A Multicenter Randomized Controlled Clinical Trial Using a New Resorbable Non-cross-linked Collagen Membrane for Guided Bone Regeneration at Dehisced Single

Implant Sites: Interim Results of a Bone Augmentation Procedure. *Clin Oral Implants Res* **2017**, *28*, e218–e226.

114. Van Assche, N.; Michels, S.; Naert, I.; Quirynen, M. Randomized Controlled Trial to Compare Two Bone Substitutes in the Treatment of Bony Dehiscences. *Clin Implant Dent Relat Res* **2013**, *15*, 558–568.
115. Veis, A.A.; Tsirlis, A.T.; Parisis, N.A. Effect of Autogenous Harvest Site Location on the Outcome of Ridge Augmentation for Implant Dehiscences. *International Journal of Periodontics & Restorative Dentistry* **2004**, *24*.
116. Wen, S.-C.; Fu, J.-H.; Wang, H.-L. Effect of Deproteinized Bovine Bone Mineral at Implant Dehiscence Defects Grafted by the Sandwich Bone Augmentation Technique. *Int J Periodontics Restorative Dent* **2018**, *38*, 79–85, doi:10.11607/prd.2931.
117. Tsai, Y.; Tsao, J.; Wang, C.; Grodin, E.; Lin, J.; Chen, C.; Ho, C.; Cochran, D.; Mau, J.L.P. Stability of Contour Augmentation of Implant-supported Single Crowns in the Esthetic Zone: One-year Cone-beam Computed Tomography Results of a Comparative, Randomized, Prospective, Two-center Clinical Study Using Two Different Bone Grafting Techniques in Early Implant Placement. *J Periodontol* **2022**, *93*, 1661–1670, doi:10.1002/JPER.21-0588.