

## Article

# Performance of 4 Pre-Trained Sentence Transformer Models in the Semantic Query of a Systematic Review Dataset on Peri-Implantitis

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**Abstract:** Systematic reviews are cumbersome yet essential to the epistemic process of medical science. Finding significant reports, however, is a daunting task because the sheer volume of published literature makes the manual screening of databases time-consuming. The use of Artificial Intelligence could make literature processing faster and more efficient. Sentence transformers are groundbreaking algorithms that can generate rich semantic representations of text documents and allow for semantic queries. In the present report, we compared four freely available sentence transformer pre-trained models (all-MiniLM-L6-v2, all-MiniLM-L12-v2, all-mpnet-base-v2, and All-distilroberta-v1) on a convenience sample of 6110 articles from a published systematic review. The authors of this review manually screened the dataset and identified 24 target articles that addressed the Focused Questions (FQ) of the review. We applied the four sentence transformers to the dataset and, using the FQ as a query, performed a semantic similarity search on the dataset. The models identified similarities between the FQ and the target articles to a varying degree, and, sorting the dataset by semantic similarities using the best-performing model (all-mpnet-base-v2), the target articles could be found in the top 700 papers out of the 6110 dataset. Our data indicate that the choice of an appropriate pre-trained model could remarkably reduce the number of articles to screen and the time to completion for systematic reviews.

**Keywords:** transformers; embeddings; natural language processing; deep learning; systematic reviews; literature search



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## 1. Introduction

Systematic reviews and literature searches serve as the foundation for evidence-based medicine, facilitating the identification of relevant research findings [1]. Based on this approach, diagnostic and therapeutic interventions should be based on the existing evidence [2]. Given the increasing volume of available research in academic literature, however, searching for pertinent manuscripts has become an arduous endeavor [3]. Reviewing the literature has thus become increasingly valued in academia [4], with systematic reviews being recognized as a crucial tool to overcome the limitations of individual studies. By pooling data across multiple studies, systematic reviews help provide a comprehensive understanding of the effectiveness of various therapies, identify research gaps, inform clinical practice guidelines, and support evidence-based decision-making by healthcare professionals, policymakers, and researchers [5]. Generating systematic reviews, however, is challenging and time-consuming.

Systematic reviews follow a predefined protocol that outlines the search strategy, inclusion and exclusion criteria, data extraction methods, and statistical analysis procedures.

This protocol ensures transparency and minimizes bias in the review process [6]. The systematic review process typically begins with the formulation of a specific and relevant research question [7]. Next, an extensive literature search is conducted using predetermined search terms across various databases like PubMed, Scopus, and Web of Science [8]. Therefore, after the initial search, studies are screened based on predefined inclusion and exclusion criteria to identify those that meet the criteria for inclusion in the review [9]. However, due to the vast amount of available literature, it can be challenging to manually assess all potential studies for relevance. The selected studies are then systematically analyzed and relevant data are extracted [10]. Statistical techniques such as meta-analysis may be employed to synthesize findings from individual studies when appropriate [11]. Additionally, each included study undergoes quality evaluation using established criteria to assess any bias present.

Automation has great potential to make systematic reviews quicker and cheaper, and recent advances in text mining, NLP, and machine learning have demonstrated that several tasks within the systematic review process can be automated or assisted by automation [12]. In recent years, there have been innovations proposed to accelerate the process of systematic reviews, and software is available to help scholars filter out the literature of interest, such as Abstractr, ASReviews, EPPI-reviewer, or RobotSearch, which relies on a convolutional neural network-based classifier to identify RCTs [13]. In particular, the development of large language models, such as BERT (Bidirectional Encoder Representations from Transformers), has shown promise in automating certain aspects of the systematic review process [14]. For example, BERT can be utilized to aid in the identification of relevant studies by improving literature retrieval capabilities through semantic understanding and contextual analysis of search terms, and software like ASReviews leverages these new architectures [15]. End-users, however, have little awareness of the underlying algorithms and models that underlie these tools. The foundation of semantic understanding of a text is the use of embeddings, i.e., numerical representations, through a vector of a given dimensionality of the meaning of a word or sentence [16]. Although vectors can be generically defined as geometric objects that represent a directed quantity, possessing both magnitude and direction, in the context of NLP, vectors can be conceived as sequences of numbers that encode the semantic information of words or phrases [17].

Although sparse vectors have been used in the semantic representation of words and texts for a long time [18], embeddings were first introduced by Mikolov and a team of researchers at Google in 2013 with an algorithm known as Word2Vec [19]. Word2vec consisted of a shallow artificial neural network that could be trained on a text or a series of texts and proceeded to model 300-dimensional embeddings for each word in such a way that embeddings of words that occurred together in the text within a pre-set context frame were more similar, while embeddings of words that never occurred together differed to a greater extent [20]. This idea, which may sound not only simple but even simplistic, is rooted in the distributional semantic theory of Harris and Firth [21], and, more importantly, has proven to be extremely effective in NLP tasks. By training such algorithms on large text datasets, it was possible to provide a way for machines to have an internal representation of the meaning of words, which would be distributed in a multidimensional semantic space according to their semantic features [22].

In 2017, a seminal paper by Vaswani et al. with the title “Attention is all you need” outlined the concept of attention mechanisms in NLP, revolutionizing the field by allowing models to capture more complex relationships and dependencies between words and sentences through specific architectures known as transformers [23]. Transformers can create richer embeddings using at least two key mechanisms: self-attention and positional encoding. Self-attention allows the model to weigh the importance of different words in a sentence and capture the relationships between them. Positional encoding is a way to provide information about the positions or order of words or tokens in a sequence by summing the embedding of each word into a positional encoding vector that, as its name suggests, encodes its position within the sequence, often relying on the sine and

cosine functions. The embeddings obtained with transformer architectures in models such as BERT or GPT (for text generations) have exceeded benchmark performances in every aspect of NLP, including tasks like machine translation, sentiment analysis, named entity recognition, and question answering. Many pre-trained models are available in the literature, and models such as SBERT have been developed to generate embeddings for whole sentences or texts, relying on a special Siamese network architecture that has proven computationally faster and more agile than previous approaches [24].

These pre-trained models can be easily applied to datasets of abstracts from the literature, as a more accurate representation of the meaning of an abstract could potentially lead to better and more precise identification of similarities between published literature and a desired query, thus reducing the need for manual screening and making literature searches faster. The purpose of the current work is to retrospectively compare the performance of four freely available pre-trained models to identify a group of target papers in a dataset that was used for a previously published systematic review in implant dentistry.

## 2. Materials and Methods

### 2.1. Dataset

The generation of the dataset was conducted during a previously published systematic review by Donos et al. [25], and it has been described elsewhere. The purpose of the review was to identify Randomized Controlled Trials, Controlled Clinical Trials, and Prospective Case Series that addressed two Focused Questions (FQs):

**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, 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 ( $\geq 12$  months) performance of reconstructive therapies in terms of pocket reduction and change in BOP/SOP?*

We chose this dataset because this corpus of articles had already been screened manually and 24 articles of interest (query target, QT) had already been identified for the systematic review, and we could use them as a measure of effectiveness for our investigation (Tables 1 and 2). The QT corpus comprised two subsets, namely the articles that addressed FQ1 (Table 1) and the articles that addressed FQ2 (Table 2).

**Table 1.** List of the target articles that meet FQ1 requirements, identified by manual search.

ID	Authors	Title	Ref.
1	Andersen H., Aass AM. and Wohlfahrt, JC.	Porous titanium granules in the treatment of peri-implant osseous defects—a 7-year follow-up study	[26]
2	Jepsen K., Jepsen S., Laine, M. L., Anssari Moin D., Pilloni A., Zeza B., Sanz M., Ortiz-Vigon A., Roos-Jansaker AM., and Renvert S.	Reconstruction of Peri-implant Osseous Defects: A Multicenter Randomized Trial	[27]
3	Wohlfahrt JC., Lyngstadaas SP., Ronold HJ., Saxegaard EE., Jan Eirik KS., and Aass AM.	Porous titanium granules in the surgical treatment of peri-implant osseous defects: a randomized clinical trial	[28]
4	Emanuel N., Machtei EE., Reichart M., and Shapira, L.	D-PLEX500: a local biodegradable prolonged release doxycycline-formulated bone graft for the treatment for peri-implantitis. A randomized controlled clinical study	[29]
5	Renvert S., Giovannoli JL., Roos-Jansaker AM., and 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	[30]
6	Ished C., Holmlun, 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	[31]
7	Ished 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	[32]

**Table 1.** *Cont.*

ID	Authors	Title	Ref.
8	Renvert S., Roos-Jansaker AM., and Persson GR.	Surgical treatment of peri-implantitis lesions with or without the use of a bone substitute—a randomized clinical trial	[33]
9	Nct	Peri-implantitis-Reconstructive Surgical Therapy	[34]

**Table 2.** List of the target articles that meet FQ2 requirements, identified by manual search.

ID	Authors	Title	Ref.
1	Froum SJ., Froum SH., and Rosen PS.	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	[35]
2	Gonzalez Regueiro I., Martinez Rodriguez N., Barona Dorado C., Sanz-Sanchez I., Montero E., Ata-Ali J., Duarte F., and Martinez-Gonzalez JM.	Surgical approach combining implantoplasty and reconstructive therapy with locally delivered antibiotic in the treatment of peri-implantitis: A prospective clinical case series	[36]
3	Isler SC., 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	[37]
4	La Monaca G., Pranno N., Annibali S., Cristalli MP., and Polimeni A.	Clinical and radiographic outcomes of a surgical reconstructive approach in the treatment of peri-implantitis lesions: A 5-year prospective case series	[38]
5	Mercado F., Hamlet S., and 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	[39]
6	Polymeri A., Anssari-Moin D., van der Horst J., Wismeijer D., Laine ML., and Loos BG.	Surgical treatment of peri-implantitis defects with two different xenograft granules: A randomized clinical pilot study	[40]
7	Roccuzzo M., Gaudio L., Lungo M., and Dalmaso P.	Surgical therapy of single peri-implantitis intrabony defects, by means of deproteinized bovine bone mineral with 10% collagen	[41]
8	Roccuzzo M., Mirra D., Pittoni D., Ramieri G., and Roccuzzo A.	Reconstructive treatment of peri-implantitis infrabony defects of various configurations: 5-year survival and success	[42]
9	Isrctn	Reconstructive surgical therapy of peri-implantitis bone defects	[43]
10	Aghazadeh A., Persson RG., 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	[44]
11	Aghazadeh A., Persson, RG., and Renvert S.	Impact of bone defect morphology on the outcome of reconstructive treatment of peri-implantitis	[45]
12	Nct	Evaluation of Photodynamic Therapy in Treatment of Peri-implantitis	[46]
13	Roos-Jansaker AM., Renvert H., Lindahl C., and Renvert S.	Submerged healing following surgical treatment of peri-implantitis: a case series	[47]
14	Roos-Jansaker AM., Lindahl C., Persson RG., and Renvert S.	Long-term stability of surgical bone regenerative procedures of peri-implantitis lesions in a prospective case-control study over 3 years	[48]
15	Roos-Jansaker AM., Persson RG., Lindahl C., and Renvert S.	Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up	[49]

Briefly, to identify relevant articles, Donos et al. implemented a search strategy using terms related to peri-implantitis. Three major databases were included in the search: MEDLINE via OVID, EMBASE, and The Cochrane Database (including CENTRAL), and the search was updated until 10 April 2022. The result of the search consisted of 6277 records that were saved as a .csv file. The abstracts for these articles can be found as Appendix A.

## 2.2. Data Pre-Processing

Data were pre-processed and analyzed using both Jupyter notebooks version 6.5.2 [50] in the Anaconda distribution running Python 3.10.10 on a local laptop computer [51] and, in parallel, remotely using the Google Colab Pro cloud-based development environment, accelerated with the NVIDIA T4 Tensor Core GPU. The corpus was pre-processed by re-

moving numbers and lowercasing all titles; stopwords, however, i.e., common grammatical words that are semantically empty [52], were not removed, to maximize the capability of transformers to create contextual embeddings. Records without an abstract ( $n = 167$ ) were removed. The final corpus contained 6110 articles. Data plotting was conducted using the Matplotlib [53] and Seaborn libraries [54].

### 2.3. Models

Four pre-trained sentence-transformer models were used to generate sentence embeddings. All models were freely available on Huggingface.com.

- (1) sentence-transformers/all-MiniLM-L6-v2. This model is based on the nreimers/MiniLM-L6-H384-uncased model and was further fine-tuned using a dataset of 1 billion sentence pairs. The embeddings' length is 384. (<https://huggingface.co/sentence-transformers/all-MiniLM-L6-v2> (accessed on 15 January 2024))
- (2) sentence-transformers/all-MiniLM-L12-v2. This model is based on the microsoft/MiniLM-L12-H384-uncased model and was further fine-tuned using a dataset of 1 billion sentence pairs. The embeddings' length is 384. (<https://huggingface.co/sentence-transformers/all-MiniLM-L12-v2> (accessed on 15 January 2024))
- (3) sentence-transformers/all-mpnet-base-v2. The model underwent pretraining on the microsoft/mpnet-base model and was subsequently fine-tuned on a dataset consisting of 1 billion sentence pairs. The embeddings' length is 768. (<https://huggingface.co/sentence-transformers/all-mpnet-base-v2> (accessed on 15 January 2024))
- (4) sentence-transformers/all-distilroberta-v1. The model underwent pretraining on the distilroberta-base model and was subsequently fine-tuned on a dataset consisting of 1 billion sentence pairs. The embeddings' length is 768. (<https://huggingface.co/sentence-transformers/all-distilroberta-v1> (accessed on 15 January 2024))

### 2.4. Sentence Encoding

The usage of a pre-trained model (model\_name in our example) for sentence transformers is straightforward, thanks to the SentenceTransformer library, and follows the general scheme:

```
from sentence_transformers import SentenceTransformer
    model = SentenceTransformer(model_name)
    embeddings = model.encode(sentences)
```

where 'sentences' is the text to encode, the abstracts in our case. We imported the .csv corpus as a pandas Dataframe, with the following structure:

Column name	
authors	6089 non-null object
title	6109 non-null object
journal	6106 non-null object
abstract	6110 non-null object
year	6110 non-null int64
volume	5623 non-null object
issue	4984 non-null float64
pages	5426 non-null object

The 'abstract' column was pre-processed as described, and the encoding method was run iteratively on it to generate sentence embeddings for every abstract and each model.

### 2.5. Semantic Text Similarity and Semantic Search

To calculate the semantic similarity across embeddings generated by the Sentence transformer model, cosine similarity was employed. This similarity metric measures the cosine of the angle between two vectors (regardless of their dimensionality), indicating

how similar or related they are in terms of their meaning. To calculate cosine similarity on our dataset, the ‘util’ tool was used. The general usage of this library is as follows:

```
from sentence_transformers import util

util.cos_sim(embedding1, embedding2)
```

Similarity was calculated both across the QT corpus (constituted by the 24 target articles only) and between each of the FQs and the whole corpus of 6110 abstracts.

### 3. Results

#### 3.1. Sentence Encoding

Sentence encoding proceeded seamlessly, but the computing time varied according to the model used. The computer we employed for this experiment was a mid-tier commercial laptop, as could be used by a scholar for a systematic review, and it was equipped with Intel(R) Core (TM) i5-10210U CPU 1.60 GHz processor and 16 Gb RAM, without dedicated GPU and running Windows 10.

This configuration took approximately 3 to 6 s to calculate the embeddings for the abstracts of the corpus when using the all-MiniLM-L6-v2 model (depending on the abstract’s length), about 4 to 7 s when using the all-MiniLM-L12-v2 model, and up to about 30–50 s when using the all-mpnet-base-v2 model, whose embeddings are twice as long as the ones of the first two models. This makes the total computational time considerably longer for a corpus of 6110 references and scarcely manageable, with several hours to days of computer work necessary to encode it all. The same procedure was repeated using the free online tool Google Colab, a cloud-based Jupyter notebook environment, which offers the choice of running code on CPU or T4 GPU architectures, and this considerably reduced runtime (Table 3).

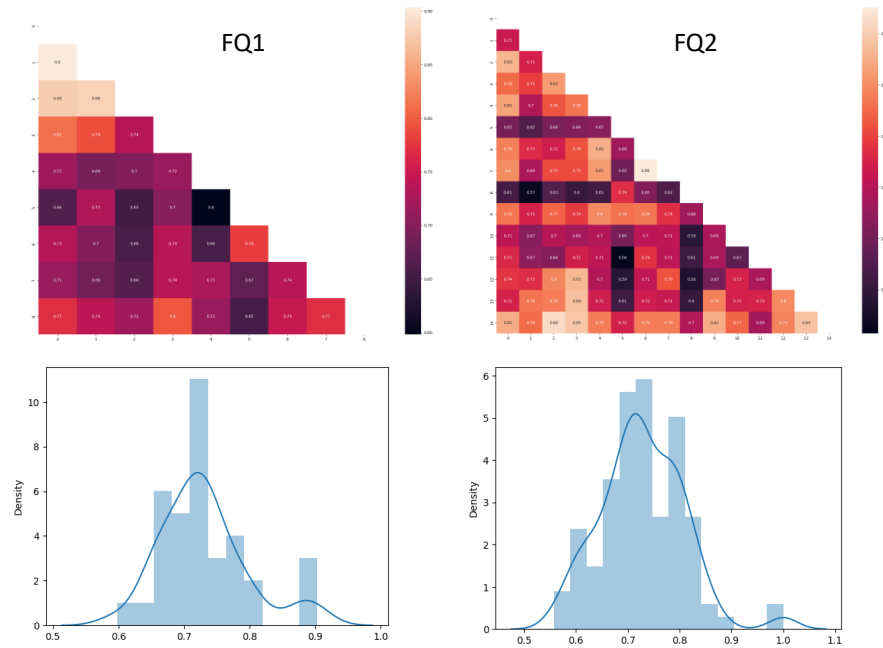
**Table 3.** Processing time for sentence encoding using different models.

	all-MiniLM-L6-v2	all-MiniLM-L12-v2	all-Mpnet-Base-v2	all-Distilroberta-v1
Local computer (no GPU)	3–6	4–7	30–50	16–30
Cloud environment (CPU)	0.16	0.12	1.4	0.75
Cloud environment (GPU)	0.01	0.02	0.03	0.02

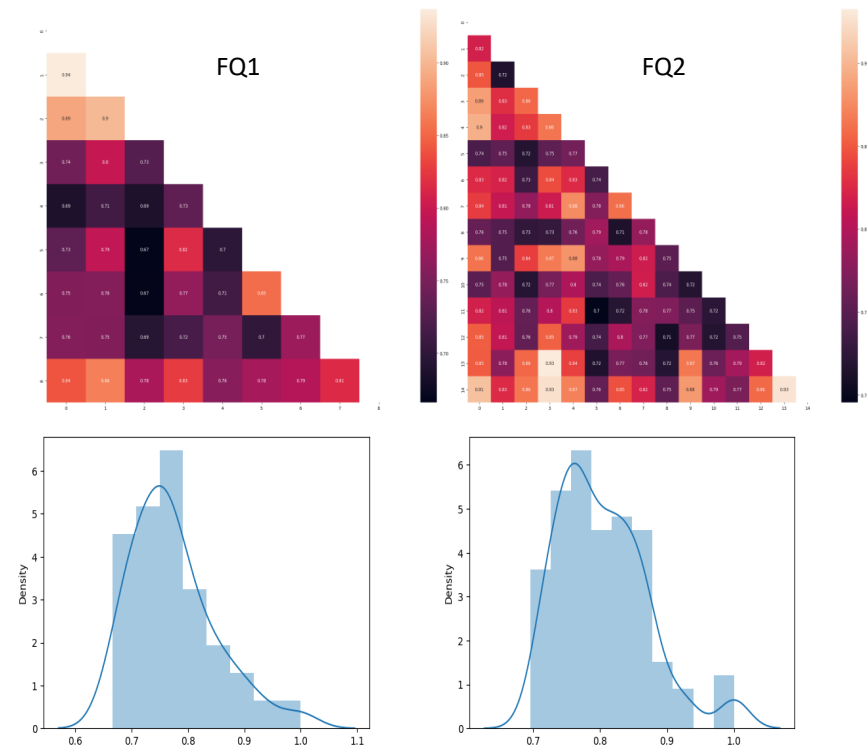
#### 3.2. Semantic Text Similarity in the QT Corpus

Figure 1 shows the cosine similarity for the abstracts that belong to the QT corpus after encoding with the smaller all-MiniLM-L6-v2 pre-trained model. The similarity matrix ranges from 0.59 to 0.9, with a mean of 0.73 (and median of 0.72) for the FQ1 subset, and ranges from 0.55 to 0.99, with a mean of 0.73 (and median of 0.72) for the FQ2 subset. The distribution of the similarity values is close to normality for both subsets (Figure 1, bottom), with skewness of 0.8 and 0.45, respectively. Figure 2 reports the cosine similarity for the abstracts of the two subsets of the QT corpus after encoding with the all-MiniLM-L12-v2 pre-trained model. The similarity score ranges from 0.60 to 0.99, with a mean of 0.71 and median of 0.69 for the FQ1 subset, and ranges from 0.55 to 0.99, with a mean of 0.74 and median of 0.74 for the FQ2 subset. The distribution of the cosine similarity values for the embeddings obtained with the all-MiniLM-L12-v2 model approximates a normal distribution for the FQ2 subset (skewness = 0.17) and is slightly right-skewed for the FQ1 subset (skewness = 1.17). Figure 3 reports the cosine similarity for the abstracts of the two subsets of the QT corpus, after encoding with the larger all-mpnet-base-v2 pre-trained model. The similarity score ranges from 0.66 to 0.99, with a mean of 0.77 and median of 0.75 for the FQ1 subset, and ranges from 0.69 to 0.99, with a mean of 0.80 and median of 0.79 for the FQ2 subset. Overall, the cosine similarity of the embeddings obtained with the all-mpnet-base-v2 model approximates a normal distribution, though slightly right-skewed

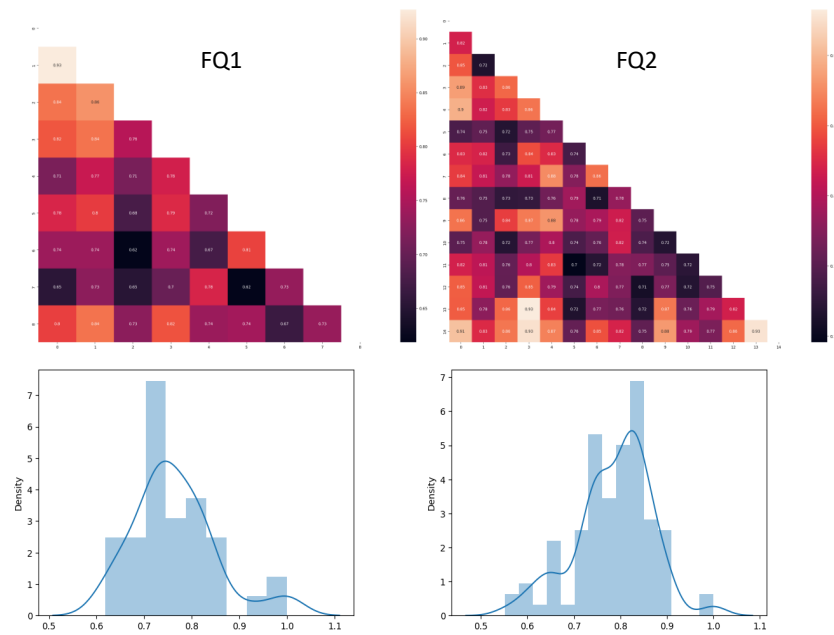
(skewness of 0.98 and 0.90, respectively), and is significantly higher than that obtained with the embeddings from the all-MiniLM-L6-v2 model.



**Figure 1.** **Top:** Cosine similarity matrix for the embeddings of the 9 FQ1 target articles and the 15 FQ2 target articles from the QT corpus generated with the all-MiniLM-L6-v2 model. **Bottom:** Distribution of the cosine similarities between the embeddings of the 9 FQ1 and the 15 FQ2 target articles, respectively.

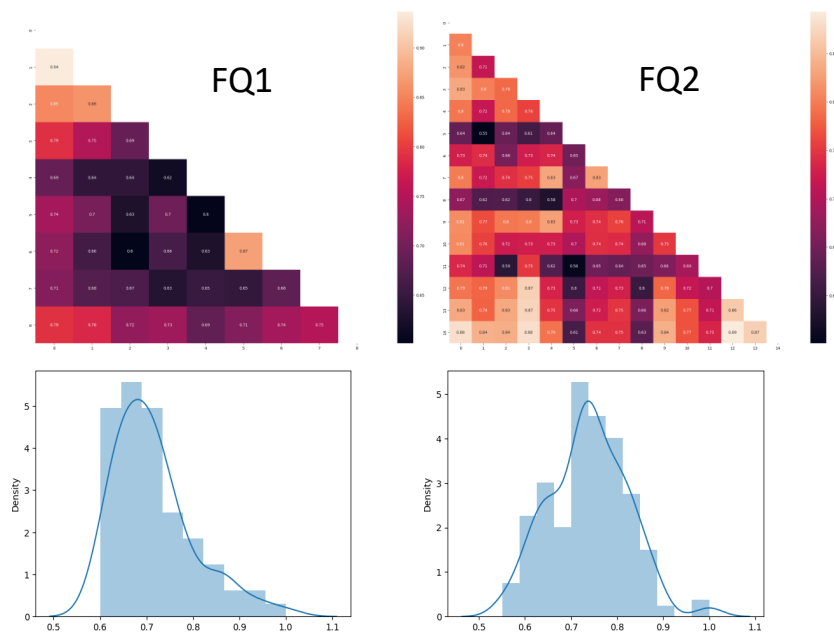


**Figure 2.** **Top:** Cosine similarity matrix for the embeddings of the 9 FQ1 target articles and the 15 FQ2 target articles from the QT corpus generated with the all-MiniLM-L12-v2 model. **Bottom:** Distribution of the cosine similarities between the embeddings of the 9 FQ1 and the 15 FQ2 target articles, respectively.



**Figure 3.** Top: Cosine similarity matrix for the embeddings of the 9 FQ1 target articles and the 15 FQ2 target articles from the QT corpus generated with the all-mpnet-base-v2 model. Bottom: Distribution of the cosine similarities between the embeddings of the 9 FQ1 and the 15 FQ2 target articles, respectively.

Figure 4 shows the cosine similarity for the abstracts of the two subsets of the QT corpus after encoding with the all-distilroberta-v1 model. This similarity matrix ranges from 0.62 to 0.99, with a mean of 0.76 (and median 0.74) for the FQ1 subset and ranges from 0.55 to 0.99, with a mean of 0.78 (and median 0.80) for the FQ2 subset; the similarity values for the QT abstracts are visibly (and significantly) higher with the models “all-mpnet-base-v2” and “all-distilroberta-v1” than with the previous two models. The skewness of the distribution is 0.86 for the FQ1 subset and 0.44 for the FQ2 subset.

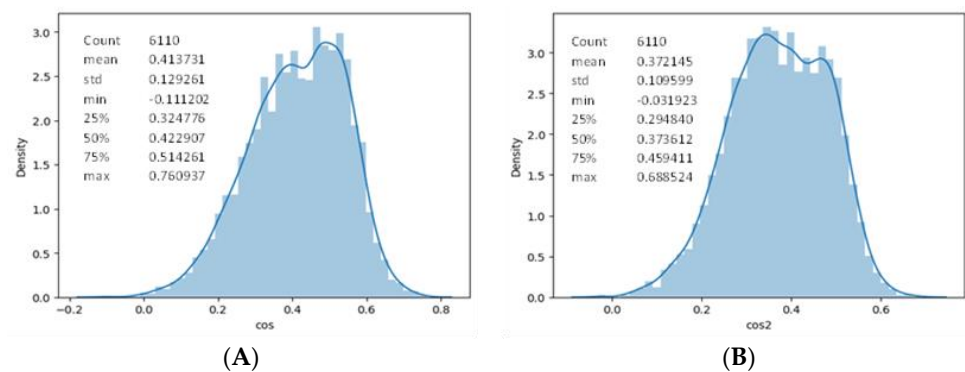


**Figure 4.** Top: Cosine similarity matrix for the embeddings of the 9 FQ1 target articles and the 15 FQ2 target articles from the QT corpus generated with the all-distilroberta-v1 model. Bottom: Distribution of the cosine similarities between the embeddings of the 9 FQ1 and the 15 FQ2 target articles, respectively.

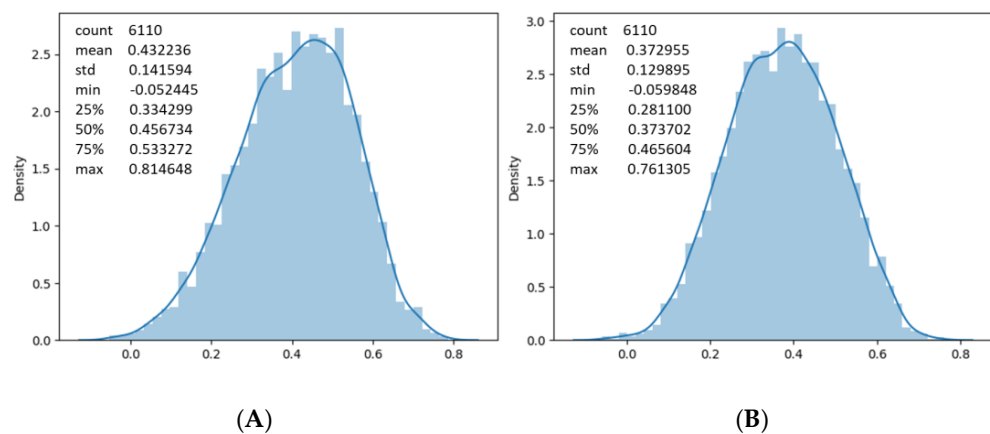


### 3.3. Semantic Text Similarity of the Whole Dataset to FQs

We then proceeded to encode FQ1 and FQ2 using the four models and computed the cosine similarity of these two queries with the whole corpus of 6110 abstracts. Figure 5 reports the distribution of the similarity score for (A) FQ1 and (B) FQ2 vs. the whole corpus, using the all-MiniLM-L6-v2 model. Overall, though both distributions are roughly normal, the abstracts of the corpus appear to have a higher similarity to FQ1 than to FQ2 (mean 0.41 vs. 0.37). Unsurprisingly, the range of similarities is wider than among the QT corpus, as the whole corpus is expected to include very diverse research papers, which may be only marginally related to the focused questions. Figure 6 reports the distribution of the similarity score for (A) FQ1 and (B) FQ2 vs. the whole corpus, using the all-MiniLM-L12-v2 model. Overall, though both distributions are roughly normal, the cosine similarity values of the abstracts of the corpus to FQ1 are higher than those to FQ2 (mean 0.41 vs. 0.37).



**Figure 5.** (A) Distribution of cosine similarity of the articles of the whole dataset to FQ1 using the all-MiniLM-L6-v2 model. (B) Distribution of cosine similarity of the articles of the whole dataset to FQ2 using the all-MiniLM-L6-v2 model.

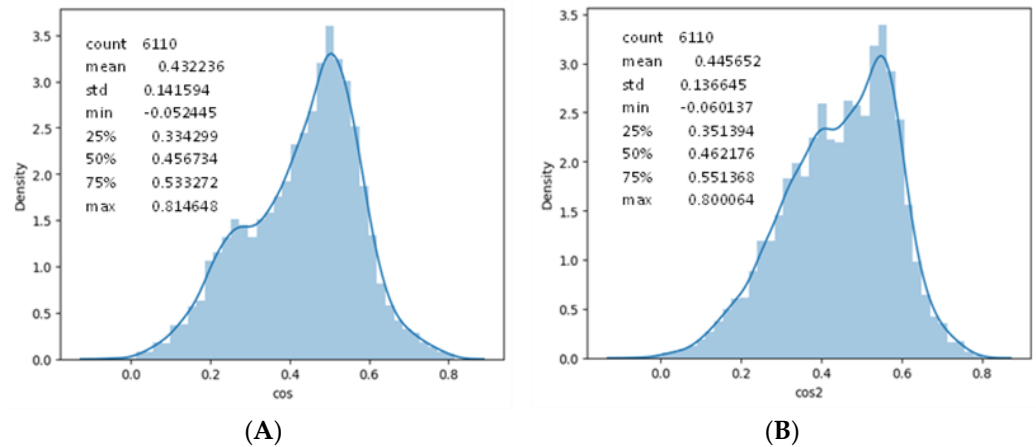


**Figure 6.** (A) Distribution of cosine similarity of the articles of the whole dataset to FQ1 using the all-MiniLM-L12-v2 model. (B) Distribution of cosine similarity of the articles of the whole dataset to FQ2 using the all-MiniLM-L12-v2 model.

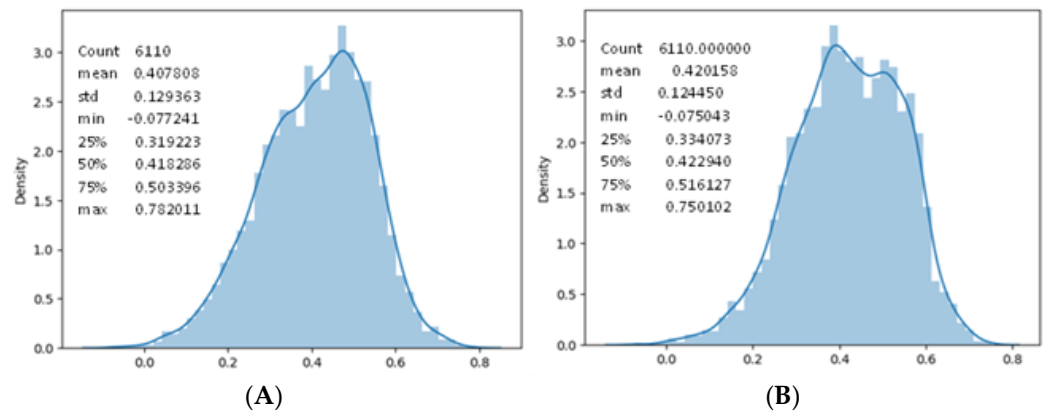
Figure 7 represents the distribution of the similarity score for (A) FQ1 and (B) FQ2 vs. the whole corpus, using the all-mpnet-base-v2 model. The distribution is left-skewed for both (A) FQ1 and (B) FQ2 vs. the total corpus. When compared to the first model, the similarity score is higher, with a mean of 0.43 for FQ1 (vs. 0.41 with all-MiniLM-L6-v2) and 0.44 for FQ2 (vs. 0.37), though the standard deviation is also slightly higher. This latter distribution appears to have lower kurtosis, which can be envisaged as a pointier peak and slimmer tails than the former model.

Figure 8 shows the distribution of the similarity score for (A) FQ1 and (B) FQ2 vs. the whole corpus, using the all-distilroberta-v1 model. The distribution is approximately

normal and differs slightly from the preceding models because its mean (0.40 and 0.42) and its standard deviation are about the same (around 0.12 for both focused questions). To better understand how effective these models were in identifying our articles of interest, we ordered all the abstracts by cosine similarity, from those with the highest similarity to the lowest, and plotted the rank of the articles of interest. Ideally, the abstracts of the QT corpus should rank in the top positions.



**Figure 7.** (A) Distribution of cosine similarity of the articles of the whole dataset to FQ1 using the all-mpnet-base-v2 model. (B) Distribution of cosine similarity of the articles of the whole dataset to FQ2 using the all-mpnet-base-v2 model.

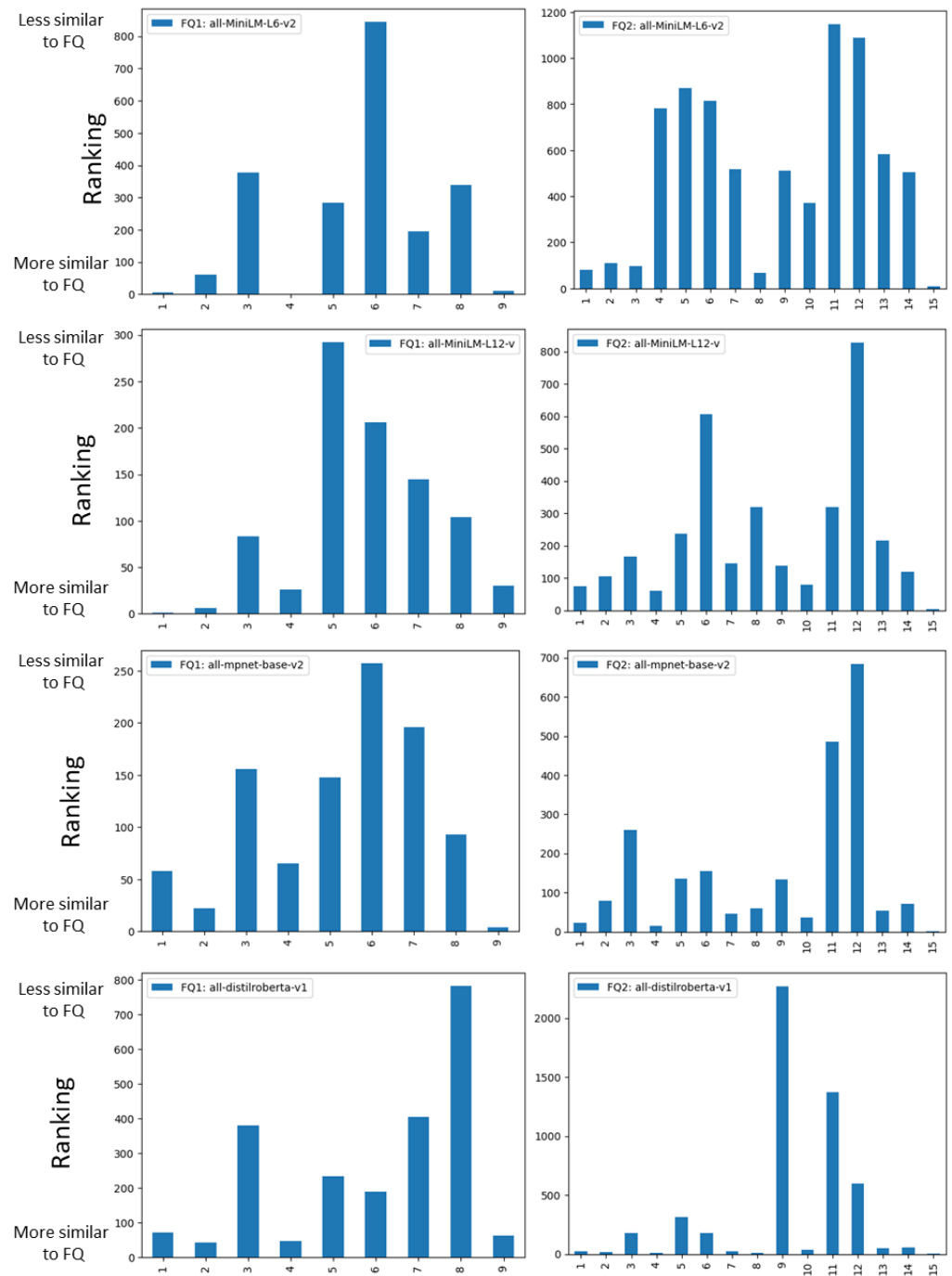


**Figure 8.** (A) Distribution of cosine similarity of the articles of the whole dataset to FQ1 using the all-distilroberta-v1 model. (B) Distribution of cosine similarity of the articles of the whole dataset to FQ2 using the all-distilroberta-v1 model.

### 3.4. Semantic Query

Figure 9 shows the rank of the target articles from the two subsets when ordered by semantic similarity to FQ1 (left column) or FQ2 (right column). When the all-MiniLM-L6-v2 model is used (Figure 9, first row) and the corpus is searched using FQ1, all target articles to FQ1 are contained in the top 844 papers, although the median rank is 128. Overall, FQ2 performs more poorly, as the median rank of the FQ2 target papers is 507, and they are all to be found in the top 1149 articles out of the total corpus. When the all-MiniLM-L12-v2 model is used (Figure 9, second row), the FQ1 target articles are contained in the first 292 papers, and the median rank is 56. Again, FQ2 tends to perform worse than FQ1, as the median rank of the QT papers is 140, though they are all to be found in the top 829 articles out of the overall corpus. When the all-mpnet-base-v2 model is used (Figure 9, third row), all the articles of the FQ1 corpus are contained in the first 257 papers, although the median rank is 79. FQ2 tends to perform slightly worse than FQ1, as the median rank of

the QT papers is 73, though they are all to be found in the top 685 articles out of the overall corpus. When the All-distilroberta-v1 model is used (Figure 9, bottom row), the results are consistent but not better than with the previous models. All the articles of interest to FQ1 are contained in the top 781 papers, with a median of 130. FQ2 tended to perform similarly to FQ1, with a median rank for the FQ2 papers of 43, but they were all to be found in the top 2271 articles out of the overall corpus.



**Figure 9.** Ranking of the target articles by similarities to FQ1 (left column) or FQ2 (right column) using the all-MiniLM-L6-v2 model, the all-MiniLM-L12-v2 model, the all-mpnet-base-v2 model, or the all-distilroberta-v1 model. Lower values indicate a higher ranking once all the 6110 are ordered by similarity, i.e., the lower the value, the more similar the article is to the FQ.

#### 4. Discussion

Transformers have emerged as a groundbreaking tool in the field of NLP, revolutionizing the ability to develop algorithms that can comprehend and generate natural language, surpassing previous benchmark performances [55]. The considerable power of transformers enables them to build effective commercial products capable of sifting through scientific literature and autonomously extracting valuable knowledge and information [56,57]. This holds tremendous value, particularly in Life Sciences, where the vast volume of publications frequently exceeds an individual's capacity or necessitates a team of experts investing significant time combing through databases for relevant insights [3]. Finding the papers of interest, discarding the background information noise, extracting useful information, and summarizing it are all steps that might soon be demanded by Artificial Intelligence [58,59]. To do that, however, it is necessary for users to improve their digital proficiency and know the strengths and limits of the models they are using.

Transformers can generate word and sentence embeddings in a highly efficient manner by incorporating contextual information, which enriches their content and subsequently improves their performance [55]. These embeddings capture the underlying semantic information of sentences, allowing for accurate comparison and similarity calculations. Additionally, transformers can be trained on extensive textual datasets, with pre-trained models readily available online to researchers and developers.

The objective of this report was to assess the effectiveness of four transformer models, particularly Sentence Transformers [24], in extracting and comparing semantic similarities between abstracts to assist scholars in selecting articles for systematic reviews. To do that, we retrospectively used data from a previously published systematic review, where clinical studies were identified that could help answer two focused questions, which were labeled as FQ1 and FQ2. The investigators who performed the systematic review had to manually scan a corpus of more than 6000 articles and extract 24 reports, mostly RCTs, that addressed the FQs; more specifically, 9 studies addressed FQ1 and 15 studies addressed FQ2. Therefore, besides possessing the whole dataset, we also had the desired corpus of documents that we wanted to identify, and this allowed us to easily evaluate the performance of our system.

Ideally, instead of going through all the 6110 articles one by one, it would have been preferable to possess an algorithm that could select those 24 articles automatically, or at least to identify a smaller subset of papers where these articles were more likely to be contained, which could relieve part of the scholars' burden. This latter task can be defined as a semantic search task, i.e., given a document, in this case, the FQs, we wanted to find the closest articles in the whole corpus. To assess the similarity between the two documents, cosine similarity was employed as a metric [60]. Abstracts were chosen among other features, e.g., instead of titles, because they contained the highest amount of information, although we knew that their length could significantly slow down computing. We then decided to use four models, choosing them from those freely available in the Huggingface repository. Two models (all-MiniLM-L6-v2 and all-MiniLM-L12-v2) were smaller and encoded 384-long embeddings, which translates into a faster deployment. The other two models, by contrast (all-mpnet-base-v2 and all-distilroberta-v1) encoded longer, 768-dimensional embeddings. Longer embeddings have the potential to contain richer and more nuanced semantic representations and could therefore perform better, though their computation speed is obviously slower. Huggingface reports an encoding speed of 14,200 sentences/s for the all-MiniLM-L6-v2 model, 7500 sentences/s for the all-MiniLM-L12-v2 model, and 2800 sentences/s for the larger all-mpnet-base-v2. Noticeably, these speed measurements were recorded on computers equipped with NVIDIA Tesla V100 GPUs, which are among the best-performing GPUs on the current market and remarkably faster than all the systems we decided to employ to try and recreate standard working conditions of a scholar in the Life Science area. All these four models had been trained with very large corpora of various origins. The deployment of these models was made very simple by the SentenceTransformer library, which required a few command-line

commands to start encoding and very little coding knowledge to be used. In addition, no specific software was required; besides, at the very minimum, the (freely available) Python interpreter of choice, or, alternatively, a cloud-based development environment [61], the abstract text was also minimally pre-processed. Numbers were removed, and the text was lower-cased, to make words more homogeneous, but no word was removed, including stopwords, i.e., very frequent words that have a purely grammatical or functional meaning (e.g., the conjunction 'and' or articles such as 'the') and are not usually considered to contain the 'gist' of the sentence [62]. Guidelines for older algorithms recommend removing stopwords to improve the creation of embeddings [63], but transformers do not need stopwords to be removed. Their inner working relies on all the lexical elements of the sentence to get context information, and more recent approaches leave stopwords untouched [64,65].

By using sentence transformers, we were able to encode all the abstracts in the dataset, calculate the cosine similarity of the embeddings of these abstracts to the embeddings of the focused questions, and sort the most similar documents. We first compared the similarity between the 24 abstracts that constituted our target, which we called the Query Target corpus, differentiating between those articles that addressed FQ1 and those that addressed FQ2. We expected that a well-performing model could be able to understand that the articles of these two QT subcorpora were somehow related because they all concerned common topics that corresponded to FQ1 and FQ2 and we, therefore, expected a good model to yield high similarity scores in the QT corpus. In this regard, the all-mpnet-base-v2 and all-distilroberta-v1 models performed the best because their mean similarity was 0.77 for FQ1, 0.8 for FQ2, and 0.76 for FQ1 and 0.78 for FQ2, respectively (Figures 3 and 4), higher than with any other model we tested.

If we review our data, we notice that we generated interesting results even just using the faster all-MiniLM-L6-v2 model to encode the corpus and the FQs. If we had sorted all the 6110 abstracts of the corpus based on their semantic similarity to FQ1 and FQ2 and had decided to limit our manual search to the top 1000 articles (e.g., to save time instead of manually examining over 6000 abstracts), by using FQ1 as a query, we would have identified all the 9 FQ1 target articles, and using FQ2 as a query, we would have missed only 2 papers out of the 15 FQ2 target articles. If we had decided to use the all-MiniLM-L12-v2, which was about as fast as the previous one, and had limited our manual search to the top 1000 papers, this time we would not have missed any article of interest, either with FQ1 or FQ2. The semantic search for this model was so good that we could have limited our manual search to the top 800 papers, further restricting the number of articles that we would have had to go through, and we would have still been able to find all the FQ1 target papers while missing only 1 FQ2 target paper, using FQ1 and FQ2, respectively. Furthermore, if we only focused on the FQ1 target papers, the top 300 papers of the corpus would have been enough to identify them, which would have meant a significant saving in hands-on time for the reviewers. Using the larger, more massive (and slower) all-mpnet-base-v2 model yielded similarly good results. To identify all the FQ1 target articles, it would be enough to limit our search to the top 300 articles, while the top 700 articles would be enough to locate the FQ2 target articles (using their respective FQs as a query). Interestingly, if we search by FQ1, all the 24 articles of interest are in the top 400 papers (see Figure A1 in Appendix B), which means that FQ1 is closer to all the 24 QT articles, not only its own 9 target papers but also the 15 FQ2 target articles, and this raises a significant issue, i.e., the importance of the formulation of the Focused Questions.

Focused Questions are commonly generated according to established criteria, such as PICO, to contain the relevant terms that will be used for database searches. Usually, these relevant terms, or keywords, are extracted from the PICO query, isolated, and combined with Boolean operators to create complex search strategies to feed into the search engine of the database [66]. This is not necessarily the case with semantic searches using sentence transformers, because they do not rely just on the presence of keywords in the sentences,

and future research should address the need to implement a new set of recommendations for queries to optimize semantic searches and improve cosine similarities with abstracts.

Another important issue is the choice of threshold to use. We mentioned how different models would allow us to limit our search to the top  $n$  fraction of articles out of the total corpus. We were able to state that because we knew our QT articles in advance, as per the design of our study. Under normal conditions, however, we would have the whole corpus we retrieved from the usual databases, and we would have the appropriate FQs, but we would not know how many target articles are present in the corpus and where they are, and it would be difficult to decide where to stop our search. We could, e.g., arbitrarily decide to limit our manual search to the top 1000 papers, which could be a reasonable number of articles to screen manually, but that would really go against most guidelines for systematic reviews, which have always stressed, among others, the need to expand the search range, include grey literature, and perform hand-searching of relevant literature and conference abstracts [67], and we could hardly justify such an arbitrary choice, which could likely lead to the loss of otherwise easily identifiable articles, just for the sake of time-saving! A preferable approach would be to have Artificial Intelligence segment the corpus in some way and identify subsets of articles that better match our FQs and can therefore contain our target. This procedure is commonly known in machine learning as clustering, and several algorithms are available to tackle this problem, both following supervised and unsupervised approaches [68]. Thus, another equally important line of research in the near future will be comparing the performance of clustering protocols to get the system to automatically identify a sensible proposal to limit our manual search based on the cosine similarities of the dataset to the available FQs.

The data we have so far indicates that sentence transformers are a viable approach that meets the requirements of scholars who desire to streamline their processing of literature searches. Unsurprisingly, the all-mpnet-base-v2 model emerges as the best-performing pre-trained model among those tested, and if faster computer set-ups are available, our data indicate that this model is preferable over the alternatives we have compared. However, its performance is only marginally better than that of faster models, such as all-MiniLM-L12-v2, which can encode sentences in about 1/10th of the time necessary to all-mpnet-base-v2, and this kind of performance can be of great advantage with corpora that contain tens of thousands of articles. Adopting this kind of model in the routine workflow could lead to abandoning one of the mainstays of literature searches for systematic reviews, i.e., defining complex search strategies to filter out undesired papers and avoid overinflating the burden for the reviewers, as already proposed by Hamel et al. [69]. A somewhat comforting-for-reviewers scenario could be envisaged, where a generic, broad, and wide-encompassing literature search is performed on the appropriate databases, which could retrieve dozens, if not hundreds, of thousands of articles with no need to restrict the search to a few thousand items to keep it manageable, and the whole burden of scanning it would be left to a semantic search algorithm, possibly combining it with keyword search to enhance results. Using both search methods, i.e., semantic searches and keyword-based searches, could enhance the search accuracy and precision, and thus its reliability, and future research will have to explore the possible synergy between these two search approaches. An even better scenario could be to be able to perform the database search using semantic search in the first place, as it is better equipped than keyword searches to find articles of interest, but that would require possessing embeddings for millions of items, which is still a lengthy procedure and still unfeasible until a consensus is reached on which model to use (which might not even happen at all, considering that models are continuously evolving), or until our computing capabilities have progressed to such an extent to make the encoding of a whole database so quick that it can be reasonably performed at the click of a button by the final users when doing their search.

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

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## Appendix A

### FQ1 target articles

#### Porous titanium granules in the treatment of peri-implant osseous defects—a 7-year follow-up study

Andersen, Heidi, Aass, Anne Merete and Wohlfahrt, Johan Caspar

**BACKGROUND:** A great number of different treatment protocols for peri-implantitis have been suggested but there is no consensus regarding the most effective intervention. The aim of the present study was to evaluate the long-term clinical and radiographic results from a study on peri-implant osseous defect reconstruction. Patients having participated in a randomized clinical study 7 years earlier were invited for a re-examination. The treatment procedures included open flap debridement (OFD) with or without defect reconstruction with porous titanium granules (PTGs). Clinical parameters (probing pocket depth and bleeding on probing) and radiographic measurements were registered. **FINDINGS:** Of the original 32 patients, 12 patients with 12 implants were finally examined after 7 years (7.3 years [6.7–8]). Patients had been maintained one to two times yearly. The PTG group showed a mean probing pocket depth of 4.3 mm  $\pm$  2.4 compared with 3.5 mm  $\pm$  1.2 in the OFD group, at the deepest site. The change between the 12 months and the 7-year examination was similar in both groups. Five of the test implants and five of the control implants had at least one site with positive bleeding on probing score. The mean radiographic defect depth change as compared to 12 months was an increase of 1.9 mm  $\pm$  2.0 in the PTG group and a mean radiographic defect depth increase of 1.3 mm  $\pm$  1.4 in the OFD group. Due to the small number of patients, a statistical analysis was not performed, but the results indicated a minimal difference in osseous defect depth as compared with baseline and between groups. No PTG exposed to the oral cavity was observed, but the graft particles were seemingly scattered in the peri-implant soft tissue. **CONCLUSIONS:** This long-term follow-up of surgical treatment of peri-implant osseous defects showed unpredictable results.

#### Reconstruction of Peri-implant Osseous Defects: A Multicenter Randomized Trial

Jepsen, K., Jepsen, S., Laine, M. L., Anssari Moin, D., Piloni, A., Zeza, B., Sanz, M., Ortiz-Vigon, A., Roos-Jansaker, A. M. and Renvert, S.

There is a paucity of data for the effectiveness of reconstructive procedures in the treatment of peri-implantitis. The objective of this study was to compare reconstruction of peri-implant osseous defects with open flap debridement (OFD) plus porous titanium granules (PTGs) compared with OFD alone. Sixty-three patients (36 female, 27 male; mean age 58.4 y [SD 12.3]), contributing one circumferential peri-implant intraosseous defect, were included in a multinational, multicenter randomized trial using a parallel-group design. After OFD and surface decontamination using titanium brushes and hydrogen peroxide, 33 defects received PTGs. The implants were not submerged. All patients received adjunctive perioperative systemic antibiotics. The primary outcome variable (defect fill) was assessed on digitalized radiographs. Clinical measurements of probing depth (PPD), bleeding on probing (BoP), suppuration, and plaque were taken by blinded

examiners. After 12 mo, the test group (OFD plus PTG) showed a mean radiographic defect fill (mesial/distal) of 3.6/3.6 mm compared with 1.1/1.0 in the control group (OFD). Differences were statistically significant in favor of the test group ( $P < 0.0001$ ). The OFD plus PTG group showed a mean reduction in PPD of 2.8 mm compared with 2.6 mm in the OFD group. BoP was reduced from 89.4% to 33.3% and from 85.8% to 40.4% for the test and control groups, respectively. There was no significant difference in complete resolution of peri-implantitis (PPD  $\leq 4$  mm and no BoP at six implant sites and no further bone loss), because this finding was accomplished at 30% of implants in the test group and 23% of implants in the control group. Reconstructive surgery using PTGs resulted in significantly enhanced radiographic defect fill compared with OFD. However, limitations in the lack of ability to discern biomaterial from osseous tissue could not be verified to determine new bone formation. Similar improvements according to clinical measures were obtained after both surgical treatment modalities (ClinicalTrials.gov NCT02406001). Copyright © International & American Associations for Dental Research 2015.

### **Porous titanium granules in the surgical treatment of peri-implant osseous defects: a randomized clinical trial**

Wohlfahrt, Johan Caspar, Lyngstadaas, Stale Petter, Ronold, Hans Jacob, Saxegaard, Erik, Ellingsen, Jan Eirik, Karlsson, Stig and Aass, Anne Merete

**PURPOSE:** Porous titanium granules (PTG) may have potential as an osteoconductive bone graft substitute to treat peri-implant osseous defects. The aim of this study was to analyze clinical and radiographic outcomes of peri-implant osseous defects after treatment with PTG., **MATERIALS AND METHODS:** This prospective, randomized, case-control, clinical 12-month study compared open-flap debridement and surface decontamination with titanium curettes and 24% ethylenediaminetetraacetic acid gel ( $n = 16$ ) to the same protocol but with the addition of PTG ( $n = 16$ ). One-, two-, and three-wall infrabony defects were included. Patients were given amoxicillin and metronidazole 3 days before surgery and for 7 days afterwards. Implants were submerged and allowed to heal for 6 months. Probing pocket depths, bleeding on probing, implant stability using resonance frequency analysis, and radiographic evaluation were performed at baseline and at 12 months. The threshold for significance was set at 0.05. **RESULTS:** Change in radiographic defect height and percent fill of the peri-implant osseous defect significantly favored patients treated with PTG. Both treatment modalities demonstrated significant improvements in probing pocket depth, but significant differences between groups were not observed. The PTG-treated implants showed an increase in implant stability quotient (ISQ) of 1.6 units, compared with a decrease of 0.7 ISQ for the control group. No adverse effects were associated with PTG treatment. **CONCLUSIONS:** Reconstruction with PTG resulted in significantly better radiographic peri-implant defect fill compared with controls; however, the results do not necessarily imply reosseointegration or osseointegration of PTG particles. Improvements in clinical parameters were seen in both groups, but no differences between groups were demonstrated.

### **D-PLEX500: a local biodegradable prolonged release doxycycline-formulated bone graft for the treatment for peri-implantitis. A randomized controlled clinical study**

Emanuel, Noam, Machtei, Eli E., Reichart, Malka and Shapira, Lior

**OBJECTIVES:** In the present pilot, multicenter, randomized, single-blinded, controlled study, surgical treatment with or without the administration of D-PLEX500 (a biodegradable prolonged release local doxycycline formulated with beta-tricalcium phosphate bone graft) was assessed for the treatment of peri-implantitis., **METHOD AND MATERIALS:** Subjects undergoing surgical treatment for intrabony peri-implantitis defects after flap elevation were randomly assigned, to adjunct D-PLEX500 placement group or to control group. Clinical and radiographic parameters were measured at 6 and 12 months., **RESULTS:** Twenty-seven subjects (average age: 64.81  $\pm$  7.61 years) were enrolled; 14 patients (18 implants) were randomized to the test group and 13 (14 implants) to the control group. There was no difference in plaque scores between the groups. There was no difference



in the changes of mean periodontal probing depth between the test and control groups between baseline and the 6-month follow-up, whereas statistically significant difference was observed after 12 months' follow-up when analyzed for all sites averaged. There was a statistically significant difference in the changes of clinical attachment levels and radiographic bone levels between the groups between baseline and 12 months. These improvements were demonstrated when analyzed at both implant and subject levels. Only D-PLEX500 treatment led to improved bone levels at both time points. The improvement in bone levels was significant in the D-PLEX500 treatment group already after 6 months, and further improved over the 12-month follow-up. Implants were lost only in the control group (14%). **CONCLUSIONS:** D-PLEX500 sustained release local antibiotic formulated with bone filler showed promising results in enabling healing of peri-implantitis lesions. The antibacterial component of the bone graft material might create favorable conditions that enable implant surface decontamination and soft and hard tissue healing over a prolonged period.

### **Surgical treatment of peri-implantitis with or without a deproteinized bovine bone mineral and a native bilayer collagen membrane: A randomized clinical trial**

Renvert, Stefan, Giovannoli, Jean-Louis, Roos-Jansaker, Ann-Marie and Rinke, Sven

**AIM:** To assess whether the use of deproteinized bovine bone mineral (DBBM) and native bilayer collagen membrane (NBCM) improved healing of peri-implantitis-related bone defects at 12 months., **MATERIALS AND METHODS:** In a multi-centre, randomized clinical trial, 32 individuals received surgical debridement (control group [CG]), and 34 received adjunct use of DBBM and NBCM (test group [TG]). Radiographic defect fill (RDF), probing pocket depth (PPD), bleeding on probing (BOP), suppuration (SUP), recession (REC), cytokines (IL-1beta, IL-1RA, IL-6, IL-8, IL-12, IP10, PDGF-BB, TNF-alpha, VEGF), and patient-reported outcomes (PROs) were evaluated at 3, 6, 9, and 12 months., **RESULTS:** RDF at the deepest site amounted 2.7 +/- 1.3 mm in TG and 1.4 +/- 1.2 mm in CG ( $p < 0.0001$ ). PPD was reduced by 1.9 mm in TG and 2.3 mm in CG ( $p = 0.5783$ ). There were no significant differences between groups regarding reductions of BOP, SUP, REC, cytokines levels, or oral health impact profile (OHIP)-14 scores at 12 months. Successful treatment (RDF  $\geq$  1.0 mm, PPD  $\leq$  5 mm,  $\leq$  1/4 site with BOP grade 1, no SUP) was identified in 32% in TG and 21% in CG. **CONCLUSIONS:** DBBM and NBCM resulted in significantly more RDF than debridement alone. No difference was found in any clinical parameters or PROs between the groups. ClinicalTrials.gov Identifier: NCT02375750. Copyright © 2021 The Authors. Journal of Clinical Periodontology published by John Wiley & Sons Ltd.

### **Effectiveness of enamel matrix derivative on the clinical and microbiological outcomes following surgical regenerative treatment of peri-implantitis. A randomized controlled trial**

Ished, C., Holmlund, A., Renvert, S., Svenson, B., Johansson, I. and Lundberg, P.

**OBJECTIVE:** This randomized clinical trial aimed at comparing radiological, clinical and microbial effects of surgical treatment of peri-implantitis alone or in combination with enamel matrix derivative (EMD). **METHODS:** Twenty-six subjects were treated with open flap debridement and decontamination of the implant surfaces with gauze and saline preceding adjunctive EMD or no EMD. Bone level (BL) change was primary outcome and secondary outcomes were changes in pocket depth (PD), plaque, pus, bleeding and the microbiota of the peri-implant biofilm analyzed by the Human Oral Microbe Identification Microarray over a time period of 12 months. **RESULTS:** In multivariate modelling, increased marginal BL at implant site was significantly associated with EMD, the number of osseous walls in the peri-implant bone defect and a Gram+/aerobic microbial flora, whereas reduced BL was associated with a Gram-/anaerobic microbial flora and presence of bleeding and pus, with a cross-validated predictive capacity (Q(2)) of 36.4%. Similar, but statistically non-significant, trends were seen for BL, PD, plaque, pus and bleeding in univariate analysis. **CONCLUSION:** Adjunctive EMD to surgical treatment of peri-implantitis was associated

with prevalence of Gram+/aerobic bacteria during the follow-up period and increased marginal BL 12 months after treatment.

### **Surgical treatment of peri-implantitis using enamel matrix derivative, an RCT: 3- and 5-year follow-up**

Isehede, C., Svenson, B., Lundberg, P. and Holmlund, A.

**OBJECTIVE:** To assess the clinical and radiographic outcomes 3 and 5 years after the surgical treatment of peri-implantitis per se or in combination with an enamel matrix derivative (EMD)., **MATERIALS AND METHODS:** At baseline, 29 patients were randomized to surgical treatment with adjunctive EMD or no EMD. One year after the surgical treatment of peri-implantitis, 25 patients remained eligible for survival analyses at the 3- and 5-year follow-up. The primary outcomes were implant loss and bone level (BL) change measured on radiographs, and the secondary outcomes, bleeding on probing, pus and plaque at each implant were analysed in 18 and 14 patients at the 3- and 5-year follow-up, respectively., **RESULTS:** After exclusion of four patients who discontinued the study, at the 3-year follow-up, 13 (100%) implants survived in the EMD group, and 10 of 12 (83%) in the non-EMD group. At the 5-year follow-up, 11 of 13 (85%) implants in the EMD group and nine of 12 (75%) in the non-EMD group survived. In multivariate modelling, BL changes and EMD treatment were positively associated with implant survival. Similarly, the same trend was seen in univariate analysis. **CONCLUSIONS:** An exploratory analysis suggests that adjunctive EMD is positively associated with implant survival up to 5 years, but larger studies are needed. Copyright © 2018 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

### **Surgical treatment of peri-implantitis lesions with or without the use of a bone substitute-a randomized clinical trial**

Renvert, Stefan, Roos-Jansaker, Ann-Marie and Persson, Gosta Rutger

**AIM:** To assess whether the treatment outcome differed between surgical debridement, with or without a bone substitute., **MATERIALS AND METHODS:** Forty-one adults with three- or four-wall peri-implant bone defects were enrolled in a 1-year RCT. Surgical debridement (control group), or in combination with a bone substitute (Endobon R) (test group) was performed., **RESULTS:** Radiographic evidence of defect fill (primary outcome) was only significant in the test group ( $P = 0.004$ ). At year 1, no bleeding on probing (BOP) in the control and test groups were 7/20 (35%) and 10/21 (47.6%), respectively ( $\chi^2 = 0.67$ ,  $P = 0.41$ ). Plaque scores did not differ by study group at baseline ( $P = 0.31$ ), or at year 1 ( $P = 0.08$ ). Mid-buccal soft tissue recession changes did not differ by groups ( $P = 0.76$ ). Successful treatment outcome (defect fill  $\geq 1.0$  mm, PPD values at implant  $\leq 5$  mm, no BOP, and no suppuration was identified in 1/20 (5.0%) control, and 9/21 (42.9%) test individuals ( $F = 7, 9$ ,  $P < 0.01$ ). Number needed to treat analysis identified an absolute risk reduction of 32.8% in benefit of the test procedure. ( $F = 7, 9$ ,  $P < 0.01$ ). **CONCLUSIONS:** Successful treatment outcome using a bone substitute was more predictable when a composite therapeutic endpoint was considered. Copyright © 2018 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

### **Peri-implantitis - Reconstructive Surgical Therapy**

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**Objective** The overall objective of the project is to evaluate the clinical efficacy of the use of a bone substitute material in reconstructive surgical therapy of peri-implantitis-associated osseous defects. **Hypothesis:** The use of a bone substitute material in reconstructive therapy of peri-implantitis increases the likelihood to achieve treatment success. **Relevance for clinical practice** The project will provide significant contribution to the understanding of outcomes using reconstructive procedures in treatment of peri-implantitis. **Study population, design and treatment procedures** The project will be conducted as a two-armed randomized controlled clinical trial of 5-year duration in 7 clinical centers. 140 systemically healthy patients with implants  $\geq 1$  year in function and diagnosed with

advanced peri-implantitis at  $\geq 1$  implants will be enrolled. Inclusion criteria Age  $\geq 18$  years  $\geq 1$  implant ( $\geq 1$  year of function) presenting with PPD  $\geq 7$  mm and BoP/Pus. Confirmed bone loss  $\geq 3$  mm at same implant(s) Exclusion criteria Treated for peri-implantitis during previous 6 months Intake of systemic or local antibiotics during previous 6 months Systemic conditions affecting peri-implant tissues Systemic conditions impeding surgical intervention Surgical procedures Surgical procedures will be performed one month after a baseline examination and initiation of plaque control. Three days before surgery a 10-day systemic antibiotic regimen will be initiated. Full thickness flaps will be elevated and inflamed tissues will be removed. The implant surfaces will be cleaned with mini-gauze soaked in saline. The osseous defect should be  $\geq 4$  mm wide and  $>3$  mm deep. The defect should in addition to the mesial and distal bone walls preferably exhibit at least a lingual or a buccal bone wall. The randomly assigned treatment strategy, stratified for smoking, will be revealed after debridement. Test procedure: The defect will be filled with Bio-Oss Collagen® and the flaps will be sutured to their previous position. Control procedure: Flaps will be sutured to their previous position. Sutures will be removed 2 weeks after treatment, followed by a 6-week control. Clinical examinations will be performed at 6, 12, 24, 36, 48 and 60 months after therapy. Maintenance therapy will be provided based on individual needs. Clinical assessments One calibrated examiner in each clinical center will perform the assessments. The following variables will be assessed at four sites around the implant: Plaque, probing pocket depth (PPD), bleeding on probing (BoP), probing attachment level (PAL) and recession (REC). Treatment success Treatment success will be defined as the absence of BoP/Pus, PPD  $\geq 5$  mm and  $\geq 1$  mm recession. Peri-implant sites showing BoP and PPD  $\geq 6$  mm at re-examination will be scheduled for further treatment. Patient-related outcome variables will be assessed at baseline and follow-up and include esthetic and functional appreciation, pain or discomfort. Radiographic assessments Intra-oral radiographs will be obtained prior to surgery (baseline) and at 1-, 3- and 5-year re-examinations. Analysis of radiographs will be performed by specialists in oral-maxillofacial radiology. The examiners will be blinded to treatment procedures. The assessment will include defect fill and crestal bone support. Power calculation A total of 122 patients (61 per group) will provide a power of 80% with alpha set at 0.05 to detect a difference of 1 mm in mean PPD change between groups, given a SD of 1.97. 140 individuals will be included to compensate for drop-out. Data analysis Mean changes for the various variables and the proportion of sites fulfilling the criteria for treatment success will be calculated. A multilevel model with the clinical center as the highest level and the implant as the lowest will be built to test the influence of measured factors on the outcomes and to compensate for potential clustering of data. Data analysis including multilevel modeling will be conducted in collaboration with a biostatistician. Schedule of investigational events 1. Screening and identification of subjects. 2. Baseline clinical examination of implants selected for the study. Case presentation and reinforcement of self-performed plaque control. Assessment of PROM. Professional mechanical infection control. 3. Radiographic examination prior to surgical therapy (within 4 weeks). 4. Surgical therapy including test and control treatment procedures at study sites. 5. 2 weeks: suture removal. Assessment of PROM. 6. 6 weeks: professional supra-mucosal cleaning and reinforcement of oral hygiene. 7. 6 months: clinical examination. 8. 12 months: clinical and radiological examination. Assessment of PROM. 9. 24 months: clinical examination. 10. 36 months: clinical and radiological examination. Assessment of PROM. 11. 48 months: clinical examination. 12. 60 months: clinical and radiological examination. Assessment of PROM.

## **FQ2 target articles**

### **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**

Froum, Stuart J., Froum, Scott H. and Rosen, Paul S.

This article presents the results of a consecutive case series of 170 treated peri-implantitis-affected implants in 100 patients with follow-up measurements from 2 to 10 years. A total of 51 implants in 38 patients previously reported on were followed for an additional 2.5 years,

and 119 additional implants in 62 additional patients were treated with the same protocol and monitored for at least 2 years posttreatment. The treatment consisted of flap reflection, surface decontamination, use of enamel matrix derivative (EMD) or platelet-derived growth factor (PDGF), and guided bone regeneration with mineralized freeze-dried bone and/or anorganic bovine bone combined with PDGF or EMD and covered with an absorbable membrane and/or subepithelial connective tissue graft. Maintenance and monitoring followed every 2 to 3 months. Two implants were lost 6 months posttreatment, for a 98.8% survival rate. Bleeding on probing was eliminated in 91% of the treated implants. Probing depth reduction averaged 5.10 mm, bone level gain averaged 1.77 mm, and soft tissue marginal gain averaged 0.52 mm. These outcomes were obtained with one surgical procedure on 140 implants, with two procedures on 18 implants, and with three procedures on 10 implants. The results to date with this layered/combined regenerative approach for the treatment of peri-implantitis appear to be encouraging.

### **Surgical approach combining implantoplasty and reconstructive therapy with locally delivered antibiotic in the treatment of peri-implantitis: A prospective clinical case series**

Gonzalez Regueiro, Iria, Martinez Rodriguez, Natalia, Barona Dorado, Cristina, Sanz-Sanchez, Ignacio, Montero, Eduardo, Ata-Ali, Javier, Duarte, Fernando and Martinez-Gonzalez, Jose Maria

**BACKGROUND:** Nonsurgical treatment, resective surgery, reconstructive surgery, or combined approaches have been proposed for the treatment of peri-implantitis, with variable results., **PURPOSE:** To evaluate the 1-year clinical and radiographic outcomes following combined resective and reconstructive surgical treatment with topical piperacillin/tazobactam antibiotic in the management of peri-implantitis., **MATERIAL AND METHODS:** Forty-three patients diagnosed with peri-implantitis were included. Surgical treatment consisted of implantoplasty of the supra-crestal component of the defect, the application of a topical antibiotic solution over the implant surface, and subsequent reconstruction of the intraosseous component of the peri-implant defect. The primary outcome was disease resolution, defined as the absence of bleeding on probing (BoP) and/or suppuration on probing (SoP), a peri-implant pocket probing depth (PPD)  $\leq 5$  mm, and no bone loss  $>0.5$  mm 1 year after surgery. Secondary outcomes included changes in BoP, PPD, SoP, and peri-implant marginal bone levels. One implant per patient was included in the analysis., **RESULTS:** The treatment success rate of the 43 dental implants included in the study was 86% at 1 year after surgery. Mean PPD and BoP decreased from  $6.41 \pm 2.11$  mm and 100% at baseline to  $3.19 \pm 0.99$  mm ( $p < 0.001$ ) and 14% ( $p < 0.001$ ) at 1 year, respectively. SoP was significantly reduced from 48.8% at baseline to 0% 1 year after surgery ( $p < 0.001$ ). Radiographically, a mean defect fill of  $2.64 \pm 1.59$  mm was recorded ( $p < 0.001$ ). **CONCLUSIONS:** The combination of a resective and reconstructive surgical approach together with locally delivered antibiotic achieved a high disease resolution rate after 1 year of follow-up and constitutes a viable option for the management of peri-implantitis. Copyright © 2021 The Authors. Clinical Implant Dentistry and Related Research Published by Wiley Periodicals LLC.

### **Regenerative surgical treatment of peri-implantitis using either a collagen membrane or concentrated growth factor: A 12-month randomized clinical trial**

Isler, S.C., Soysal, F., Ceyhanli, T., Bakirarar, B. and Unsal, B.

**BACKGROUND:** Platelet concentration based membranes, as well as collagen membranes in combination with bone substitutes, have demonstrated successful outcomes in regeneration of peri-implant bone defects (PBD)., **PURPOSE:** The aim of this study was to evaluate the clinical and radiographic outcomes of regenerative surgical treatment (RST) of peri-implantitis using a bone substitute combined with two different bioresorbable barrier membranes, either collagen membrane (CM) or concentrated growth factor (CGF), during 12-month follow-up., **MATERIALS AND METHODS:** Fifty two patients, who had at least one peri-implantitis lesion was treated by using a bone substitute in combination with CGF or CM. After surgical procedures, implants were allowed for submerged healing.

Clinical assessments were conducted at baseline, 6 and 12 months postoperatively, while radiographic evaluation was performed at baseline and 12 months. **RESULTS:** Significant reductions were obtained in the mean gingival index (GI), bleeding on probing (BOP), probing depth (PD), clinical attachment level (CAL) and mucosal recession (MR) values at both 6 and 12 months postoperatively compared to baseline for both treatment procedures ( $P < 0.05$ ). At 6 months, no statistically significant difference was observed for all clinical parameters between the groups, whereas the mean PD, CAL and vertical defect depth (VDD) values were statistically significant in favor of the CM group at 12 months ( $P < 0.05$ ). The mean defect fill (DF) in the CM group ( $1.99 \pm 0.76$ ) was not statistically significantly different from that observed in the CCF group ( $1.63 \pm 1.00$ ) ( $P = 0.154$ ). **CONCLUSIONS:** The outcomes of the present study suggest that both regenerative approaches yielded significant improvements in both clinical and radiographic assessments. The procedure using a collagen membrane in combination with a bone substitute showed better results at 12 months in RST of peri-implantitis. Copyright © 2018 Wiley Periodicals, Inc.

### **Clinical and radiographic outcomes of a surgical reconstructive approach in the treatment of peri-implantitis lesions: A 5-year prospective case series**

La Monaca, Gerardo, Pranno, Nicola, Annibali, Susanna, Cristalli, Maria Paola and Polimeni, Antonella

**OBJECTIVES:** The aim of this study was to evaluate the 5-year clinical and radiographic outcomes following reconstructive therapy of peri-implantitis lesions using mineralized dehydrated bone allograft and resorbable membrane in the nonsubmerged mode of wound healing. **MATERIALS AND METHODS:** Thirty-four patients with at least one implant diagnosed with peri-implantitis were treated by mechanical debridement; chemical decontamination using hydrogen peroxide (3%), chlorhexidine (0.2%), and a tetracycline hydrochloride solution; and bone defect filling with mineralized dehydrated bone allograft and resorbable membrane. Clinical and radiographic assessments were obtained during 5-year follow-up. The primary outcome was the absence of additional marginal peri-implant bone loss  $\geq 1.0$  mm after surgery, and the composite outcome included the additional marginal peri-implant bone loss, absence of probing depth (PD)  $\geq 5$  mm, and absence of bleeding on probing (BoP)/suppuration. **RESULTS:** According to the primary and composite outcomes, the success rate of 34 implants included in the study was 100% and 91% ( $N = 31$ ), at 1 year after surgery, and decreased progressively to 77% ( $N = 26$ ) and to 59% ( $N = 20$ ) at 5-year follow-up, respectively. Five years following treatment, only the BoP reduction was statistically significant compared to baseline ( $p < 0.001$ ), and no difference was found in PD ( $p = 0.318$ ) and in marginal peri-implant bone level ( $p = 0.064$ ). **CONCLUSIONS:** At 1-year follow-up, the surgical reconstructive therapy showed clinical improvement and radiographic defect filling. However, the results appeared to be unpredictable over time, due to a progressive decrease in the bone filling of the peri-implant defects and an increase in the mean PD. Copyright © 2018 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

### **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**

Mercado, Faustino, Hamlet, Stephen and Ivanovski, Saso

**OBJECTIVES:** There is limited evidence regarding the long-term efficacy of regenerative treatment for peri-implantitis. The aim of this study was to evaluate a combination therapy of deproteinized bovine bone mineral with 10% collagen (DBBMC), enamel matrix derivative (EMD) and Doxycycline in the regeneration of bone defects associated with peri-implantitis. **METHODS:** Thirty patients diagnosed with peri-implantitis (BoP/suppuration, probing depth greater than 4 mm, minimum radiographic bone loss of 20%, at least 2 years in function) were enrolled in the study. Clinical measurements included probing depths, recession, radiographic bone fill, gingival inflammation and bleeding on probing/suppuration. Following surgical access and debridement, the implant surfaces

were decontaminated with 24% EDTA for 2 min, and the bone defects were filled with a combined mixture of DBBMC, EMD and Doxycycline powder. The defects were covered with connective tissue grafts where necessary. Clinical measurements were recorded after 12, 24 and 36 months., RESULTS: The mean probing depth and bone loss at the initial visit was 8.9 mm (+/-1.9) and 6.92 mm (+/-1.26), respectively. Both mean probing depth and bone loss reduced significantly from baseline to 3.55 mm (+/-0.50) and 2.85 mm (+/-0.73) at 12 months, 3.50 (+/-0.50) and 2.62 mm (+/-0.80) at 24 months and 3.50 mm (+/-0.50) and 2.60 mm (+/-0.73) at 36 months. 56.6% of the implants were considered successfully treated (according to Successful Treatment Outcome Criterion: PD < 5 mm, no further bone loss >10%, no BoP/suppuration, no recession >0.5 mm for anterior implants and >1.5 mm for posterior implants) after 36 months. CONCLUSION: Regenerative treatment of peri-implantitis using a combined mixture of DBBMC, EMD and Doxycycline achieved promising results. The benefits of this protocol incorporating EMD should be tested in randomized clinical trials. Copyright © 2018 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

### **Surgical treatment of peri-implantitis defects with two different xenograft granules: A randomized clinical pilot study**

Polymeri, Angeliki, Anssari-Moin, David, van der Horst, Joyce, Wismeijer, Daniel, Laine, Marja L. and Loos, Bruno G.

OBJECTIVES: To investigate whether xenograft EB (EndoBon) is non-inferior to xenograft BO (Bio-Oss) when used in reconstructive surgery of peri-implant osseous defects., MATERIALS AND METHODS: Dental patients with one implant each demonstrating peri-implantitis were randomized to receive surgical debridement and defect fill with either BO or EB. Changes in bone level (BL) and intrabony defect depth (IDD) evaluated radiographically were the primary outcomes. The secondary outcomes included changes in probing pocket depth (PPD), bleeding on probing (BoP), and suppuration on probing (SoP). All outcomes were recorded before treatment and at 6 and 12 months post-treatment., RESULTS: Twenty-four patients (n = 11 BO, n = 13 EB) completed the study. Both groups demonstrated significant within-group improvements in all clinical and radiographic parameters at 6 and 12 months ( $p \leq 0.001$ ). At 12 months, both groups presented with IDD reductions of 2.5–3.0 mm on average. The inter-group differences were not statistically significant at all time points and for all the examined parameters ( $p > 0.05$ ). While the radiographic defect fill in both groups exceeded > 1 mm and can be considered treatment success, successful treatment outcomes as defined by Consensus Reporting (no further bone loss, PPD  $\leq 5$  mm, no BOP, and no SoP) were identified in 2/11 (18%) BO and 0/13 (0%) EB individuals (Fisher's exact test,  $p = 0.199$ ). CONCLUSIONS: Within the limitations of this pilot study, the application of xenograft EB showed to be non-inferior to xenograft BO when used in reconstructive surgery of peri-implant osseous defects. Copyright © 2020 The Authors. Clinical Oral Implants Research published by John Wiley & Sons Ltd.

### **Surgical therapy of single peri-implantitis intrabony defects, by means of deproteinized bovine bone mineral with 10% collagen**

Roccuzzo, Mario, Gaudio, Luigi, Lungo, Marco and Dalmaso, Paola

AIM: To evaluate the efficacy of a reconstructive surgical procedure in single peri-implantitis intrabony defects., METHODS: Seventy-five patients with one peri-implantitis crater-like lesion with pocket depth (PD)  $\geq 6$  mm, were included. Each defect was assigned to one characteristic class, by an independent examiner. After implant decontamination, defects were filled with deproteinized bovine bone mineral with 10% collagen., RESULTS: At 1-year follow-up, four patients were lost and six implants removed. Treatment success, PD  $\leq 5$  mm and absence of suppuration/bleeding on probing (BOP), was obtained in 37 (52.1%) of the 71 implants examined. PD was significantly reduced by 2.92 +/- 1.73 mm ( $p < 0.0001$ ). BOP decreased from 71.5 +/- 34.4% to 18.3 +/- 28.6% ( $p < 0.0001$ ). The mean number of deep pockets ( $\geq 6$  mm) decreased from 3.00 +/- 0.93 to 0.85 +/- 1.35 ( $p < 0.0001$ ). CONCLUSIONS: These results confirm the possibility to successfully treat

peri-implantitis lesions. There is lack of evidence of whether or not the resolution of the peri-implant disease is associated with the defect configuration. Due to the fact that complete resolution does not seem a predictable outcome, the clinical decision on whether implants should be treated should be based on several patient related elements. Copyright © 2016 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

#### **Reconstructive treatment of peri-implantitis infrabony defects of various configurations: 5-year survival and success**

Roccuzzo, Mario, Mirra, Davide, Pittoni, Dario, Ramieri, Guglielmo and Roccuzzo, Andrea

**AIM:** To present the 5 years outcomes of a reconstructive surgical protocol for peri-implantitis defects with different morphologies, by means of deproteinized bovine bone mineral with 10% collagen (DBBMC)., **MATERIAL AND METHODS:** The original population of this case series consisted of 75 patients with one crater-like defect and probing depth (PD)  $\geq 6$  mm. After flap elevation, defects were assigned to one characteristic class and treated by means of DBBMC. Following healing, patients were enrolled in an individualized supportive periodontal/peri-implant (SPT) program., **RESULTS:** Fifty-one patients reached the 5 years examination, as 11 patients were lost to follow-up and 13 implants were removed. Overall treatment success was registered in 29 patients (45.3%). Mean PD and BOP significantly decreased at one year and remained stable for the rest of observation period. No correlation was found between implant survival rate and defect configuration ( $p = 0.213$ ). Patients, who did not fully adhere to the SPT, experienced more complications and implant loss than those who regularly attended recall appointments ( $p = 0.009$ ). **CONCLUSIONS:** The proposed reconstructive treatment resulted in a high 5 years implant survival rate in patients who fully adhered to SPT. The resolution of the peri-implantitis defect does not seem significantly associated with the defect configuration at the time of treatment. Copyright © 2021 The Authors. Clinical Oral Implants Research published by John Wiley & Sons Ltd.

#### **Reconstructive surgical therapy of peri-implantitis bone defects**

Isrctn

**INTERVENTION:** The test group will be treated with xenograft cover with a resorbable collagen membrane. Control group will be treated with xenograft only. The intervention will be realized in a single session and the follow-up will be 12 months after the surgical procedure. Randomization will be carried out by means of 5 blocks by a sequence generated by the computer. **CONDITION:** Intraosseous peri-implant defects; Oral Health **PRIMARY OUTCOME:** Probing depth (PS) is measured in 6 locations per implant. It consists of probing from the margin of the peri-implant mucosa to the most apical part of the peri-implant defect at baseline, at 6 months and at 12 months. **SECONDARY OUTCOME:** 1. Filling of the radiographic defect is measured using intraoral radiographs of the implant at baseline, 6 months and 12 months. The defect that is appreciated in the initial radiography with the filling in the following ones will be compared; 2. Mucosal recession is measured at one vestibular point of each implant. Measured from the apical margin of the implant-supported restoration to the margin of the peri-implant mucosa at baseline, at 6 months and at 12 months; 3. Bleeding on probing is measured in 6 locations per implant in basal at 6 months and 12 months; 4. Plaque control is measured in 6 locations per implant in basal at 6 months and 12 months; 5. Presence of complications is measured using membrane exposure at healing period. It will be checked if there is primary closure of the lesion or if there is membrane exposure; 6. Intervention time. Is measured by a chronometer since the first incision until the last suture; 7. Patient satisfaction and morbidity are measured using a visual analogic scale at 2 weeks, 6 months and 12 months to know the postoperative morbidity and perception and satisfaction with the procedure; 8. Volumetric changes are measured using an intraoral scanner and a digital computer program that superimposes an initial scanner with the posterior ones to see the volumetric changes at baseline, at 6 months and 12 months.; **INCLUSION CRITERIA:** 1. Show radiographically peri-implant intraosseous defects of at least 3 mm depth. 2. Depth of clinical probing = 5 mm with

bleeding and/or suppuration. 3. Intra-surgically, the infra-osseous defect must have at least one intraosseous component of 3 mm and a width of no more than 4 mm. 4. The implant to be treated must have been in function for at least 12 months.

#### **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**

Aghazadeh, A., Rutger Persson, G. and Renvert, S.

**BACKGROUND:** Limited evidence exists on the efficacy of regenerative treatment of peri-implantitis., **MATERIAL AND METHODS:** Subjects receiving antibiotics and surgical debridement were randomly assigned to placement of autogenous bone (AB) or bovine-derived xenograft (BDX) and with placement of a collagen membrane. The primary outcome was evidence of radiographic bone fill and the secondary outcomes included reductions of probing depth (PD) bleeding on probing (BOP) and suppuration., **RESULTS:** Twenty-two subjects were included in the AB and 23 subjects in the BDX group. Statistical analysis failed to demonstrate differences for 38/39 variables assessed at baseline. At 12 months, significant better results were obtained in the BDX group for bone levels ( $p < 0.001$ ), BOP ( $p = 0.004$ ), PI ( $p = 0.003$ ) and suppuration ( $p < 0.01$ ). When adjusting for number of implants treated per subject, a successful treatment outcome PD  $\leq 5.0$  mm, no pus, no bone loss and BOP at 1/4 or less sites the likelihood of defect fill was higher in the BDX group (LR: 3.2, 95% CI: 1.0–10.6,  $p < 0.05$ ). **CONCLUSIONS:** Bovine xenograft provided more radiographic bone fill than AB. The success for both surgical regenerative procedures was limited. Decreases in PD, BOP, and suppuration were observed. Copyright © 2012 John Wiley & Sons A/S.

#### **Impact of bone defect morphology on the outcome of reconstructive treatment of peri-implantitis**

Aghazadeh, A., Persson, R.G. and Renvert, S.

**OBJECTIVES:** To assess if (I) the alveolar bone defect configuration at dental implants diagnosed with peri-implantitis is related to clinical parameters at the time of surgical intervention and if (II) the outcome of surgical intervention of peri-implantitis is dependent on defect configuration at the time of treatment, **MATERIALS AND METHODS:** In a prospective study, 45 individuals and 74 dental implants with  $\geq 2$  bone wall defects were treated with either an autogenous bone transplant or an exogenous bone augmentation material. Defect fill was assessed at 1 year, **RESULTS:** At baseline, no significant study group differences were identified. Most study implants (70.7%,  $n = 53$ ) had been placed in the maxilla. Few implants were placed in molar regions. The mesial and distal crestal width at surgery was greater at 4-wall defects than at 2-wall defects ( $p = 0.001$ ). Probing depths were also greater at 4-wall defects than at 2-wall defects ( $p = 0.01$ ). Defect fill was correlated to initial defect depth ( $p < 0.001$ ). Defect fill at 4-wall defects was significant ( $p < 0.05$ ). **CONCLUSIONS:** (I) The buccal-lingual width of the alveolar bone crest was explanatory to defect configuration, (II) 4-wall defects demonstrated more defect fill, and (III) deeper defects resulted in more defect fill.

#### **Evaluation of Photodynamic Therapy in Treatment of Peri-implantitis**

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**Treatment procedure** After clinical parameters were recorded and samples were taken, all patients underwent a single episode of non-surgical therapy. It implied a mechanical method for debridement of implants and remaining dentition in order to reduce signs of inflammation. Instructions for oral hygiene were proposed in the same visit. Peri-implantitis surgical treatment was conducted by one experienced surgeon two weeks after non-surgical therapy. After granulation tissue removal and mechanical implant surface cleaning with graphite curettes (Straumann Dental Implant System Straumann AG, Basel, Switzerland), decontamination of implant surface was conducted. In the study group, for the decontamination of implant surfaces and peri-implant tissues photodynamic therapy was performed (HELBO, Photodynamic Systems GmbH, Wels, Austria), while in the control group, after



removal of granulation tissue, 1% gel of chlorhexidine (Chlorhexamed®- Direkt) was put on the implant surface. One minute after exposing the implant surface with CHX, it was irrigated for 1 min by saline. Bone augmentation and bio-resorbable membrane were applied in peri-implant defects using the bovine bone substitute and collagen membrane (Bio-Oss and Bio Gide, GeistlichPharma; Dembone). The mucoperiosteal flaps were repositioned and sutured [17, 19]. Patients were prescribed antibiotics (Amoxicillin, 500 mg, three per day, 5 days). It was recommended that patients don't use mouthwash during the postoperative period. Clinical, immunological and microbiological parameters were measured and assessed baseline, three, six, 12 and 24 months postoperatively. Immunological parameters (IL-17, IL-1, IL-6) were analysed by ELISA while microbiological samples were collected before the therapy, during the surgery, and at follow-up periods. Assessment of implant macro- and micro-design were additionally assessed.

### **Submerged healing following surgical treatment of peri-implantitis: a case series**

Roos-Jansaker, Ann-Marie, Renvert, Helena, Lindahl, Christel and Renvert, Stefan

**OBJECTIVES:** The aim was to study a regenerative surgical treatment modality for peri-implantitis employing submerged healing., **MATERIAL AND METHODS:** Twelve patients, having a minimum of one osseointegrated implant with peri-implantitis, with a progressive loss of  $\geq 3$  threads (1.8 mm) following the first year of healing were involved in the study. After surgical exposure of the defect, granulomatous tissue was removed and the implant surface was treated using 3% hydrogen peroxide. The bone defects were filled with a bone substitute (Algipore), a resorbable membrane (Osseoquest) was placed over the grafted defect and a cover screw was connected to the fixture. The implant was then covered by flaps and submerged healing was allowed for 6 months. After 6 months the abutment was re-connected to the supra-structure., **RESULTS:** A 1-year follow-up demonstrated clinical and radiographic improvements. Probing depth was reduced by 4.2 mm and a mean defect fill of 2.3 mm was obtained. **CONCLUSION:** Treatment of peri-implant defects using a bone graft substitute combined with a resorbable membrane and submerged healing results in defect fill and clinical healthier situations.

### **Long-term stability of surgical bone regenerative procedures of peri-implantitis lesions in a prospective case-control study over 3 years**

Roos-Jansaker, Ann-Marie, Lindahl, Christel, Persson, G. Rutger and Renvert, Stefan

**OBJECTIVES:** To evaluate the extent of bone fill over 3 years following the surgical treatment of peri-implantitis with bone grafting with or without a membrane., **MATERIAL AND METHODS:** In a non-submerged wound-healing mode, 15 subjects with 27 implants were treated with a bone substitute (Algipore(R)) alone and 17 subjects with 29 implants were treated with the bone substitute and a resorbable membrane (Osseoquest(R)). Implants with radiographic bone loss  $\geq 1.8$  mm following the first year in function and with bleeding and/or pus on probing were included. Following surgery, subjects were given systemic antibiotics (10 days) and rinsed with chlorhexidine. After initial healing, the subjects were enrolled in a strict maintenance programme., **RESULTS:** Statistical analysis failed to demonstrate changes in bone fill between 1 and 3 years both between and within procedure groups. The mean defect fill at 3 years was  $1.3 \pm 1.3$  mm if treated with the bone substitute alone and  $1.6 \pm 1.2$  mm if treated with an adjunct resorbable membrane, ( $p = 0.40$ ). The plaque index decreased from approximately 40–10%, remaining stable during the following 2 years. **CONCLUSION:** Defect fill using a bone substitute with or without a membrane technique in the treatment of peri-implantitis can be maintained over 3 years. Copyright © 2011 John Wiley & Sons A/S.

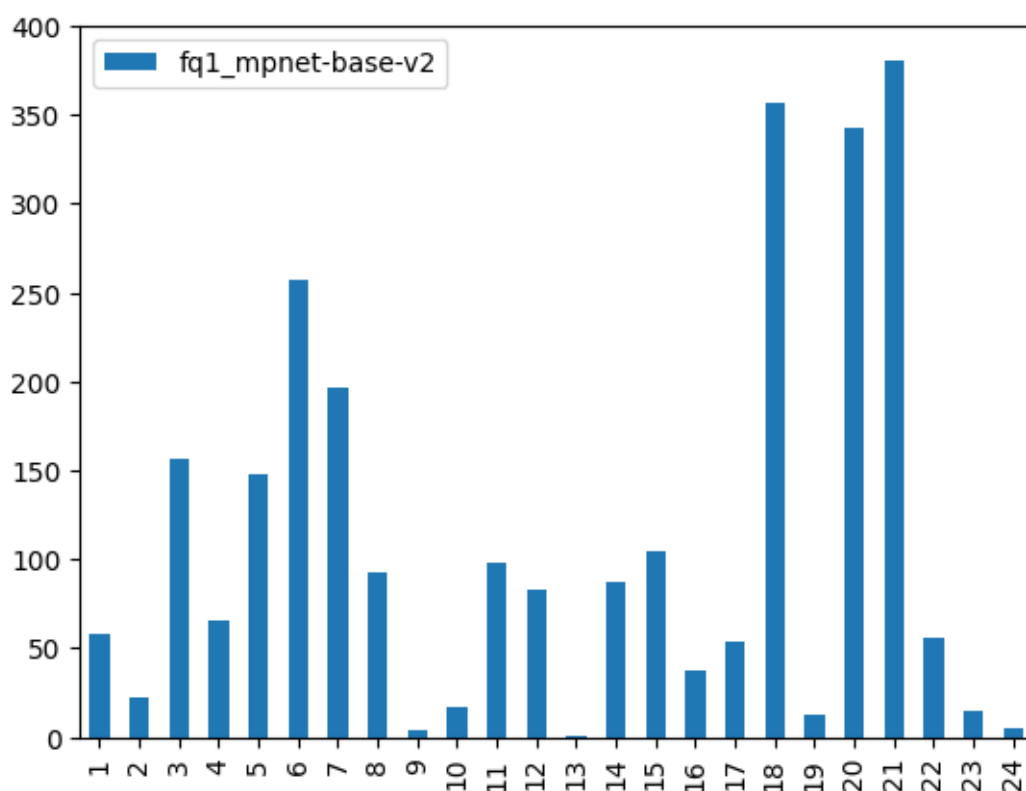
### **Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up**

Roos-Jansaker, Ann-Marie, Persson, Gosta Rutger, Lindahl, Christel and Renvert, Stefan

**AIM:** To compare two regenerative surgical treatments for peri-implantitis over 5 years., **MATERIAL & METHODS:** Twenty-five individuals with peri-implantitis remained

at study endpoint. They were treated with a bone substitute and a resorbable membrane (13 individuals with 23 implants) [Group 1], or with bone substitute alone (12 individuals with 22 implants) [Group 2]. All study individuals were kept on a strict maintenance programme every third month., RESULTS: Five-year follow-up demonstrated clinical and radiographic improvements in both groups. No implants were lost due to progression of peri-implantitis. Probing depths were reduced by 3.0 +/- 2.4 mm in Group 1, and 3.3 +/- 2.09 mm in Group 2 (NS). In both groups, radiographic evidence of bone gain was significant ( $p < 0.001$ ). At year 5, the average defect fill was 1.3 mm (SD +/- 1.4 mm) in Group 1 and 1.1 mm (SD +/- 1.2 mm) in Group 2 (mean diff; 0.4 95% CI -0.3, 1.2,  $p = 0.24$ ). Bleeding on probing decreased in both groups. Baseline and year 5 plaque scores did not differ between groups and was reduced from 50% to 15%. CONCLUSION: Both procedures resulted in stable conditions. Additional use of a membrane does not improve the outcome. Copyright © 2014 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

## Appendix B



**Figure A1.** Ranking of all the 24 target articles by similarities to FQ1 using the all-mpnet-base-v2 model. Lower values indicate a higher ranking once all the 6110 are ordered by similarity, i.e., the lower the value, the more similar the article is to the FQ.

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