LITHUANIAN UNIVERSITY OF HEALTH SCIENCES

MEDICAL ACADEMY

FACULTY OF ODONTOLOGY

DEPARTMENT OF MAXILLOFACIAL SURGERY

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THE USE OF PLATELET-RICHED FIBRIN IN SINUS FLOOR ELEVATION SURGERY: A SCIENTIFIC LITERATURE REVIEW

Master's thesis of the Master's degree study program "Odontology"

Supervisor of the Master's thesis

Prof. Gintaras Juodžbalys

Kaunas, 2024

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The thesis was done by graduate student: ……..

Oren Babich, 5th year, group 16

2023-04-20

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2024-04-20

Kaunas, 2024

EVALUATION OF THE SCIENTIFIC LITERATURE REVIEW MASTER'S THESIS REVIEWER'S FORM

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5	Search methods andstrategy	Is the selection process of articles (screening, eligibility for systematic reviewor, if applicable, for meta-analysis) described? Is the process of data selection from articles described (types of research,participants, interventions, factors analysed, and indicators)? Were all the variables, for which data were searched and described, listed anddescribed? What assumptions or simplifications were made? Were the key measurement indicators (relative risk, mean differences)identified?	
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ABBREVIATION LIST

FDBA- freeze-dried bone allograft

DBBM- deproteinized bovine bone mineral

MSFE-maxillary sinus floor elevation

PRF- platelet reach fibrin

L-PRF- Leukocyte platelets reach fibrin

ISQ- implant stability quotient

NR- not reported

SUMMARY

RELEVANCE AND AIM: This thesis addresses the efficacy of Platelet-Rich Fibrin (PRF) in maxillary sinus floor elevation (MSFE) together with bone plastic material, focusing on new bone formation, bone height, implant stability quotient (ISQ), and Schneiderian membrane thickness. The objective is to critically assess the impact of PRF on these parameters to improve clinical outcomes in dental implantology.

MATERIALS AND METHODS: A systematic review and meta-analysis were conducted, analyzing studies from PubMed/Medline, Cochrane, and Science Direct databases, 2018 to 2024 that compared maxillary sinus floor elevation MSFE using bone plastic material with and without PRF. This review focused on patients 18 years and older who had undergone MSFE before dental implant placement. It systematically examined five studies, encompassing randomized controlled trials, and reported on 112 MSFE procedures conducted in 84 patients.

RESULTS: The meta-analysis reveals a marginal significance in new bone formation with PRF, suggesting a trend towards beneficial outcomes that were not statistically significant. No significant impact on bone height was observed. However, a notable improvement in ISQ was recorded, indicating enhanced implant stability with PRF. The Schneiderian membrane thickness did not show significant changes post-treatment with PRF.

CONCLUSION: While PRF shows promise in enhancing implant stability, its effects on new bone formation and Schneiderian membrane thickness are inconclusive, highlighting the need for further research. PRF did not significantly affect bone height. The findings support PRF's potential as a beneficial adjunct in MSFE, particularly for implant stability.

Keywords: Maxillary Sinus Floor Augmentation, Platelet-Rich Fibrin, Implant Stability.

SANTRAUKA

AKTUALUMAS IR TIKSLAS: pagal literatūros duomenis ištirti trombocitais praturtinto fibrino (TPF) efektyvumą augmentuojant viršutinio žandikaulio ančio dugną, sutelkiant dėmesį į naujos kaulinės medžiagos susiformavimą, kaulo aukštį, implanto stabilumo koeficientą (ISK) ir Schneiderio membranos storį. Tikslas yra kritiškai įvertinti TPF poveikį šiems parametrams, siekiant pagerinti klinikinius rezultatus dantų implantacijoje.

MEDŽIAGA IR METODAI: Atlikta sisteminė apžvalga ir meta-analizė, analizuojant tyrimus iš „PubMed/Medline“ ‚Cochrane“ ir „Science Direct“ duomenų bazių, 2018-2024 m., kur buvo lyginama viršutinio žandikaulio ančio dugno augmentacija kaulo pakaitalais su ir be TPF. Buvo tirti vyresni nei 18 metų pacientai, kuriems buvo atlikta viršutinio žandikaulio ančio dugno augmentacija prieš įsodinant dantų implantus. Sistemiškai išnagrinėti penki tyrimai, apimantys atsitiktinių imčių kontroliuojamus tyrimus, kur 84 pacientams atlikta 112 operacinių procedūrų.

REZULTATAI: Meta-analizė atskleidė teigiamą TPF poveikį naujos kaulinės medžiagos formavimui, nors šis poveikis nebuvo statistiškai reikšmingas. Kaulo aukštis nepasikeitė reikšmingai. Tačiau užfiksuotas pastebimas ISK pagerėjimas, rodo padidėjusį implantato stabilumą naudojant TPF. Schneiderio membranos storis po gydymo TPF neparodė reikšmingų pokyčių.

IŠVADA: Nors TPF rodo teigiamą poveikį didinant implantato stabilumą, jo poveikis naujos kaulinės medžiagos formavimui ir Schneiderio membranos storiui lieka neaiškus, pabrėžiant tolesnių tyrimų poreikį. TPF neturėjo reikšmingo poveikio kaulo aukščiui. Rezultatai patvirtina TPF potencialą papildant viršutinio žandikaulio ančio dugno pakėlimo operacijos priemonių potencialą, ypač siekiant implanto stabilumo.

Raktiniai žodžiai: viršutinio žandikaulių ančio dugno augmentacija, trombocitais praturtintas fibrinas, implantato stabilumas.

INTRODUCTION

Implant placement in the posterior maxilla has long posed a significant challenge due to factors such as poor bone quality, ridge atrophy, and sinus floor expansion following tooth extraction [1].

Tatum (1977, 1986), Boyne and James (1980), and Wood and Moore (1988) were the initial researchers to delineate a method for augmenting the maxillary sinus floor, wherein autogenous bone grafts were introduced into the maxillary sinus floor through a lateral bone window before the placement of dental implants. The utilization of autogenous bone grafts is widely acknowledged as the benchmark for bone augmentation procedures (Burchardt 1987) and is imperative for facilitating osseointegration (Hing 2004) [2].

In response to promising outcomes reported in the literature, an increasing number of clinicians and patients are turning to implant-supported restorations in the posterior maxilla. Consequently, techniques for maxillary sinus elevation and augmentation have gained popularity [3].

To address the need for improved maxillary bone height, several surgical techniques have been proposed, with a focus on integrating and placing dental implants. Maxillary sinus floor augmentation often involves the use of biologic or synthetic grafting materials, either independently or in combination with autogenous bone grafts [4].

Various kinds of biomaterials have been utilized for maxillary sinus floor augmentation, encompassing autografts, allografts, xenografts, alloplasts, and growth factors. Determining the optimal graft material has remained contentious. Autogenous bone graft stands as the benchmark in augmentation procedures owing to its osteoinductive, osteogenic, and osteoconductive properties [5-6].

Utilizing autogenous bone grafts is linked to the risk of donor site morbidity and unpredictable graft resorption [7-9].

In the 1970s, Ross et al. made a pivotal discovery regarding the regenerative potential of platelets. They found that platelets contain a variety of growth factors responsible for cell mitosis, increased collagen production, blood vessel growth, and other essential elements for tissue healing and regeneration [10].

One valuable tool that has emerged in implantology is Platelet-Rich Fibrin (PRF).

It offers diverse applications, such as enhancing grafts with slow-releasing osteoinductive properties (I-PRF), serving as a complete substitute for grafted bone (solid PRF), or acting as a membrane in

various regenerative procedures, including maxillary sinus membrane grafting and connective tissue grafting. Additionally, PRF can be blended with bone graft materials to improve outcomes [11].

As platelet-rich fibrin (PRF) was introduced to promote bone formation and stimulate bone graft healing, its utilization has garnered significant attention. Studies have indicated that PRF exhibits a superior affinity for osteoblasts, suggesting that it exerts a more robust and enduring effect on the differentiation and proliferation of these cells compared to platelet-rich plasma (PRP) [12,13].

The combined application of platelet-rich fibrin (PRF) and autologous bone grafts has demonstrated promising outcomes, characterized by reduced bone resorption, and augmented bone volume and quality [14,15].

This systematic review aims to critically assess the impact of PRF on maxillary sinus floor elevation and outline the specific aspects of:

1. New bone formation
2. Bone height
3. Implant stability quotient (ISQ)
4. Schneiderian membrane thickness

Hypothesis:

This systematic review hypothesizes that the PRF has a positive effect on maxillary sinus floor elevation and has a better effect on bone augmentation outcomes compared to maxillary sinus floor elevation with bone graft alone.

1. SEARCH METHODS AND STRATEGY

1.1 The protocol for systematic review

The institutional approval was obtained from the Bioethics Centre at the Lithuanian University of Health Sciences to conduct the present systematic review and meta-analysis, registration code: Nr. 2024-BEC2-01 (Annex 1). PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement criteria were followed for guiding this systematic review [16]. According to the database search tool applied, research publications were found in databases such as PubMed/Medline, Cochrane, and ScienceDirect.

1.2 Focus question

The following focus question was framed according to the problem, intervention, comparison, and outcome (PICO) process (Table 1): What is the effect of PRF on maxillary sinus floor elevation.

Table 1. PICO framework

Component	Description
Population (P)	Healthy adult patients who need maxillary sinus floor elevation for a dental implant.
Intervention (I)	Maxillary sinus floor augmentation with bone plastic material and PRF
Comparison (C)	Maxillary sinus floor augmentation with bone graft alone
Outcome (O)	New bone formation, Bone height, ISQ, Bone Density, Schneiderian membrane thickness

1.3 Types of Publication

This systematic review covered human studies that were published in the English language.

1.4 Types of studies

The review included all human randomized clinical trials, from January 2018 until December 2024 on patients who had done maxillary sinus floor elevation before dental implant placement which are 18 years and older. Articles with patients that underwent maxillary sinus floor elevation with PRF only.

1.5 Information sources

The literature was sourced from PubMed/Medline, Cochrane, and Science Direct databases. Filters were used to ensure that the studies included were in English and were published between January

2018 and December 2024. The reference lists of the chosen papers were manually searched for additional related publications. Grey literature, letters, editorials, PhD thesis, abstract case series, case reports, cross-sectional studies, reviews, unpublished literature as well as other databases were not included in the search strategy of the present systematic review.

1.6 Type of population

Healthy adult patients without any systematic disease maxillary sinus floor elevation in the posterior zone.

1.7 Literature search and screening

Research publications were searched from January 29th, 2018 until December 29th, 2024 based on Preferred reporting items for systematic reviews and meta-analysis (PRISMA) [16] guidelines in PubMed/Medline, Cochrane, and Science Direct databases using the database's search tool. Articles were chosen according to the inclusion and exclusion criteria. Titles and abstracts were initially screened, and full-text papers were then separated for review. The use of different combinations of keywords was used: Platelet-Rich Fibrin, Maximillary Sinus Floor Augmentation, Bone Graft, Dental Implants (Table 2).

Table 2. Search and screening

1st concept	((": platelet rich fibrin "[Mesh]) OR "Maxillary sinus floor augmentation "[Mesh]) OR "Dental Implants"[Mesh]
2nd concept	(("Platelet Rich Fibrin "[Mesh]) OR " Maxillary Sinus Floor Augmentation" [Mesh]) OR "Dental Implants"[Mesh] OR “Bone Graft” (TW)
3rd concept	(("Platelet-Rich Fibrin "[Mesh]) And "Sinus Floor Augmentation"[Mesh]) And "Dental Implants"[Mesh] And” Bone Graft” [Mesh] (TW)
4th concept	(("Platelet-Rich Fibrin "[Mesh]) And ("Maxillary Sinus Floor Augmentation "[Mesh])

Text word (TW)

1.8 Inclusion and exclusion criteria for the study selection

Inclusion criteria

- Articles from 2018 to 2024
- Adult patients 18+

- Maxillary sinus floor elevation for dental implants using bone plastic material
- Maxillary sinus elevation with using bone plastic material and PRF
- Posterior region of maxillary sinus floor elevation
- Clinical trials
- randomized controlled trials (RCTs),
- prospective and retrospective cohort studies and case-control studies.
- In ENGLISH
- Full text
- Follow-up

Exclusion criteria

- Systemic review
- Literature review
- Clinical studies on patients with less than 10 patients
- Studies other than human
- Patients that less than 18 years old
- Anterior maxillary sinus floor elevation

1.9 Sequential search strategy

The methodology for this systematic review was executed in a series of distinct stages. Initially, a search was conducted to identify articles using specific keywords previously mentioned. Following this, any duplicates found across various databases were removed. Next, each publication was subjected to a detailed assessment to evaluate its relevance and conformity with the established selection criteria, which was based on an analysis of the full text. Publications that successfully met these criteria were subsequently included in this systematic review.

1.10 Data extraction

According to the aim and tasks of the review in the form of variables, data extracted from the articles were. The data items extracted are listed below.

1.11 Data items

- First author and publication year
- Study design
- Total number of patients
- Mean age
- Group of study

- Type of bone graft
- Type of PRF
- Maxillary sinus floor augmentation in the posterior region
- Maxillary sinus floor elevation with PRF only
- Outcome measure – new bone formation, bone height, ISQ, bone density, Schneiderian membrane thickness
- Follow-up examination

1.12 The risk of bias assessment

The five studies that met the inclusion criteria were assessed for methodological quality by two researchers using the JBI Critical Appraisal Checklist for randomized controlled trials (Annex 2). The RCT checklist contains 13 assessment criteria. Every criterion was given a rating of 'yes', 'no', 'unclear' or 'not applicable. The checklists do not have a specific way to summarize if the risk is high or low, so there was no appropriate way to classify them as having high or low risk of bias, but whether a study is of low, moderate, or high quality. In this systematic review, all the prospective studies have high quality and low probability of containing bias, with strategies that did not mention addressing incomplete follow-up. In contrast, the randomized controlled clinical trials in this review followed some protocols to reduce the risk of bias. The results of risk of bias assessment are summarized in Table 3.

Table 3. Risk of bias JBI

Study	Year	Study design	Checklist											
			Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Nizam et al. 2018 [17]	2018	Randomized controlled trial	+	-	+	-	-	+	-	+	+	+	-	+	-
Pichotano et al. 2019 [18]	2019	Randomized Controlled Trial	+	-	+	-	-	+	-	-	+	+	+	+	?
Salimzade et al. 2022 [19]	2022	Randomized Controlled Trial	+	-	+	-	-	+	-	+	+	+	-	+	+
Almeida Malzoni et al. 2023 [20]	2023	split-mouth Randomized Controlled Trial	+	-	+	-	-	+	-	+	+	+	+	+	+
Shiezadeh et al. 2023 [21]	2023	Randomized Controlled Trial	+	-	+	-	-	+	-	+	+	+	+	+	+

1.13 Synthesis of the results

Relevant data points from the previously mentioned studies were systematically gathered and structured into tabular formats for ease of comparison and analysis. Table n. 4 are organized according to year of publication, study design, patients, group of study, bone graft, PRF type, area of elevation and age table n. 5 are summarized the outcome of each study, new bone formation, bone height, ISQ, Schneiderian membrane thickness.

1.14 Statistical analysis

The meta-analysis utilized the Cohen's d measure within a random-effects model. This approach accounts for both the within-study variance and the between-study variance, offering a more nuanced view of the treatment's effectiveness across different research contexts. The effect size provides a numerical representation of the magnitude of the treatment's impact, with confidence intervals offering a range within which the true effect size is likely to fall, The meta-analysis was carried out using SPSS software, version 29.0, while the management of articles was facilitated by Mendeley reference management software, version 2.79 (available at www.mendeley.com).

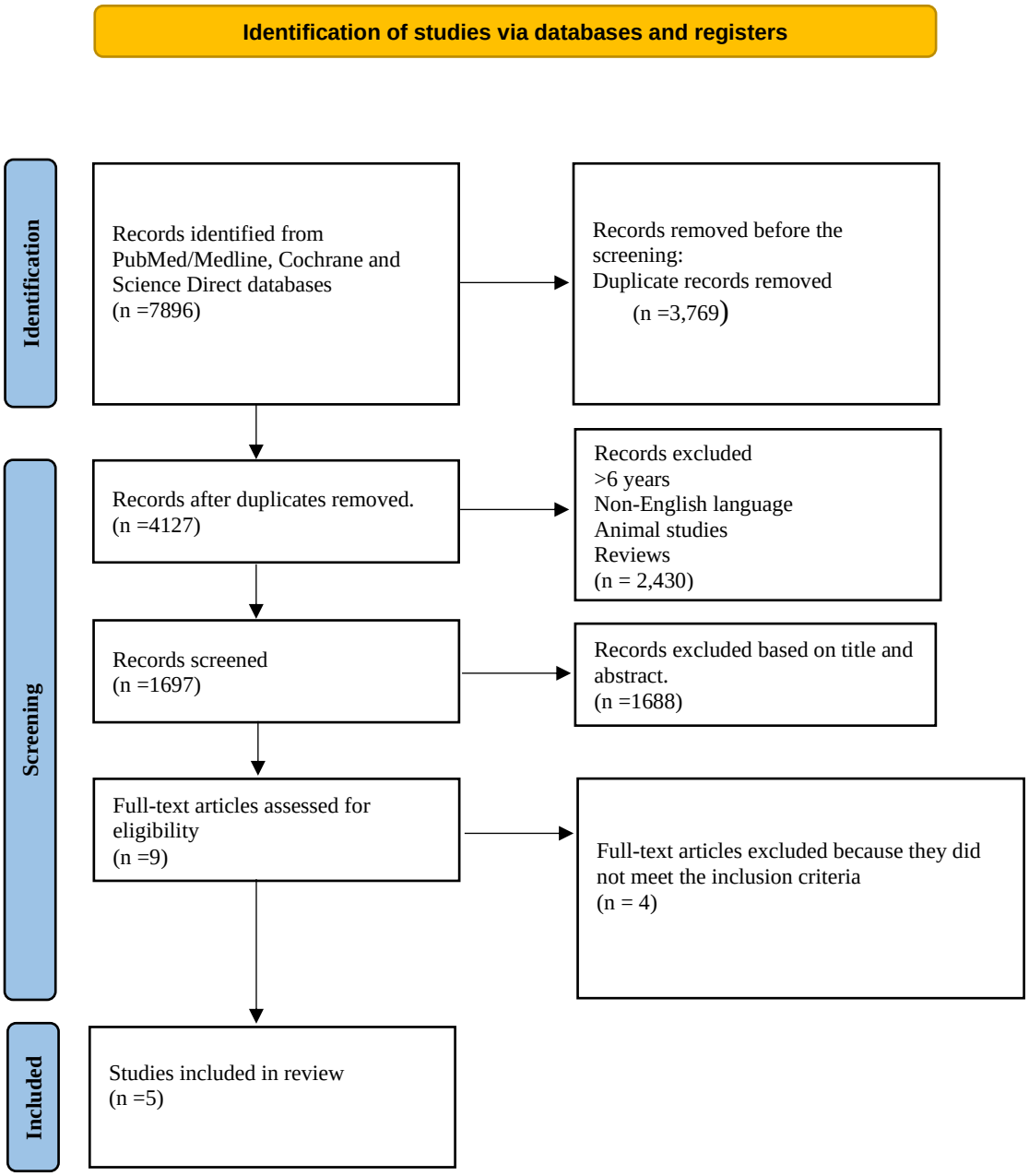

Fig. 1. PRISMA flow diagram summarizing the search strategy and study selection.

2. SYSTEMIZATION AND ANALYSIS OF DATA

2.1 Study selection

During the database exploration phase, the search across PubMed/Medline, Science Direct, and the Cochrane Library identified 2630, 2322, and 2944 articles respectively, adding up to an initial tally of 7896 potentially relevant articles. Post elimination of 3769 duplicate entries, 4127 articles remained under consideration. The next phase of scrutiny led to the exclusion of 2430 articles due to reasons such as being published more than 6 years ago, written in languages other than English, on animal research, or being review articles. An additional 1675 articles were disregarded after evaluating their titles and abstracts for relevance, narrowing the selection down to 9 articles for full review based on inclusion and exclusion criteria. Four articles were not included in this article because of the materials used by test groups [22-24], the article with 3 groups of study [25]. Ultimately, 5 records were meticulously reviewed and met the stringent criteria for inclusion in this systematic review.

2.2 Study characteristics

This review systematically examined five studies, encompassing randomized controlled trials, and reported on 112 maxillary sinus floor elevation procedures conducted in 84 patients. Three of the studies [5,8,9] utilized deproteinized bovine bone mineral (DBBM) in their maxillary sinus floor elevation (MSFE) procedures. Shiezadeh et al. [6] opted for an allograft material for MSFE, while Salimzade [7] employed a xenograft. Four of these articles [5, 7-9] incorporated leukocyte-platelet-reach fibrin (L-PRF) in the test groups, whereas one study [6] used platelet-rich fibrin (PRF) for its test group in MSFE scenarios. The MSFE procedures across all five articles were performed in the posterior region of the maxilla. The characteristics of the studies included are detailed in Table 4.

Table 4. Characteristics of included study.

Author	Study design	Patients	Age	Group of study		Bone graft	PRF type
				Test group	Control group		
Nizam et al. 2018 [17]	Randomized controlled trial	13	mean age ± SD; 49.92 ± 10.37	MSFE DBBM +L-PRF (n=13)	MSFE DBBM alone (n=13)	(DBBM)	L-PRF
Pichotano et al. 2019 [18]	Randomized controlled trial	12	Mean (age of 54.17 ± 6.95 years)	MSFE DBBM+ L-PRF (n=13)	MSFE DBBM alone (n=13)	(DBBM)	L-PRF
Salimzade et al. 2022 [19]	Randomized controlled trial	15 (30 MSFE)	the mean age of 53.6± 0.18 years	MSFE PRF with bone graft (n=15)	MSFE bone graft with membrane (n=15)	xenograft	L-PRF
Almeida Malzoni et al. 2023 [20]	Randomized controlled trial	24	mean age of 54.08±10.07	MSFE L-PRF with bone graft (n=24)	MSFE only bone graft (n=12)	(DBBM)	L-PRF
Shiezadeh et al. 2023 [21]	Randomized controlled trial	20	Group with PRF: mean (42.7 5.79 years) Group without PRF: (40.3 4.83 years)	MSFE PRF with bone graft (n=10)	MSFE-only bone graft (n=10)	Allograft	PRF

FDBA- freeze-dried bone allograft

DBBM- deproteinized bovine bone mineral

MSFE-maxillary sinus floor elevation

PRF- platelet reach fibrin

L-PRF- leukocytes platelet reach fibrin

2.3 Outcome

All the 5 studies are compered the effect of PRF combine with bone graft to bone graft only on the MSFE. Table 5 describes the effect of the test and control groups on: new bone formation, bone height, ISQ, Schneiderian membrane thickness.

2.3.1 New bone formation

Almeida Malzoni et al. [20] show in the test group using L-PRF+DBBM, new bone formation was significantly higher (18.35 ± 5.62%) compared to the control group using DBBM alone (12.95 ± 5.33%) with a p-value of 0.0135. In Shiezadeh et al. [21] employing PRF showed a new bone formation percentage of 43.25% in Group A compared to 38.25% in Group B (without PRF), indicating a non-significant trend towards improved outcomes with PRF (p=0.087). Article Nizam et al.[17] present the comparison between the test group (with PRF) and the control group (without PRF) showed nearly identical percentages of new bone formation (21.38% vs. 21.25%, respectively), suggesting no significant difference with a p-value of 0.96. Pichotano et al.[18] demonstrated a significant difference in new bone formation with the test group (with PRF) showing a higher percentage (44.58%) compared to the control group (30.02%) with a p-value of 0.0087 (Table 5).

2.3.2 Bone height

Almeida Malzoni et al. [20] bone height increase in the control group was 0.48 cm^3. In the test group, DBBM4 resulted in a bone height of 0.58 cm^3 and DBBM8 in 0.72 cm^3. The article does not specify a p-value directly related to bone height differences between these groups. Shiezadeh et al. [21] the bone height in Group A (with PRF) was 2.74 mm compared to 2.72 mm in Group B (without PRF). This comparison indicates a minimal difference, with the p-value not explicitly stated for bone height. Nizam et al. [17] bone height was reported as 13.60 mm in the test group (with PRF) versus 13.53 mm in the control group (without PRF). The p-value for this comparison was 0.88, indicating no statistically significant difference in bone height between the groups. Pichotano et al. [18] this study does not provide direct measurements of bone height increase but focuses on the residual graft material, with the test group showing significantly less residual graft (3.59% ± 4.22) compared to the control group (13.75% ± 9.99), with a p-value of 0.0111 for this comparison (Table 5).

2.3.3 ISQ

Almeida Malzoni et al. [20] this study reported an ISQ comparison between the test group (L-PRF+DBBM) and the control group (DBBM), with the test group showing ISQ values ranging from LPRF+DBBM4 (72.19) to LPRF+DBBM8 (75.56). The p-value for this comparison was less than 0.0001, indicating a statistically significant difference favouring the test group. Pichotano et al. [18] indicate a comparison between the control group and the test group, with the control group having an

ISQ of 75.13 ± 5.69 and the test group an ISQ of 60.9 ± 9.35. The p-value for this comparison is 0.0003, suggesting a statistically significant difference between the two groups (Table 5).

2.3.4 Schneiderian membrane thickness

In article by Salimzade et al.[19] the control group, the baseline value was 1.85, and after 2 months, it increased to 2.54. In the test group, the baseline was 2.17, and after 2 months, it decreased to 1.77. This p-value is relatively high 0.2, indicating the results may not be statistically significant, and any observed differences might be due to random variation rather than a real effect (Table 5).

Table 5. Outcome variables of included studies

Author	New bone formation	Bone height	ISQ	Schneiderian membrane thickness	Follow-up
Nizam et al. 2018 [17]	Test group (with PRF) 21.38 ± 8.78%vs. Control group (without PRF) 21.25 ± 5.59 % (p = 0.96)	Test group (with PRF) 13.60 ± 1.09) vs. Control group (without PRF 13.53 ± 1.20;(p = 0.88)	NR	NR	6 months follow-up
Pichotano et al. 2019 [18]	test group (with PRF) (44.58% ± 13.9%) vs. Control group (without PRF) (30.02% ± 8.42%; (P = .0087)	residual graft in the control group was (13.75% ± 9.99%) vs. Test group (3.59 ± 4.22) (P = .0111)	control group (75.13 ± 5.69) vs. Test Group (60.9 ± 9.35) P = (0.0003)	NR	Immediately after implant placement,4 and 8 months after sinus augmentation.
Salimzade et al. 2022 [19]	NR	NR	NR	Control group Baseline 1.85, after 2 months 2.54; Test group Baseline 2.17, after 2 months 1.77 (p=0.2)	2 months follow-up
Almeida Malzoni et al. 2023 [20]	test group (L-PRF+DBBM) (18.35 ± 5.62%) control group (DBBM) 12.95 ± 5.33%) (p=0.0135)	Control group – mean t1-t2 0.48(cm3) Test group – DBBM4 0.58 (cm3) -DBBM8 0.72(cm3)	Test goup-LPRF+DBBM4 to LPRF+DBBM8 (72.19±5.43) and control (75.56±4.60) p= (<0.0001)	NR	1-year follow-up
Shiezadeh et al. 2023 [21]	Group A (with PRF) 43.25% vs. Group B (without PRF) 38.25% (p=0.087).	Group A (with PRF) 2.74 mm vs. Group B (without PRF) 2.72 mm)	NR	NR	Average of 33 months follow-up

ISQ- implant stability quotient

NR- not reported

PRF- platelet reach fibrin

L-PRF- platelet reach fibrin

3. META-ANALYSIS

Meta-Analysis: Continuous Outcomes of New Bone Formation with Raw Data

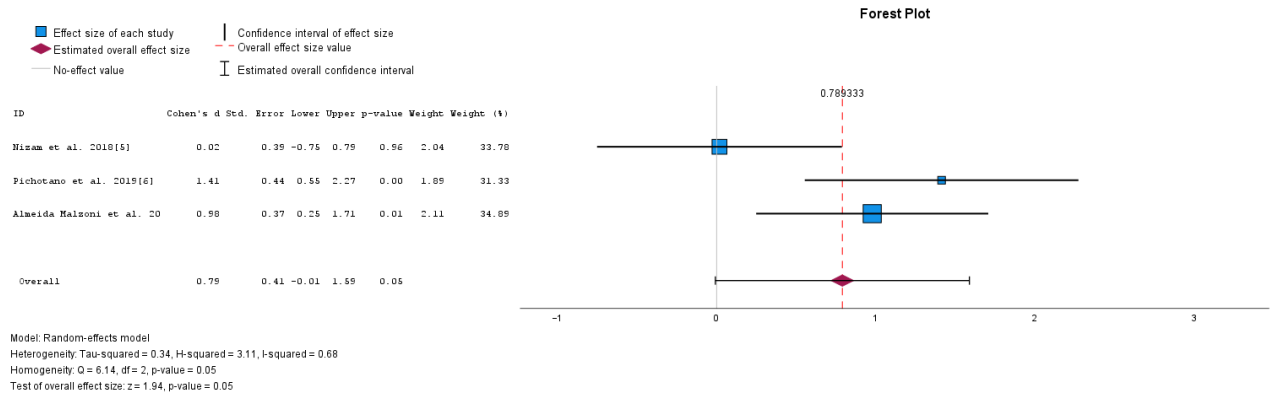

Fig 2.jpg **Forest Plot New Bone Formation**

Meta-Analysis Summary

Data Type	Raw
Outcome Type	Continuous
Effect Size Measure	Cohen's d
Model	Random-effects
Weight	Inverse-variance[a]
Estimation Method	REML
Standard Error Adjustment	None

effects weights including both within- and between-study variance.

Case Processing Summary

	N	Percent
Included	3	60,0%
Missing	2	40,0%
Invalid[a]	0	0,0%
Total	5	100,0%

variance or standard error, or insufficient study size.

Effect Size Estimates

	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval	
					Lower	Upper
Overall	,789	,4071	1,939	,052	-,008	1,587

Meta-Analysis: Continuous Outcomes of Bone Height with Raw Data

Meta-Analysis Summary

Data Type	Raw
Outcome Type	Continuous
Effect Size Measure	Cohen's d
Model	Random-effects
Weight	Inverse-variance[a]
Estimation Method	REML
Standard Error Adjustment	None

effects weights including both within- and between-study variance.

Case Processing Summary

	N	Percent
Included	4	80,0%
Missing	1	20,0%
Invalid[a]	0	0,0%
Total	5	100,0%

variance or standard error, or insufficient study size.

Effect Size Estimates

	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval	
					Lower	Upper
Overall	-,005	,2321	-,020	,984	-,460	,450

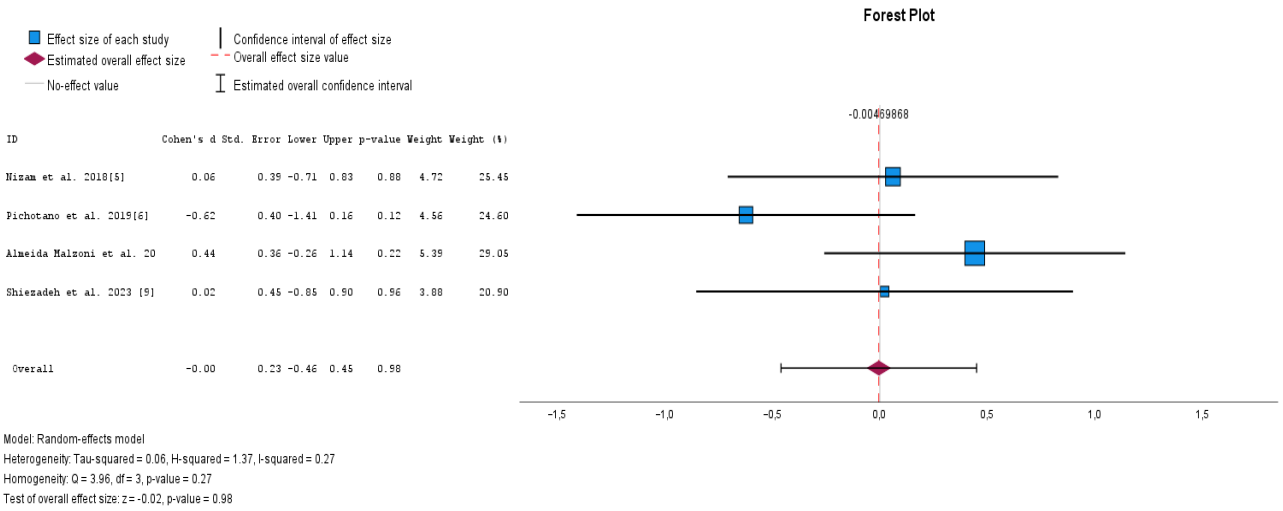

Fig 3.jpg **Forest Plot Bone Height**

4. DISCUSSION

Most of the PRF In this systematic review, the impact of Platelet-Rich Fibrin (PRF) on Maxillary Sinus Floor Elevation (MSFE) for dental implants is explored. The following parameters were examined: new bone formation, bone height, implant stability quotient (ISQ), bone density, and Schneiderian membrane thickness during MSFE with or without PRF. Studies within this review underscore the presence of crucial components in PRF, including fibrin matrix, platelets, growth factors, leukocytes, and stem cells [26]. These elements collectively contribute to the efficacy of PRF in various regenerative processes. The prevailing focus of clinical research on PRF in implantology centers is around enhancing clinical outcomes in sinus floor elevations. PRF is particularly investigated as a standalone grafting material, often employed simultaneously with implant placement [27].

The five articles encompassed in this study collectively demonstrate the effectiveness of PRF in Maxillary Sinus Floor Elevation.

The varied results across these studies underscore the complexity of bone regeneration and the potential role of PRF. While Almeida Malzoni et al. [20] and Pichotano et al. [18] provide strong evidence supporting the beneficial effects of PRF in enhancing new bone formation, Shiezadeh et al.[21] and Nizam et al. [17] present more nuanced outcomes, suggesting that the effectiveness of PRF might be influenced by specific conditions or variables not fully explored in these studies. According to meta-analysis of new bone formation indicated a marginal significance level with a p-value of 0.052. Since this value is slightly above the conventional threshold, it suggests that the difference in new bone formation observed due to the treatment with PRF might not be considered statistically significant.

The collective findings from these studies suggest a nuanced understanding of factors influencing bone height increase. The use of DBBM appears to enhance bone height more effectively than the control treatments, as indicated by the results from Almeida Malzoni et al.[20]. This could imply that the osteoconductive properties of DBBM provide a scaffold that promotes bone growth more effectively than other materials or the absence of such materials. In the meta-analysis concerning bone height, the overall effect size was -0.005 with a very high p-value of 0.984, which indicates there was no statistically significant difference in bone height as a result of the treatment.

In contrast, the use of PRF, as explored by Shiezadeh et al.[21] and Nizam et al. [17] does not show a significant impact on bone height increase. This could be due to the role of PRF primarily in enhancing healing and not necessarily in providing a structural basis for bone growth. The minimal

differences observed, and the lack of statistical significance suggest that while PRF may have benefits in wound healing or reducing inflammation, its direct contribution to bone height may be limited.

The significance of residual graft material reduction in the test group, as reported by Pichotano et al. [18] suggests an interesting angle for future research. The correlation between lower residual graft material and possibly more effective bone regeneration or remodeling highlights the complexity of bone healing processes and the potential for certain treatments to facilitate more natural bone structure restoration.

The findings from these studies highlight the importance of material choice and treatment method in achieving optimal implant stability. The significant improvement in ISQ values with the use of L-PRF in combination with DBBM suggests that this combination not only promotes bone growth but also enhances the stability of the implant in the newly formed bone. The mechanism behind this could involve the synergistic effect of L-PRF's growth factors and DBBM's osteoconductive properties, facilitating faster and stronger bone integration with the implant.

On the other hand, the reduced ISQ values in the test group reported by Pichotano et al. [18] raise questions about the materials or methods used in this group. Without specific details on the treatment differences, it's challenging to pinpoint the cause of reduced stability. However, it suggests that not all treatment combinations or materials yield the same positive effect on implant stability, emphasizing the need for careful selection based on evidence of effectiveness.

The increase in membrane thickness in the control group could be interpreted in several ways. It may reflect a natural variability in membrane thickness over time, or it could indicate a response to physiological factors or interventions that were not controlled for in the study. Without statistical significance, it is challenging to draw concrete conclusions about the clinical relevance of this increase.

The decrease in thickness in the test group is intriguing, as it suggests that the intervention might have had a potential effect on reducing membrane thickness. However, the lack of statistical significance (p-value of 0.2) cautions against overinterpreting this result. It's possible that the intervention could influence membrane thickness in a beneficial way, but the evidence from this study alone is insufficient to confirm such an effect.

Recent investigations have unveiled encouraging results concerning the use of PRF in facilitating bone regeneration. Research by Mazor et al. [28] and Diss et al. [29] has shown that in the context of direct sinus lifts using the lateral window approach, initial postoperative panoramic X-rays (conducted 8–10 days following the procedure) displayed implants positioned within the sinus cavity

without dense tissue envelopment, with the PRF filler appearing radiolucent. However, at the six-month mark post-sinus lift, the area around the implants in the sinus cavity was characterized by dense, bone-like tissue. Radiological evaluations consistently demonstrated significant bone augmentation, with gains ranging from 7 to 13 mm using longer implants. In this methodology, implants acted as stabilizers to demarcate the required bone volume, with the shape of the implant not affecting the new sinus floor's location. Furthermore, in the study by Diss et al. [29] that applied the Bone Added Osteotome Sinus Floor Elevation (BAOSFE) Technique, PRF was employed as a grafting substance. Their results showed a bone increase of 5.8 and 5.2 mm on the mesial and distal sides of the implant, respectively. Although the findings from both studies were akin, the significance of the research outcomes was notably profound.

This systematic review possesses certain limitations that merit consideration. Primarily, variations exist in the maxillary sinus floor elevation technique, diverse dental implant types employed, and various conditions that could impact the outcomes. The acknowledgment of limitations in the studies includes factors such as sample size. Additional research is warranted to conclusively establish and substantiate the efficacy of Platelet-Rich Fibrin (PRF) in maxillary sinus floor elevation.

Looking ahead, it is imperative to recognize the evolving landscape of regenerative dentistry and the continuous refinement of techniques and materials used in maxillary sinus floor elevation. While the studies reviewed here contribute valuable insights, they also underscore the need for more comprehensive investigations. Future research endeavors could delve into exploring the optimal combination of PRF with other biomaterials or growth factors, aiming to enhance its efficacy in bone regeneration. Additionally, a deeper understanding of the specific conditions that may influence the outcomes of PRF in MSFE is essential. Investigations into the long-term effects, such as the stability of newly formed bone and the durability of implant integration, could shed light on the sustained benefits of PRF in clinical practice. Furthermore, considering the dynamic nature of dental implant technology, future studies may also explore the potential synergies between PRF and emerging implant designs or surfaces, potentially unlocking novel approaches for achieving superior clinical outcomes. As the field progresses, embracing a multidisciplinary approach that integrates insights from biomaterial science, molecular biology, and clinical practice will be crucial in advancing our understanding and harnessing the full regenerative potential of Platelet-Rich Fibrin in the context of maxillary sinus floor elevation.

CONCLUSION

1. New bone formation with the use of PRF is not statistically significant by conventional standards.
2. There is no demonstration of a statistically significant impact on increasing bone height.
3. The ISQ demonstrates a significant positive impact of PRF when used in conjunction with MSFE.
4. The impact of PRF on Schneiderian membrane thickness does not demonstrate significant changes.

5. ACKNOWLEDGEMENT

It has been a distinct honor to work under the mentorship of Professor Gintaras Juodžbalys. His exceptional guidance and profound expertise have profoundly impacted my academic and personal development. Professor Juodžbalys's dedication to mentoring goes beyond traditional boundaries, offering deep insights and fostering a commitment to excellence. I am immensely grateful for his inspirational support and the invaluable knowledge imparted to me, which has significantly shaped my professional path. My appreciation for his mentorship is deep and enduring.

6. PRACTICAL RECOMMENDATION

PRF be considered as an adjunctive treatment in MSFE procedures, particularly in cases where patients exhibit poor bone quality and volume, necessitating augmentation for successful dental implant integration. PRF's potential to enhance implant stability, as evidenced by improvements in the ISQ.

Furthermore, future studies should clarify the mechanisms through which PRF contributes to tissue regeneration and how these effects can be optimized in clinical practice.

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ANNEX 1

LIETUVOS SVEIKATOS MOKSLŲ UNIVERSITETO
BIOETIKOS CENTRAS

Medicinos akademija (MA) Nr. 2024-BEC2-017
Vientisųjų studijų programa - Odontologija (anglų kalba)
5 k. studentas: Oren Babich
Darbo vadovas: Profesorius Gintaras Juodžbalys
Veido ir žandikaulių chirurgijos klinika

DĖL PRITARIMO TYRIMUI

LSMU Bioetikos centras, įvertinęs pateiktus dokumentus, moksliniam-tiriamajam darbui tema „The effect of platelet-rich fibrin in maxillary sinus floor elevation“ P R I T A R I A .

dr. Aušra Urbonienė 2024-01-12 13:18:11

** Pastaba: šis pritarimas neatleidžia tiriamąjį mokslinį darbą vykdančių asmenų nuo prievolės laikytis Bendrojo duomenų apsaugos reglamento nuostatų ir nuo atsakomybės gauti nacionalinio arba regioninio bioetikos komiteto leidimą, jei toks leidimas būtinas pagal LR Biomedicininių tyrimų etikos įstatyme numatytus reikalavimus.*

ANNEX 2

Assessor:	Date of Appraisal:	Record Number:
Study Author:	Study Title:	Study Year:

Internal Validity		Choice - Comments/Justification	Yes	No	Unclear	N/A
Bias related to selection and allocation						
1	Was true randomization used for assignment of participants to treatment groups?		☐	☐	☐	☐
2	Was allocation to treatment groups concealed?		☐	☐	☐	☐
3	Were treatment groups similar at the baseline?		☐	☐	☐	☐
Bias related to administration of intervention/exposure						
4	Were participants blind to treatment assignment?		☐	☐	☐	☐
5	Were those delivering the treatment blind to treatment assignment?		☐	☐	☐	☐
6	Were treatment groups treated identically other than the intervention of interest?		☐	☐	☐	☐
Bias related to assessment, detection and measurement of the outcome						
7	Were outcome assessors blind to treatment assignment?		Yes	No	Unclear	N/A
	Outcome 1		☐	☐	☐	☐
	Outcome 2		☐	☐	☐	☐

	Outcome 3		☐	☐	☐	☐
	Outcome 4		☐	☐	☐	☐
	Outcome 5		☐	☐	☐	☐
	Outcome 6		☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐

8	**Were outcomes measured in the same way for treatment groups?**		**Yes**	**No**	**Unclear**	**N/A**
	Outcome 1		☐	☐	☐	☐
	Outcome 2		☐	☐	☐	☐
	Outcome 3		☐	☐	☐	☐
	Outcome 4		☐	☐	☐	☐
	Outcome 5		☐	☐	☐	☐
	Outcome 6		☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐

9	**Were outcomes measured in a reliable way**		**Yes**	**No**	**Unclear**	**N/A**
	Outcome 1		☐	☐	☐	☐
	Outcome 2		☐	☐	☐	☐
	Outcome 3		☐	☐	☐	☐

	Outcome 4		☐	☐	☐	☐
	Outcome 5		☐	☐	☐	☐
	Outcome 6		☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐

Bias related to participant retention

10	**Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?**					
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
	Outcome 2		**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
	Outcome 3		**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐

Outcome 4			**Yes**	**No**	**Unclear**	**N/A**
Result 1			☐	☐	☐	☐
Result 2			☐	☐	☐	☐
Result 3			☐	☐	☐	☐
Outcome 5			**Yes**	**No**	**Unclear**	**N/A**
Result 1			☐	☐	☐	☐
Result 2			☐	☐	☐	☐
Result 3			☐	☐	☐	☐
Outcome 6			**Yes**	**No**	**Unclear**	**N/A**
Result 1			☐	☐	☐	☐
Result 2			☐	☐	☐	☐
Result 3			☐	☐	☐	☐
Outcome 7			**Yes**	**No**	**Unclear**	**N/A**
Result 1			☐	☐	☐	☐
Result 2			☐	☐	☐	☐
Result 3			☐	☐	☐	☐

Statistical Conclusion Validity

11	**Were participants analysed in the groups to which they were randomized?**		

Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 2		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 3		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 4		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 5		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐

Outcome 6		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 7		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐

12	**Was appropriate statistical analysis used?**					
Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 2		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 3		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐

Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 4		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 5		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 6		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐
Outcome 7		**Yes**	**No**	**Unclear**	**N/A**
Result 1		☐	☐	☐	☐
Result 2		☐	☐	☐	☐
Result 3		☐	☐	☐	☐

		Yes	**No**	**Unclear**	**N/A**

13	**Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?**		☐	☐	☐	☐

Overall appraisal: **Include:** ☐ **Exclude:** ☐ **Seek Further Info:** ☐

Comments:

Table 3 – The JBI Critical Appraisal Tool for RCTs