

# INPLASY

## Efficacy of Probiotics on Clinical Parameters and Human Immune Response in Peri-Implant Diseases: A systematic Review and Meta-Analysis of Randomized Clinical Studies

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### ADMINISTRATIVE INFORMATION

**Support** - None.

**Review Stage at time of this submission** - Completed but not published.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202410051

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 January 2024 and was last updated on 12 January 2024.

### INTRODUCTION

**Review question / Objective** Are probiotics able to favorably modify clinical and immunological biomarkers determinants of peri-implant pathologies? The aim of the present systematic and meta-analytic approach of randomized clinical studies was to evaluate the efficacy of probiotics in the treatment of peri-implant oral diseases.

**Condition being studied** Peri-implant oral diseases (peri-implant mucositis and peri-implantitis) are a group of pathologies of an infectious nature, which describe, in the case of peri-implant mucositis, an inflammatory lesion of the mucosa surrounding a dental implant, while in peri-implantitis the supporting bone is affected. The most important parameter for the diagnosis of peri-implant mucositis is bleeding on probing, with a gentle pressure of less than 0.25 N; however, in peri-implantitis alterations appear at the level of

the crestal bone and the presence of purulent liquid in the affected areas is frequent. This last aspect is the reason why peri-implantitis, unlike mucositis, is considered an irreversible pathology.

### METHODS

**Search strategy** Two reviewers (NL-V, AL-V) independently searched four electronic databases (MEDLINE/PubMed, Embase, Cochrane Central, Web of Science,) until December 2023, using the terms Medical Subject Headings (MeSH): Peri-Implantitis\* / diagnosis OR Peri-Implantitis\* / prevention & control OR Mucositis\* AND Dental Implants\* AND Dental Plaque\* AND Probiotics / therapeutic use\* AND Lactobacillus\* AND Probiotics\* / therapeutic use\* AND Humans\*. In addition, a manual search and consultations in the gray literature were performed; the bibliographic references of the included studies were also consulted to obtain the most information and avoid bibliographic bias.

**Participant or population** Adult subjects with mucositis, peri-implantitis, or both.

**Intervention** Probiotic treatment.

**Comparator** Conventional treatment or no treatment.

**Study designs to be included** Randomized Controlled Trials.

**Eligibility criteria** (i) randomized clinical trials (single or double blind) that included in the study more than 10 subjects  $\geq$  18 years of age; (ii) with peri-implant pathologies; (iii) that provided data on clinical parameters and/or immunological follow-up indicative of peri-implant disease; (iv) with statistical methods that included mean numerical values and standard deviation, together with units with which to quantify mediator levels; (v) published in English.

**Information sources** Electronic databases (MEDLINE/PubMed, Embase, Cochrane Central, Web of Science). In addition, a manual search and consultations in the gray literature were performed; the bibliographic references of the included studies were also consulted to obtain the most information and avoid bibliographic bias.

**Main outcome(s)** Evaluate the efficacy of probiotics in the treatment of peri-implant oral diseases. Observe the effects of treatment on clinical parameters indicative of mucositis or peri-implantitis ( $\Delta$  PD;  $\Delta$  PI;  $\Delta$  BoP) and/or immunological parameters ( $\Delta$  IL- $\beta$ ;  $\Delta$  IL-6;  $\Delta$  IL-8).

**Quality assessment / Risk of bias analysis** Quality assessment: Joanna Briggs Institute for RCTs (JBI MASTARI). Risk of bias analysis: Cochrane Risk of Bias Tool (RoB2).

**Strategy of data synthesis** Data were analyzed using Review Manager software (RevMan Software. Version 5.4.1; The Cochrane Collaboration, Copenhagen, Denmark; 2020). Meta-analyses were performed for studies assessing peri-implantitis, mucositis and for different clinical and immunological variables, as well as a meta-analysis of pooled studies. All were based on mean difference (MD) and standard deviation (SD) to estimate continuous data and to evaluate categorical data, 95% confidence intervals (CI). Heterogeneity was considered unimportant with  $I^2 = 0-30\%$ ; moderate,  $I^2 = 40-50\%$ ; substantial  $I^2 = 60-75\%$  and considerable  $I^2 \geq 75\%$ . The threshold for statistical significance was set as  $p < 0.05$ . Due to the homogeneity of

results, a fixed-effects meta-analysis was performed.

**Subgroup analysis** Two meta-analyses were performed, one for studies evaluating probiotics in mucositis and one for studies evaluating probiotics in peri-implantitis. Clinical and immunological parameters and an analysis of grouped variables in both cases (mucositis and peri-implantitis) were analyzed independently.

**Sensitivity analysis** It was not necessary.

**Language restriction** English Language.

**Country(ies) involved** Spain.

**Keywords** Probiotic; Prebiotic; Peri-implant disease; Mucositis, Peri-implantitis; Immune-Response.

**Contributions of each author**

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