Study Title and Responsible Entity

We invite you to voluntarily participate in a clinical investigation entitled "Probiotics as adjuvants in non-surgical periodontal treatment: a randomized and placebo-controlled clinical trial", within the scope of the PhD in Biomedical Sciences of the Instituto Universitário Egas Moniz (IUEM), the entity responsible for this study, under the guidance of Professor Nuno Taveira and Prof. Dr Ricardo Castro Alves.

It is important for you to understand why this project is being developed and what its implications are. This document should help you make a free and informed decision about whether or not you wish to participate in this study.

Please take the time to read the following information carefully and talk to others if you wish. If something isn't clear to you, or if you feel you need additional information, don't hesitate to ask.

Participation in this study is voluntary, but if you decide not to participate, the clinical care for you by the Dental Clinic of the Instituto Universitário Egas Moniz (IUEM) will not be affected, in the present and in the future.

Your participation in the study is not remunerated, the administration of the products necessary for the development of the study is free of charge.

If you voluntarily decide to participate in this study, you will be asked to date and sign an Informed Consent Form before any specific study procedure is performed. You will receive a copy of this information sheet, and a copy of the signed informed consent form.

Study Objectives

The main objective of this randomized, placebo-controlled clinical trial, to be carried out at the Dental Clinic of the Instituto Universitário Egas Moniz (IUEM), is to evaluate the effectiveness of probiotics in the treatment of periodontitis, as a complement to conventional mechanical therapy. The secondary objectives of this study are to evaluate the effects of probiotics on the composition of oral microorganisms and on inflammation associated with periodontitis.

The clinical trial in which you will participate is placebo-controlled. This means that the activity of probiotics against periodontitis will be compared with the activity of a substance without therapeutic properties (placebo). The clinical trial is randomized, which means that the choice of participants taking probiotics or placebo is random.

Periodontitis is an oral disease caused by bacteria that accumulate around the tooth. Conventional treatment of periodontitis involves mechanical removal of plaque and local administration of antibiotics or antiseptics, which may have limited effectiveness due to bacterial resistance. It is necessary to look for alternatives to conventional therapeutic and preventive approaches. Probiotics can play an important role in this context. Probiotics are non-pathogenic bacteria that are naturally present in multiple foods (eg yogurts). Probiotics are regularly used to treat/prevent intestinal diseases and have also been proposed for the treatment and management of oral diseases including periodontitis.

Procedures in which it participates

Completion of a brief questionnaire with sociodemographic data and clinical history (5 minutes, 1st consultation); Conducting a standard periodontal examination, in which several measurements are taken around the teeth (10 minutes, 1st visit); Collection of biological

samples of gingival exudate with sterile paper strips (10 minutes, 1st visit); Performing a "scaling" consisting of mechanical cleaning of the teeth (15 minutes, 1st appointment).
At the first appointment, you will receive instructions on oral hygiene and taking probiotics/placebo. The probiotics used will be L. reuteri DSM 17938 and L. reuteri ATCC PTA 5289 that had promising results in short-term studies. The probiotics and placebo will be administered twice a day (one in the morning and one in the evening, after brushing the teeth) for 3 months, in the form of tablets.
The study has an expected duration of 6 months. The participant will be evaluated at baseline, and at 3 and 6 months. Assessment at 3 and 6 months consists of performing the standard periodontal examination and taking biological samples as explained above. The rate of adherence to taking the probiotics/placebo and potential adverse effects will be assessed at 3 months using questionnaires (Appendix 2).

Who can participate in the Study (Appendix 1)
Adults aged 18-65 years with periodontal health.
Who cannot participate in the Study (Appendix 1)
People who did not sign the informed consent; pregnant and lactating women; participants with inflammatory bowel diseases, diabetes, infectious diseases, transplant recipients; participants who regularly take the following medications (NSAIDs, corticosteroids, cyclosporine, and medications that reduce salivary flow or cause a dry mouth sensation); participants who took antibiotics and/or probiotics in the last 3 months;
participants who use antiseptics regularly; drug and/or alcohol users and smokers;
participants who received chemotherapy and/or radiotherapy for less than 1 year;
participants who received periodontal treatment for less than 6 months; participants with a mental illness that prevents autonomous decision-making; participants with lactose intolerance, gluten intolerance or allergy to one of the components of the probiotics/placebo.

Possible Benefits for Participants
Participation in the study is altruistic, with no monetary compensation for the participant. This study may contribute to improving your oral health. In case of positive results, the analyzed probiotics may be recommended for the prevention and maintenance of oral health. Your participation will provide the acquisition of knowledge that may benefit you and third parties in the future.

Possible risks for Participants
Therapy with probiotics can cause some side effects, namely gastrointestinal changes (eg gastric pain, nausea, diarrhea, change in peristalsis, change in taste) although these changes are rare. To assess potential side effects, you will need to complete a side effects questionnaire at the 3 month evaluation visit. Minimal discomfort may occur during the collection of biological samples.
If you become ill during this study, you should notify the team responsible for the study (Appendix 3).

Voluntary Participation and Right of Abandonment

The participant can withdraw from the study at any time, refuse and/or interrupt his/her collaboration in the study, without having to present any justification, however, he/she must inform the responsible team not to be contacted again. The participant can even decide whether to keep their data or prefer to have them destroyed/withdrawn from the study, within the scope of the right to erase their personal data. Your decision to discontinue participation in the study will not affect your clinical follow-up at the Dental Clinic of the Instituto Universitário Egas Moniz (IUEM).

The study, or parts thereof, may be interrupted at any time by decision of the health authorities or the Egas Moniz Ethics Commission (CEEM), responsible for its audit regarding compliance with appropriate conduct, in the safeguarding of rights and well-being. of the participants.

If the study takes longer than planned, you will be informed in good time and you will be free to voluntarily decide whether or not you want to continue to participate in the study.

Participant's responsibility

As a participant in a research study, it is your responsibility to attend scheduled evaluation appointments, as well as maintain good communication, whenever established and/or necessary with the responsible team. To facilitate the evaluation and communication periods, the participant will receive a card with scheduled appointments and contact details of those responsible (Annex 3). You will be notified by message one week before and the day before the assessment appointments. We ask that the participant provide their contact details, in order to make this communication possible. The contacts of those responsible for the study are made available to clarify any doubts that arise during the study, to communicate absences from appointments, study abandonment or emergency situations/side effects.

Sample Identification, Right to Confidentiality and Data Protection

Participants' data will be treated confidentially and are protected in accordance with the provisions of the General Data Protection Regulation (RGPD), Law 58 of 2019, and in accordance with the ethical standards approved by the Egas Moniz Ethics Commission (CEEM).

To guarantee the confidentiality and protection of the data collected, the anonymization procedure of your data will be carried out immediately after signing the Informed Consent, which will be valid for the entire duration of the study. This process consists of assigning a code made up of numbers and letters to each participant, so that they are not identifiable by their name, but only by the code. Decoding can only be carried out by those responsible for the study, who will be responsible for the database, in accordance with the legal provisions in force.

The biological samples collected within the scope of this study, duly anonymized, will be transferred for laboratory analysis to be carried out in foreign laboratories (Canada and Spain), with the consent of the participant, expressed in the informed consent statement. By signing this Informed Consent, you allow leftover samples to be retained for the duration of the project.

The study team will maintain confidentiality about the medical records of your participation in this Study, which will not be made available to the public. The participant has the right to

obtain access to his/her personal data and to receive a copy of the Study results. The biological samples collected will not be used for commercial purposes.

Data Retention Term and/or Deletion
The samples will be kept for a period of 4 years at the IUEM Dental Clinic under the responsibility of the team linked to the project. The samples will be destroyed after this period. An extension of the conservation of the samples may be requested, which will imply contacting the donors again to obtain their authorization.

Communication and Dissemination of Study Results
The results of the Study will be disseminated through doctoral reports, presentation at conferences, submission for publication in scientific journals and academic thesis. The information collected will be handled by the person(s) responsible for the study.
The results will be available at the end of the study and the participant has the right to access their data after analysis of the results. The participant must request it from the team responsible for the Study. The participant will not be identified in any report or publication of the Study.

Contacts:
Questions about the study, study procedures or any other questions can be directed to the persons listed on the consultation card (Appendix 3).

Principal Investigators of the Study:
Professor Doctor Nuno Taveira and Prof. Doctor Ricardo Alves
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Thank you so much for taking the time to read the Study Information. Do not hesitate to ask for clarification on any question that the approach to this document may have raised.

(Scratch what does not matter)
I ACCEPT/I DO NOT ACCEPT to participate in this study, confirming that I have been informed about the conditions of the study and that I have no doubts.

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(Signature of the participant or, in the case of minors, of the parent or legal guardian)