ISRCTN11832395 https://doi.org/10.1186/ISRCTN11832395

Feasibility study: Can reducing periodontal infection (gum disease) slow the progression of cognitive impairment associated with Alzheimer's disease?

Submission date
20/10/2022

Recruitment status
No longer recruiting

Registration date
31/10/2022

Overall study status
Completed

Last Edited
04/09/2025

Condition category
Oral Health

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Alzheimer’s disease has recently been linked to oral health and certain bacteria that are found in the mouth (oral bacteria). We want to see whether, with appropriate dental treatment we can improve Oral health (oral hygiene, how well we clean our teeth and gums) and reduce the number of oral bacteria in people living with memory loss. If the study is successful, we want to complete a bigger study to see if keeping teeth and gums clean can slow the progression of Alzheimer’s disease

Who can participate?
Adults aged 60+ years with Mild Cognitive Impairment (MCI) or early-stage Alzheimer's Disease (AD) and capacity to consent will be recruited to the study. As well as a diagnosis of AD or MCI, participants must have gum disease, which will be assessed at screening by a study dentist. As gum disease is very prevalent as we get older it is likely that most participants who are screened will have sufficient gum disease to qualify for study inclusion. Participants will be asked to have a study partner who can attend at least the first appointment when the capacity to consent is determined.

What does the study involve?
Eligible participants who give informed consent will be allocated at random to either the control or the treatment group. Control group participants will be told they have gum disease, provided with a gum health care leaflet and an electric toothbrush, and advised to attend their dentist, but will not receive study treatment. Treatment group participants will be given the same gum health leaflet and an electric toothbrush, and allocated to a dental practice for gum disease treatment delivered by specially trained dentists in a way that is personal to the participant. Both study groups will assessed for cognition and gum health at screening, 6 and 12 months and samples of blood and saliva will be taken at these visits so that the bacterial load and levels of some inflammatory proteins can be monitored over the course of the study. At the 12-month appointment participants will be asked to take part in a short interview to gather their thoughts

about the study. For participants who join the study at the start of recruitment there will be a final 18-month assessment of cognition. Participants in the control group will be offered study treatment after they have completed the study.

What are the possible benefits and risks of participating?
The dental treatment the participant will be given will be routine. Every effort will be made to alleviate any pain or discomfort with a dental cause. Risks of treatment will be no greater than those encountered when they attend an appointment with their own dentist.
When necessary, an injection to numb the mouth before treatment will be given to minimise any discomfort. A gel will be applied prior to the injection to minimise any discomfort from the injection itself.
The participant will be asked to have an X-ray to determine what treatment is needed. This is a normal requirement prior to dental treatment, and the dose of radiation that they receive from the X-ray is low. The X-rays will enable the dentist to spot problems and signs of disease that may not be visible on the surface of your teeth and gums when the dentist examines them. The X-rays are necessary to reach a diagnosis and formulate the best treatment plan.
If it is thought to be necessary, the participant will be asked to take a short course of antibiotics, and it is possible that they could be allergic to the antibiotic prescribed. The dentist will take a full medical history to make sure they are not prescribing something that they are known to be allergic to. They will also provide advice to the participant and project partner regarding what to do and who to contact if they feel unwell after taking the antibiotics. As with all antibiotics, there is a risk of gut problems which can cause symptoms whilst taking a course of antibiotics or up to 2 months afterwards. Noticeable symptoms may be changed bowel movements, diarrhoea, fever, loss of appetite, nausea, abdominal pain or tenderness. This can be caused by the bacteria Clostridium difficile and associated disease and if they notice any of these changes, they should arrange a consultation with their general medical practitioner (doctor).
When blood is taken there will be a sharp scratch from the needle, but this should not last long and is no different to giving blood for a blood test.

Where is the study run from?
University Hospitals Bristol and Weston NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
July 2022 to July 2025

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Nikki Hellin, nikki.hellin@bristol.ac.uk

Study website
https://www.bristol.ac.uk/dental/research/mysmile/

Contact information

Type(s)
Scientific

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
315223

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 53909, NIHR 203048, IRAS 315223

Study information

Scientific Title
The Oral Health for Brain Health (Mysmile) Study

Acronym

Mysmile

Study objectives
Most gum diseases are preventable and patients with active disease can be treated and returned to oral health. Therefore, stabilising gum health manages an important risk-factor for inflammatory diseases, including Alzheimer's Disease (AD). This clinical study will test the feasibility of a large-scale trial aiming to demonstrate whether our intervention with intensive dental care for periodontitis, facilitating a lessening of bacteria-induced inflammation, can achieve oral health in AD patients and slow their AD-disease progression.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/11/2022, West of Scotland Research Ethics Committee 5 (West of Scotland Research Ethics Service, Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK; +44 (0)141 3140213; WoSREC5@ggc.scot.nhs.uk), ref: 22/WS/0137

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Oral and dental health, Alzheimer's disease

Interventions
At screening, consent will be taken by a researcher trained in taking informed consent from those suffering from memory loss, a project partner will be present at the screening appointment before capacity to consent has been confirmed. This researcher will then assess cognition and confirm cognitive eligibility scores and then the study dentist will conduct the dental assessment and confirm dental eligibility. This will take place at one site and in one appointment to minimise study visits. The study dentist or a member of the dental team qualified in venepuncture will take as sample of blood and ask participants to swish a mouthful of mouthrinse and expectorate into a pot. The dental team will then provide eligible participants with an electric toothbrush, interdental brushes and toothpaste and gum health leaflet, and details of how the participant would like to be contacted about the study will be collected.

As confirmation of cognitive and dental scores is required for stratification eligible participants will not be told which group they have been randomised to on the day of screening as this would add too much time to the visit, instead they will be contacted by the means agreed the following day or after the weekend. Eligible participants will be randomised to control or treatment groups, and stratified so that each group has roughly equivalent numbers of individuals with MCI and mild periodontitis.

When contacted regarding the group they have been randomised to, those in the control group will be encouraged to seek dental treatment, and reminded that they can get study treatment at the end if they would like it. Those randomised to the treatment group will be told which dental practice this will be in, and we will endeavour to identify a practice near to the participant.

The practices who have agreed to deliver the dental treatment are those who provide training for newly qualified dental practitioners and are located in and around Bristol, a small number of participants will also be treated by clinicians on dental training pathways at Bristol Dental Hospital. The dentists in these practices/at the dental hospital will be trained by the Chief Investigator and senior study dentist, both periodontologists. They will also be on had to support the foundation dentists/specialty training pathway dentists as needed to ensure that the study treatment is carried out as planned. The dental intervention is based on standard treatment for periodontitis, but with a focus on the participant and comprises (1) Behaviour motivation and support for participants to attain and maintain effective plaque removal and reduce gum inflammation by a personalised, tailored oral hygiene regimen and motivational advice to maximise home-compliance (2) the reduction/elimination of plaque and calculus below the gum line with standard mechanical
therapies and antibiotics if indicated clinically, (3) further treatment of any oral sites that respond poorly to initial treatment, (4) provision of supportive periodontal care per 2021 UK-guidelines to maintain oral health. This treatment will take on average 3 appointments within the first 3-4 months, but could require more visits as it is dependent on how well the participant responds to the treatment and is able to undertake oral hygiene at home. Participants in the treatment group will be made aware of the potential number of visits. Participants in the treatment group will also be sent motivational communications about aspects of oral hygiene to help remind them about taking care of their gums.

All participants will be asked to return to the Brain Centre at Southmead Hospital 6 and 12 months after their screening appointment for further memory and dental assessments and give further samples of blood and saliva. At the 12-month appointment participants will be approached to take part in a short interview to gain their feedback about their experience of taking part in the study. This will be audio recorded. After 18 months those who are recruited at the start of the study will be invited to have one final cognitive assessment. It is anticipated that this might be via a zoom link or similar as the cognitive assessors used remote assessments successfully during the pandemic, and this will avoid the need to travel, but can be in person if the participant prefers. This additional 18 month time point was requested by the funder, but they acknowledged that due to the funding timeframe those recruited at the end of the recruitment period would not have time to complete this assessment. This 18 month assessment will just provide a slightly longer follow up period.

Intervention Type
Behavioural

Primary outcome measure

Feasibility outcomes measured using patient records at the end of the study:
1. Recruitment rates
2. Compliance rates-intervention
3. Completion rates-data collection

Secondary outcome measures
1. Periodontal scores. Periodontal assessment: Bleeding on Probing (BOP) (yes/no); periodontal pocket depths (mm)-four gingival sites/tooth; dental plaque- O'Leary plaque index (yes/no)-four surfaces/tooth at screening, 6 months, 12 months
2. Cognitive scores. Cognitive assessment: Clinical Dementia Rating Sum of Boxes (CDR-SB): an appropriate and widely used primary outcome measures for early and late dementia. Alzheimer's Disease Assessment Scale Cognitive subscale (ADAS-Cog11), and Bristol Activities of Daily Living Scale (BADLS), measuring functional ability at screening, 6 months, 12 months, 18 months
3. Blood levels of markers that are indicative of inflammation. Blood/saliva (laboratory research): Assessed for inflammatory response and bacterial load to confirm that bacteraemia and that pathogens have been reduced by the treatment at screening, 6 months, 12 months
4. Qualitative data (mini interview) regarding the perceived acceptability and success of the intervention at the end of the study

Overall study start date
01/07/2022

Completion date
23/07/2025

Eligibility

Key inclusion criteria
1. Diagnosis of either amnesic or multidomain mild cognitive Impairment with memory loss or early-stage Alzheimer's disease
2. Capacity to consent
3. Periodontitis (periodontal pockets of >4 mm with bleeding on probing)
4. Aged 60 years or over
5. A project partner to attend at least the first study appointment
6. A minimum of 6 teeth

Participant type(s)
Patient

Age group
Adult

Lower age limit
60 Years

Sex
Both

Target number of participants

Planned Sample Size: 80; UK Sample Size: 80 (80 participants were planned to be screened in order to reach the recruitment target of 50 participants randomised onto the study)

Total final enrolment
53

Key exclusion criteria
1. Lack of one or more of the inclusion criteria
2. Uncontrolled diabetes
3. Uncontrolled dental disease that is not periodontitis
4. Scores of >=3 on the American Society of Anaesthesiologists Physical-Status-Classification-System

Date of first enrolment
09/01/2023

Date of final enrolment
01/08/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Dental Hospital
Lower Maudlin Street
Bristol
United Kingdom
BS1 2LX

Study participating centre
Chipping Manor Dental Practice - Cirencester
56 Ashcroft Road
Cirencester
United Kingdom
GL7 1QX

Study participating centre
Ashley Down Dental Care
382 Gloucester Rd
Horfield
Bristol

United Kingdom
BS7 8TR

Study participating centre
Bupa Dental Care Gloucester
124 Stroud Rd
Gloucester
United Kingdom
GL1 5JN

Study participating centre
Bupa Dental Care Dursley
40-42 Parsonage St
Dursley
United Kingdom
GL11 4AE

Study participating centre
Millennium Dental Care
130 Montreal Ave
Bristol
United Kingdom
BS7 0NQ

Study participating centre
Portishead Dental Practice
52 Nore Rd
Portishead
Bristol
United Kingdom
BS20 6JY

Study participating centre
Redland Park Dental Surgery
9 Redland Park
Bristol
United Kingdom
BS6 6SA

Study participating centre
The Rodney Dental Practice
31 Rodney Road
Cheltenham
United Kingdom
GL50 1HX

Study participating centre
Yate Centre Dental Surgery
2a North Walk
Yate
Bristol
United Kingdom
BS37 4AP

Study participating centre
My Dentist Filton Road Dental Practice
94 - 96 Filton Road
Horfield
Bristol
United Kingdom
BS7 0PD

Study participating centre
Nelson Street Dental Practice
17-18 Nelson Street
Stroud
United Kingdom
GL5 2HN

Study participating centre
Rhiwbina Dental Surgery
25-27 Heol y Deri
Cardiff
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CF14 6HB

Sponsor information

Organisation
University Hospitals Bristol and Weston NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan
The anonymised participant data (clinical scores and questionnaire data) generated during the current study will be shared once the data has been published and will be stored in the publicly available University of Bristol Research Data Repository/https://data.bris.ac.uk/data/ with a DOI maintained for a minimum of 20 years. Data will be made available as restricted access to bonafide researchers who provide a methodologically sound proposal and evidence of ethical approval (if required), subject to the agreement of the University of Bristol Data Access Committee for analysis to achieve aims in the approved proposal.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.0	15/12/2022	12/05/2023	No	No
HRA research summary			28/06/2023	No	No