ISRCTN14412713 https://doi.org/10.1186/ISRCTN14412713

The impact of open-label dummy pills (placebo) on chronic pain

Submission date
11/03/2025

Recruitment status
No longer recruiting

Registration date
18/03/2025

Overall study status
Completed

Last Edited
17/03/2025

Condition category
Oral Health

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

Plain English summary of protocol

Background and study aims
The purpose of this research study is to better understand how open-label placebo (OLP) influences pain perception and expectations over time. OLP is a treatment in which individuals knowingly take a pill with no active medication, yet it may still provide pain relief. This study examines the effects of OLP use in mitigating chronic pain in temporomandibular disorder (TMD). The findings will help inform future research on the role of OLP in chronic pain management.

Who can participate?
Adults with chronic orofacial pain primarily diagnosed with TMD.

What does the study involve?
This is a crossover study conducted over 90 days with 2 periods of 45 days. Participants are divided into three groups. Group 1 will start OLP during period 1 and stop taking OLP during period 2. Group 2 will not take OLP in period 1 and will start to take OLP in period 2. Group 3 will take no OLP for a total of 45 days.
Throughout the study, they will record daily pain intensity, unpleasantness, mood, and anxiety through ecological momentary assessments (EMA). Pain relief expectations are assessed weekly using a visual analogue scale (VAS).

What are the possible benefits and risks of participating?
Participants may or may not experience pain relief from taking OLP. Risks include loss of confidentiality, privacy concerns, and potential psychological discomfort from completing daily assessments.

Where is the study run from?
University of Maryland, Baltimore

When is the study starting and how long is it expected to run for?
Aptil 2021 to January 2023

Who is funding the study?
National Institute of Dental and Craniofacial Research (NIDCR)

Who is the main contact?
Dr. Luana Colloca, colloca@umaryland.edu

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Luana Colloca

ORCID ID
https://orcid.org/0000-0002-6503-4709

Contact details
School of Nursing, University of Maryland, Baltimore, 655 West Lombard Street Room 731
Baltimore
United States of America
21201
+1 4107068244
colloca@umaryland.edu

Additional identifiers

Study information

Scientific Title
Comparing open-label placebo and standard of care for chronic pain in temporomandibular disorders

Acronym
OLP-TMD

Study objectives
The study hypothesis is that:
1. OLP use will attenuate chronic pain intensity (primary outcome) in temporomandibular disorders (TMD) as compared to the standard of care.
2. The OLP use will reduce pain interference, decrease anxiety, improve mood and sleep quality (secondary outcomes) in TMD as compared to the standard of care.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 20/04/2021, University of Maryland, Baltimore Institutional Review Board (IRB) (620 W. Lexington St. Second Floor Baltimore, MD 21201, Baltimore City, 21201, United States of America; +1 (410) 706-5037; hrpo@umaryland.edu), ref: HP-00068315

Primary study design
Interventional

Study design
Single-center open-label randomized crossover study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Reducing chronic pain in participants with temporomandibular disorders

Interventions
This is a free-choice, randomized, cross-over design study lasting a total of 90 days, with two periods of 45 days. At informed consent, participants choose whether they want to take open-label placebo (OLP) pills as part of their daily intervention regimen for chronic pain treatment. Those who agree to take OLP are randomized to Group 1 or Group 2. Both Groups 1 and 2 complete a period of OLP intervention and a period of standard care without OLP. Group 1 starts OLP in period 1 and stops taking OLP in period 2 (standard care). Group 2 does not take OLP in period 1 and starts taking OLP in period 2. Those who do not agree to take OLP (Group 3) are monitored using the same daily survey throughout the study.

Intervention Delivery and Randomization
The intervention is delivered by trained research staff who introduce participants to OLP during an initial session. Participants receive instructions in person. The intervention is home-based, with participants self-administering the placebo pills according to a structured regimen. Randomization is performed using a computer-generated sequence, ensuring balanced allocation between the groups. There is no wash-out period between the two intervention phases, as OLP has no pharmacological effects.

OLP Pills
The pills are composed of magnesium stearate and microcrystalline cellulose PH-102 (inert chemicals). If participants agree to receive the placebo (i.e., Zeebo®) pills, they take one pill per day as an adjuvant to their usual treatments.

OLP Instructions
Groups 1 and 2 are introduced to the analgesic effects of OLP through discussions with experimenters about its effectiveness in three ways. First, participants view a figure from a previous publication demonstrating that both individuals with temporomandibular disorders and healthy, pain-free participants benefit equally from placebo effects. Participants are informed that despite experiencing long-term chronic pain, their ability to respond to placebo effects in laboratory settings is the same as that of healthy pain-free individuals. This provides theoretical and mechanistic support for the use of OLP as a non-pharmacological treatment for chronic pain. Second, some participants receive additional reinforcement about OLP benefits by watching a

video of participant testimonies. In this video, three individuals with Parkinson’s disease and chronic pain describe how their symptoms improved after using OLP. Third, enrolled participants are required to take one pill per day for a total of 45 days.

Follow-Up and Monitoring
Participants complete daily electronic surveys to track their pain levels and adherence to the intervention. The total study duration is 90 days, with 3-, 4-, and 6-month follow-up. Data collection is conducted remotely, and participants receive periodic reminders to ensure high retention and compliance.

Intervention Type
Supplement

Primary outcome(s)
Pain intensity measured using a 0 to 100 Visual Analog Scale (VAS), with 0=no pain at all to 100=maximum tolerable pain, daily for 90 days, with 3-, 4-, and 6-month follow-up

Key secondary outcome(s)
The following secondary outcome measures are assessed for 90 days, with 3-, 4-, and 6-month follow-up:
1. Pain unpleasantness, mood, and anxiety measured using a 0 to 100 VAS, with 0=no unpleasantness at all/worst mood/not anxious to 100=maximum unpleasant/best mood/most anxious, daily
2. Pain interference, pain behavior, anxiety, depression, and sleep disturbance measured using the Patient-Reported Outcomes Measurement Information System (PROMIS) weekly
3. Expectations measured using a 0 to 100 VAS with the question "how much pain relief do you expect due to the intervention?" weekly

Completion date
15/01/2023

Eligibility

Key inclusion criteria
1. Fluency in English
2. Aged between 18 and 70 years old
3. Having TMD for more than 3 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
42

Key exclusion criteria
1. The presence of degenerative neuromuscular disease
2. Untreated cardiovascular disease
3. Neurological disease
4. Severe psychosis such as mania, bipolar disorders, and schizophrenia (self or first order family members)
5. A positive toxicology test result on opioid, cocaine, amphetamine, and methamphetamine will disqualify the participant because the use of those illicit medications might alter the placebo responses

Date of first enrolment
20/04/2021

Date of final enrolment
12/10/2022

Locations

Countries of recruitment
United States of America

Study participating centre
University of Maryland, Baltimore
655 West Lombard Street Room 743
Baltimore
United States of America
21201

Sponsor information

Organisation
University of Maryland, Baltimore

ROR
https://ror.org/04rq5mt64

Funder(s)

Funder type
Government

Funder Name
National Institute of Dental and Craniofacial Research

Alternative Name(s)
NIH National Institute of Dental and Craniofacial Research, National Institute of Dental Research, Instituto Nacional de Investigación Dental y Craneofacial, El Instituto Nacional de Investigación Dental y Craneofacial, NIDCR, NIDR

Funding Body Type
Government organisation

Funding Body Subtype
Research institutes and centers

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The dataset generated during and/or analysed during the current study will be available upon request from Dr. Luana Colloca (colloca@umaryland.edu), or Dr. Wang (yang.wang@umaryland.edu).

Type of data being shared: The study will share de-identified data, including aggregated pain scores, expectation measures, and adherence rates. No personally identifiable information will be included in the shared dataset.
Timing for Availability: Data will be made available after the completion of the study and following publication of the primary results.
Consent from Participants: Informed consent is obtained from all participants before enrollment. Participants are informed about the purpose of data collection, the anonymization process, and their rights to withdraw from the study at any time without consequences.
Data Anonymization: All shared data will be fully anonymized to protect participant confidentiality. Identifying information will be removed, and data will be stored securely in compliance with data protection regulations.
Ethical and Legal Restrictions: The study follows ethical guidelines set by the institutional review board (IRB) and complies with relevant legal requirements for data protection and privacy.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 01.2021		17/03/2025	No	Yes