

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

<b>Submission date</b> 11/03/2025	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 18/03/2025	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 17/03/2025	<b>Condition category</b> Oral Health	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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?

April 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

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## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**

**ClinicalTrials.gov number**  
Nil known

**Secondary identifying numbers**  
Nil known

## 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

### **Study design**

Single-center open-label randomized crossover study

### **Primary study design**

Interventional

### **Secondary study design**

Randomised cross over trial

### **Study setting(s)**

Home

### **Study type(s)**

Treatment

### **Participant information sheet**

See study outputs table

### **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 measure**

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

#### **Secondary outcome measures**

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

#### **Overall study start date**

20/04/2021

#### **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

## Age group

Mixed

## Lower age limit

18 Years

## Upper age limit

70 Years

## Sex

Both

## Target number of participants

120

## 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

**Sponsor details**  
655 W Lombard Street  
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**Sponsor type**  
University/education

**Website**  
<http://www.umaryland.edu/>

**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, Instituto Nacional de Investigación Dental y Craneofacial, El Instituto Nacional de Investigación Dental y Craneofacial, National Institute of Dental Research, NIDCR, NIDR

**Funding Body Type**

Government organisation

### Funding Body Subtype

National government

### Location

United States of America

## Results and Publications

### Publication and dissemination plan

Planned publication in a peer reviewed journal

### Intention to publish date

31/12/2025

### 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?
<a href="#">Participant information sheet</a>	version 01.2021		17/03/2025	No	Yes