

# INPLASY PROTOCOL

To cite: Ritto et al.  
Approaching different stages  
of the disease and the  
correlated treatment on Molar  
Incisor Hypomineralization  
(MIH): a systematic review and  
meta-analysis. Inplasy protocol  
202230127. doi:  
10.37766/inplasy2022.3.0127

Received: 23 March 2022

Published: 23 March 2022

**Corresponding author:**  
Fernanda Ritto

fernanda-ritto@ouhsc.edu

**Author Affiliation:**  
Oklahoma University

**Support:** No support.

**Review Stage at time of this  
submission:** Piloting of the  
study selection process.

**Conflicts of interest:**  
None declared.

## Approaching different stages of the disease and the correlated treatment on Molar Incisor Hypomineralization (MIH): a systematic review and meta-analysis

Ritto, FP<sup>1</sup>; Tiwana, K<sup>2</sup>; Dacus, Z<sup>3</sup>; Schmitz, T<sup>4</sup>; Canellas, JV<sup>5</sup>;  
Borges, MAP<sup>6</sup>.

**Review question / Objective:** This systematic review aims to define and evaluate the treatments available for two different stages of the Molar Incisor Hypomineralization (MIH) defect. On stage I, the lesion is classified as Mild and is characterized by demarcated opacities without posteruptive breakdown. On stage II, the lesion is classified as Severe and is characterized by posteruptive breakdown of enamel. To this end, the proposed study will answer the following question: What are the treatments available and their results for the two different stages of MIH on permanent teeth?

**Condition being studied:** Mild and Severe Molar Incisor Hypomineralization (MIH). MIH is an enamel defect that occurs during the mineralization on the second stage of the formation of the enamel called maturation phase. This disease affects the outer layer of enamel, making the structure soft and undercalcified. The appearance of the lesion can be white opaque to yellow brown depending on the stage ( mild or severe).

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 March 2022 and was last updated on 01 June 2022 (registration number INPLASY202230127).

### INTRODUCTION

**Review question / Objective:** This systematic review aims to define and evaluate the treatments available for two different stages of the Molar Incisor Hypomineralization (MIH) defect. On stage I, the lesion is classified as Mild and is

characterized by demarcated opacities without posteruptive breakdown. On stage II, the lesion is classified as Severe and is characterized by posteruptive breakdown of enamel. To this end, the proposed study will answer the following question: What are the treatments available and their

results for the two different stages of MIH on permanent teeth?

**Rationale:** MIH is an enamel defect and the cause is not yet fully established. The levels of decalcification and porosity of the enamel as well as the extension and the location of the defect will define the treatment. Despite the significant increase in studies related to MIH, this topic is still considered a challenge for the dental community. Clinical trials have investigated results on different treatments for MIH. However, the disease has different stages. As the stages come with different characteristics and symptoms, different treatments choices has to be addressed. It's being difficult for the clinicians to identify the best treatment for each stage.

**Condition being studied:** Mild and Severe Molar Incisor Hypomineralization (MIH). MIH is an enamel defect that occurs during the mineralization on the second stage of the formation of the enamel called maturation phase. This disease affects the outer layer of enamel, making the structure soft and undercalcified. The appearance of the lesion can be white opaque to yellow brown depending on the stage ( mild or severe).

## METHODS

**Search strategy:** 1) MEDLINE via PubMed (((((Molar Incisor Hypomineralization) OR (MIH)) OR (Dental Enamel Hypoplasia) OR (Dental Enamel Hypoplasia[MeSH Terms])) OR ("Tooth Demineralization/therapy"[Mesh])) AND (((((((((Randomized controlled trial[Publication Type]) OR controlled clinical trial[Publication Type]) OR randomized[Title/Abstract]) OR placebo[Title/Abstract]) OR randomly[Title/Abstract]) OR trial[Title])) OR "Clinical Trials as Topic"[Mesh:NoExp])) NOT ((animals[MeSH Terms]) NOT humans[MeSH Terms]))

2) Cochrane Central Register of Controlled Trials (via Ovid): ((molar incisor hypomineral\*.mp. OR mih.mp. OR dental enamel hypopla\*.mp. OR ((tooth or teeth or dental or enamel) adj3 demineral\*).mp.) AND (randomized controlled trial.pt. OR

controlled clinical trial.pt. OR random\*. ti, ab,kw. OR placebo.ti,ab,kw. OR trial.ti. OR clinical trials as topic/)) NOT (exp Animals/ NOT exp Humans/)

3) EMBASE (Molar Incisor Hypomineralization OR MIH OR Dental Enamel Hypoplasia (Mesh) OR Tooth demineralization/therapy (Mesh) (((((((((Randomized controlled trial[Publication Type]) OR controlled clinical trial[Publication Type]) OR randomized[Title/Abstract]) OR placebo[Title/Abstract]) OR randomly[Title/Abstract]) OR trial[Title])) OR "Clinical Trials as Topic"[Mesh:NoExp])) NOT ((animals[MeSH Terms]) NOT humans[MeSH Terms].

**Participant or population:** We will include clinical studies investigating treatments for Molar Incisor Hypomineralization (mild and severe stages) on permanent dentition in Children from 6 to 15 years old. No restrictions regarding gender, or ethnicity will be applied.

**Intervention:** Evaluate and compare treatments in molar-incisor Hypomineralization in two different stages of the disease (mild- stage I and severe – stage II).The treatments are varnish and laser therapy for pain reduction, sealant, composites, onlays, crowns or any other available method restoration treatment.

**Comparator:** In this systematic review each MIH treatment related to the stage I and to the stage II will be compared with each other. The treatments for each stage will be compared separately. There will be no reference as an ideal treatment.

**Study designs to be included:** We will include only randomized controlled trials (RCTs).

**Eligibility criteria:** Studies will be selected according to the PICOS criteria (Participant, intervention, comparator, outcomes, and study design) outlined in the referred sections. Only clinical trials related to Molar-Incisor Hypomineralization treatments in permanent dentition will be included. No restriction of country,

publication status, setting or language will be applied. Studies involving another disease or comparing different types of anterior defect related to trauma and hereditary like fluorosis and amelogenesis imperfect will be excluded. Finally, studies for treatment in primary dentition will be excluded.

**Information sources:** We will search the following electronic bibliographic databases: EMBASE, MEDLINE via PubMed, and Cochrane Central Register of Controlled Trials (CENTRAL). We will use the PICOS strategy for research question construction and evidence search. The reference lists of the articles identified will be cross-checked. Furthermore, and studies from the 'grey literature' will be screened through the following trial registry platform: ClinicalTrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)). A comprehensive manual search will be done in the relevant journals of Dentistry: European Journal of Paediatric Dentistry, International Journal of Paediatric Dentistry, Caries Research, Dental Materials and Operative Dentistry. We will contact study correspondent authors to clarify any doubts. Finally, the reference lists of the included studies will be checked to identify additional potential primary studies.

**Main outcome(s):** Stage I non-cavitated lesions: Measurements 1) Maintain Structural Integrity (yes/no); 2) Reduce the dental pain ( yes/no) 3) Restoration Survival. ( USPHS criteria/ USPHS modified or Ryge criteria Stage II cavitated lesions 1) Restoration Survival (USPHS criteria/ USPHS modified or Ryge criteria RETENTION (A- no loss of restorative material/ C- Any loss of restorative material; COLOR MATCH – A- matches tooth / B- acceptable mismatch / C- Unacceptable mismatch; MARGINAL DISCOLORATION – A- no discoloration/ B- discoloration without axial penetration/C- discoloration with penetration; SECONDARY CARIES – A- no caries present/ C- cáries present ; ANATOMIC FORM- A-continuous/ B- Slight discontinuity, clinically acceptable/ C- Discontinuous, failure; MARGINAL

ADAPTION – A- closely adapted, no etectable margin/ B- detectable margin, clinically acceptable, C- marginal crevice, clinical failure; SURFACE TEXTURE- A- Enamel-like surface/ B- Surface rougher than enamel, clinically acceptable; C- Surface unacceptable rough.

**Data management:** Two review authors will independently search the databases and, upon retrieving study titles and abstracts, identify RCTs to be screened for final selection. The review authors will independently screen the full texts of these included RCTs. Any discrepancies will be solved by discussion. The references will be imported into EndNote X9 software (Thompson Reuters, Philadelphia, PA, USA) where duplicates will be automatically removed. The quantitative analysis will be performed using R software version 3.6.2 or if available a later version. In case of network meta-analyses, we will use a frequentist methods (netmeta package) for the Mac OS X computer system.

**Quality assessment / Risk of bias analysis:** Two review authors will independently assess the risk of bias. Any discrepancies will be solved by discussion. Study quality in terms of sequence generation, allocation concealment, blinding, the completeness of outcome data, selective reporting and other biases will be assessed with the Cochrane Collaboration risk of bias tool.

**Strategy of data synthesis:** A narrative synthesis will be presented to summarize the findings and characteristics of the included studies. Initially, the studies will be qualitatively analyzed, compared, and discussed based on the risk of bias of each study. If possible, a pairwise meta-analysis for direct evidence and a network meta-analysis for direct and indirect evidence of eligible comparisons will be accomplished. For studies reporting the primary outcome as a continuous variable, the average will be estimated by meta-analysis, with 95% confidence interval to indicate precision. The odds ratio (OR) will be estimated for dichotomous. Initially, we will pool the results using a random-effects meta-analysis. Heterogeneity will be assessed

---

using both the  $\chi^2$  test and the I<sup>2</sup> statistic. We will consider an I<sup>2</sup> value greater than 50% indicative of substantial heterogeneity. In addition to the heterogeneity assessment using the I<sup>2</sup> statistic. We will investigate the assumption of transitivity and similarity based on clinical and methodological characteristics. A frequentist NMA model will be adopted throughout our analysis. Furthermore, each therapy at each endpoint will be ranked according to their P-score, a frequentist analog to surface under the cumulative ranking curve (SUCRA), which indicated the performance of each treatment.

Author 6 - Marcio Antônio Paraíso Borges.  
Email: marcioparaizo2@hotmail.com  
PUC - Pontifical Catholic University of Rio de Janeiro

**Subgroup analysis:** None planned.

**Sensitivity analysis:** None planned.

**Language:** No language restriction will be imposed.

**Country(ies) involved:** USA and Brazil.

**Keywords:** molar incisor hypomineralization, dental enamel hypoplasia, MIH, children, permanent dentition, treatment survival, posteruptive breakdown; systematic review; meta-analysis.

**Dissemination plans:** The results of this systematic review will be disseminated through peer reviewed journal.

**Contributions of each author:**

Author 1 - Fernanda Ritto.

Email: fernanda-ritto@ouhsc.edu

Oklahoma University

Author 2 - Karen Tiwana.

Email: karen-tiwana@ouhsc.edu

Oklahoma University

Author 3 - Zachary Dacus.

Email: zachary-dacus@ouhsc.edu

Oklahoma University

Author 4 - Troy Schmitz.

Email: troy-schmitz@ouhsc.edu

Oklahoma University

Author 5 - João Vitor Canellas.

Email: canellas@inplasy.com

INPLASY, Inc.