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ADMINISTRATIVE INFORMATION

Support - No financial support was received for this study.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202650019

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 May 2026 and was last updated on 5 May 2026.

INTRODUCTION

Review question / Objective What is the efficacy of methotrexate in patients with vitiligo ?

Population (P): Patients with vitiligo.

Exposure (E): methotrexate administered as monotherapy or in combination with other therapeutic modalities, including phototherapy.

Outcomes (O): Repigmentation, disease stabilization (halt of progression).

Objective:

To evaluate the efficacy of methotrexate in patients with vitiligo, either as monotherapy or in combination with phototherapy or other treatments.

Condition being studied Vitiligo is an acquired depigmenting skin disorder characterized by the progressive loss of melanocytes, resulting in well-defined depigmented macules. It affects approximately 0.5–2% of the global population and

has a significant impact on patients' quality of life. The disease is considered to have an autoimmune basis, involving cytotoxic CD8+ T cells and proinflammatory cytokines that lead to melanocyte destruction.

METHODS

Search strategy A systematic search was conducted in the PubMed, Web of Science, LILACS, and Scopus databases. The search strategy combined terms related to the population ("vitiligo") and the intervention ("methotrexate"), using synonyms and MeSH terms where appropriate. To maximize sensitivity, no terms related to clinical outcomes such as repigmentation or disease progression were included.

A publication year filter was applied, including studies published between 2016 and April 2026, in order to identify recent evidence. A total of 288 records were retrieved. Duplicate records were removed, and the remaining studies were initially

screened by title and abstract. Studies meeting the inclusion and exclusion criteria were then selected for full-text review.

Participant or population Patients of any age and sex with a clinical diagnosis of vitiligo, regardless of disease type, duration, or extent.

Intervention Methotrexate administered via systemic (oral, subcutaneous, or intramuscular) or topical routes, either as monotherapy or in combination with other therapeutic modalities, including phototherapy.

Comparator No specific comparator is required.

Study designs to be included Case reports and case series evaluating the use of methotrexate in patients with vitiligo.

Eligibility criteria Studies that met the following criteria were included: patients with a clinical diagnosis of vitiligo, regardless of age, sex, clinical subtype, or extent of the disease. Cases in which treatment included methotrexate via any route of administration (oral, subcutaneous, intramuscular, or topical) were considered, whether as monotherapy or in combination with other therapeutic modalities, including phototherapy. Regarding study design, although the search had no restriction on study type, according to the established eligibility criteria, only case reports and case series that described the clinical course of patients treated with methotrexate and reported relevant clinical outcomes such as repigmentation, disease stabilization, progression, or treatment-related events were considered for analysis. Studies published in any language were included.

Exclusion criteria. Studies in which methotrexate was not administered as a treatment for vitiligo or in which specific clinical outcomes attributable to methotrexate were not described were excluded. Duplicate publications identified during the selection process were also excluded.

Information sources Electronic databases including PubMed, Web of Science, Scopus, and LILACS were searched.

Main outcome(s) The primary outcomes will include repigmentation and disease stabilization (halt of progression), disease progression and treatment-related adverse events.

Quality assessment / Risk of bias analysis The methodological quality of the included studies will be assessed using appropriate tools for descriptive

studies, such as the Joanna Briggs Institute (JBI) critical appraisal checklists for case reports and case series. Two reviewers will independently perform the assessment, and disagreements will be resolved by consensus.

Strategy of data synthesis A narrative synthesis will be conducted due to the expected heterogeneity of the included studies. The results will be summarized descriptively, focusing on repigmentation, disease stabilization, progression, and adverse events associated with methotrexate treatment.

Subgroup analysis No subgroup analysis is planned.

Sensitivity analysis No sensitivity analysis is planned.

Language restriction No language restrictions will be applied.

Country(ies) involved México.

Keywords Vitiligo; Methotrexate; Autoimmune.

Contributions of each author

Author 1 - Laura Marcela Ochoa Ramírez - Conceived and designed the study, conducted the literature search, performed data extraction, carried out the research process, and drafted the manuscript.

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Author 2 - Taide Laurita Arista-Ugalde - Supervised the study process and provided methodological guidance, ensuring the accuracy and rigor of the protocol.

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