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Candidate molecular endotypes and dynamic risk prediction in anti-MDA5-positive dermatomyositis-associated interstitial lung disease: a systematic scoping review

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 October 2026 and was last updated on 4 October 2026.

INTRODUCTION

Review question / Objective Among people with anti-MDA5-positive dermatomyositis across pulmonary states, which molecular programs recur, what clinical, imaging and multi-omics approaches predict ILD progression, RP-ILD or mortality, and what evidence supports decision-timed risk stratification?

Rationale This scoping review maps molecular programs across pulmonary states together with clinical, imaging and multi-omics prediction, sampling landmarks and validation. The links between molecular states and decision-timed risk stratification remain fragmented.

Condition being studied Anti-MDA5-positive dermatomyositis is an autoimmune inflammatory disease with variable skin, muscle and lung involvement. Interstitial lung disease (ILD) may be absent, chronic or rapidly progressive (RP-ILD), the

latter associated with high short-term mortality. The review concerns molecular endotypes and prognostic tools across these pulmonary states.

METHODS

Participant or population Human patients with anti-MDA5-positive dermatomyositis, including clinically amyopathic disease, across no detectable ILD, chronic ILD and RP-ILD.

Intervention Not applicable as a treatment comparison. Molecular, clinical, imaging, radiomic and multi-omics markers and prediction approaches were mapped; treatment exposure was charted when reported.

Comparator No comparator was required. Pulmonary states or risk groups were compared descriptively where the source provided such data.

Study designs to be included Peer-reviewed human observational, patient-derived mechanistic and prediction-model studies, plus focused evidence syntheses. Primary studies and syntheses were distinguished in the evidence map.

Eligibility criteria English-language, peer-reviewed human reports were eligible if they contained relevant anti-MDA5 and pulmonary molecular, clinical, imaging or prediction evidence. Animal-only studies, inadequately reported abstracts, editorials, non-English reports and reports outside these domains were excluded. Overlapping data were not double-counted.

Information sources PubMed/MEDLINE, Ovid MEDLINE, Web of Science Core Collection and Embase, from database inception through 22 August 2026. No additional information sources are reported in the manuscript.

Main outcome(s) Main mapped outcomes were ILD status or progression, RP-ILD and mortality, together with recurrent molecular programs and prediction-model performance at each source's reported sampling and outcome times.

Quality assessment / Risk of bias analysis Prediction and monitoring studies received structured methodological appraisal informed by PROBAST+AI: selection, predictor and outcome definitions, sample size and events, development, validation, calibration and transportability. This contextualized performance; no formal uniform risk-of-bias rating or GRADE assessment was performed across all sources.

Strategy of data synthesis Molecular findings and prediction studies were charted by biological process, data modality and clinical decision time. Tables summarized cohorts, sampling landmarks, outcomes, model performance and validation; narrative synthesis mapped recurring programs and methodological gaps. No meta-analysis or pooled effect estimate was performed because designs, assays, endpoints and time points differed.

Subgroup analysis Descriptive groupings considered pulmonary state (no ILD, chronic ILD or RP-ILD), assay or data modality and sampling landmark. No formal subgroup effect estimates or interaction tests were performed.

Sensitivity analysis No formal quantitative sensitivity analysis was performed because no effect estimates were pooled. Interpretation considered overlapping cohorts, small samples,

sampling timing and external validation where reported.

Country(ies) involved China.

Keywords anti-MDA5; dermatomyositis; interstitial lung disease; multi-omics; molecular endotype; dynamic prediction; machine learning; radiomics.

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