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Association Between MDM2 Expression and Prognosis in Patients With Malignant Tumors: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

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 24 May 2026 and was last updated on 24 May 2026.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aims to evaluate whether elevated MDM2 expression is associated with poor prognosis in patients with malignant tumors. The population includes patients with pathologically confirmed human cancers. The exposure is high or positive MDM2 expression, mainly assessed by immunohistochemistry or mRNA-based methods. The comparator is low or negative MDM2 expression. The main outcomes include overall survival and other prognostic endpoints such as disease-free survival, progression-free survival, relapse-free survival, cancer-specific survival, biochemical recurrence, recurrence, progression, and tumor-related death. Hazard ratios with 95% confidence intervals will be pooled to assess the prognostic value of MDM2 expression.

Condition being studied Malignant tumors are a major cause of cancer-related morbidity and mortality worldwide. Patient prognosis varies substantially across tumor types and clinical settings. MDM2 is an important regulator of the p53 pathway and has been reported to be overexpressed in various human cancers. This review will focus on malignant tumors and evaluate whether elevated MDM2 expression is associated with poor clinical prognosis.

METHODS

Participant or population Patients with pathologically or histologically confirmed human malignant tumors, regardless of tumor type, stage, age, sex, region, or treatment background.

Intervention Not applicable. The exposure of interest is elevated or positive MDM2 expression,

mainly assessed by immunohistochemistry or mRNA-based methods.

Comparator Patients with low, negative, or reference-level MDM2 expression as defined in the original studies.

Study designs to be included Original clinical observational studies, including retrospective or prospective cohort studies, reporting the association between MDM2 expression and prognosis in patients with malignant tumors.

Eligibility criteria Eligible studies must include patients with human malignant tumors, assess MDM2 expression directly, and report clinical prognostic outcomes such as OS, DFS, PFS, RFS, CSS, DSS, recurrence, progression, biochemical recurrence, or tumor-related death. Studies must provide HRs with 95% CIs or sufficient data for extraction. Reviews, editorials, comments, letters, case reports, animal or in vitro studies, SNP/polymorphism-only studies, amplification-only studies, and studies without relevant prognostic outcomes will be excluded.

Information sources PubMed, Embase, and the Cochrane Library will be systematically searched. Reference lists of eligible articles and relevant reviews will also be screened manually to identify additional studies.

Main outcome(s) The primary outcome will be the association between elevated MDM2 expression and overall prognosis in patients with malignant tumors, measured by hazard ratios (HRs) with 95% confidence intervals (CIs). Overall survival will be prioritized when available. Other eligible prognostic outcomes will include disease-free survival, progression-free survival, relapse-free survival, recurrence-free survival, cancer-specific survival, disease-specific survival, biochemical recurrence, recurrence, progression, and tumor-related death.

Quality assessment / Risk of bias analysis The methodological quality of included observational studies will be assessed using the Newcastle-Ottawa Scale (NOS). The assessment will consider selection of study groups, comparability of cohorts, and ascertainment of outcomes. Studies with higher NOS scores will be considered to have better methodological quality. Disagreements during quality assessment will be resolved by discussion or by consultation with a third reviewer if necessary.

Strategy of data synthesis Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) will be used as the effect measures. When both univariate and multivariate results are available, multivariate Cox regression estimates will be preferentially extracted. The primary quantitative synthesis will be based on studies reporting multivariate Cox regression results. The natural logarithm of HRs and standard errors will be calculated for meta-analysis. A random-effects model will be used to pool effect estimates because clinical and methodological heterogeneity is expected across tumor types. Heterogeneity will be assessed using the I^2 statistic and Cochran's Q test. Studies reporting only univariate or less-adjusted estimates will be considered in supplementary or sensitivity analyses.

Subgroup analysis Subgroup analyses will be performed according to tumor histological origin and geographic region when sufficient data are available. Tumor histological origin will be categorized as epithelial-derived and non-epithelial-derived malignancies. Geographic region will be categorized as Europe/Americas and Asia-Pacific regions. Subgroup analyses will mainly be based on the primary multivariate Cox regression dataset.Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) will be used as the effect measures. When both univariate and multivariate results are available, multivariate Cox regression estimates will be preferentially extracted. The primary quantitative synthesis will be based on studies reporting multivariate Cox regression results. The natural logarithm of HRs and standard errors will be calculated for meta-analysis. A random-effects model will be used to pool effect estimates because clinical and methodological heterogeneity is expected across tumor types. Heterogeneity will be assessed using the I^2 statistic and Cochran's Q test. Studies reporting only univariate or less-adjusted estimates will be considered in supplementary or sensitivity analyses.

Sensitivity analysis Sensitivity analysis was performed using the metainf command in Stata to assess the robustness and reliability of the pooled results.

Country(ies) involved China.

Keywords MDM2; cancer; malignant tumors; prognosis; survival; biomarker; meta-analysis; systematic review.

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