# INPLASY PROTOCOL

To cite: Lu et al. The metabolic syndrome and its components as prognostic factors in colorectal cancer: A Meta-analysis and Systematic Review. Inplasy protocol 202280050. doi: 10.37766/inplasy2022.8.0050

Received: 14 August 2022

Published: 14 August 2022

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**Support:** **NSFC No. 81770559 , 81370500.**

**Review Stage at time of this submission:** **Completed but not published.**

**Conflicts of interest:**
**None declared.**

# The metabolic syndrome and its components as prognostic factors in colorectal cancer: A Meta-analysis and Systematic Review

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**Review question / Objective:** **To explore the impact of individual components and synergies of Metabolic syndrome (MetS) on the prognosis of patients with colorectal cancer (CRC).**
**Condition being studied:** **MetS manifests as a group of clinical syndromes including diabetes or glucose intolerance, hypertension, obesity, dyslipidemia, with multiple metabolic diseases occurring simultaneously. Sedentary lifestyle, chronic stress, imbalanced diet and lipodystrophy may increase the risk of MetS. Patients with MetS are associated with a higher risk for metabolic and cardiovascular disorders, including chronic kidney disease, peripheral vascular disease, coronary artery disease, and stroke. The incidence of MetS has increased dramatically worldwide and has become a major public health problem due to aging, urbanization, and lifestyle changes. In recent years, many lines of evidence have indicated that MetS has hormonal and systemic effects that increase susceptibility to various cancers. Epidemiological studies have shown that MetS and / or its components are associated with an elevated risk of cancer, including CRC. CRC is the third most common neoplasm and the fourth most lethal malignancy worldwide, accounting for 10.2% of all cancers. Although MetS increases the risk of CRC, the impact of MetS on CRC prognosis remains controversial after the diagnosis of CRC is established.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 August 2022 and was last updated on 14 August 2022 (registration number INPLASY202280050).

## INTRODUCTION

**Review question / Objective:** **To explore the impact of individual components and synergies of Metabolic syndrome (MetS) on the prognosis of patients with colorectal cancer (CRC).**

**Rationale:** The prognostic analysis of CRC is mainly based on clinical factors such as completeness of surgery, TNM stage and number of lymph nodes procured, and secondarily on relevant pathologic features such as microsatellite instability and grade. Despite these prognostic factors, prognostic and predictive factors guiding treatment strategies are still lacking in many clinical situations. Therefore, these factors need to be recognized clinically in order to improve treatment and outcomes. To address this issue, we conducted this meta-analysis and systematic study aiming to explore whether MetS affects the prognosis of CRC patients MetS increases the risk of CRC, the impact of MetS on CRC prognosis remains controversial after the diagnosis of CRC is established.

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## METHODS

**Participant or population:** Patients with colorectal cancer.

**Intervention:** Patients with MetS.

**Comparator:** Patients without MetS.

**Study designs to be included:** Prospective or retrospective observational cohort studies.

**Eligibility criteria:** This study evaluated the MetS and its components as prognostic factors in CRC. The inclusion criteria were: (1) Patients: patients with CRC, (2) Intervention: with MetS (3) Control: without MetS (4) Outcome: HR of survival, Odds ratio (OR) of postoperative complications (5) Study design: prospective or retrospective observational cohort studies.

**Information sources:** Four electronic databases including PubMed, Embase, Cochrane Library and ScienceDirect.

**Main outcome(s):** Survival: HR of overall mortality, CRC-specific mortality and DFS. HR of survival between patients with and without MetS was calculated. Postoperative outcomes: Odds ratios of postoperative complications and postoperative mortality.

**Quality assessment / Risk of bias analysis:** To assess the risk of bias of observational studies, we followed the Newcastle-Ottawa Quality Assessment Scale. The scale assigns stars (up to 9 stars) based on the quality of selection, comparability, exposure and outcome of study participants.

**Strategy of data synthesis:** A random-effects model Inverse Variance method was used to estimate the summarized effect size, assuming heterogeneity always exist. We reported the pooled estimates as the weighted mean difference along with their respective 95% CI.

**Subgroup analysis:** We also meta-analyzed the effect of any single component of the

MetS, including diabetes mellitus, hypertension, dyslipidemia, and obesity. We also meta-analyzed the all-cause mortality, CRC specific mortality and DFS of each single component in an attempt to find which of the above prognostic outcomes was associated with each single component. However, we pooled only those studies that had been included to assess Mets and provided single-component prognostic results, and did not search separately for studies that assessed only the impact of a single component on CRC.

**Sensitivity analysis:** None.

**Country(ies) involved:** China.

**Keywords:** colorectal cancer, metabolic syndrome, prognostic, diabetes, glucose intolerance.

**Contributions of each author:**
Author 1 - Bo Lu - Conceived and designed the study, screened and extracted data, performed the statistical analyses, drafted the manuscript, and revised the manuscript.
Author 2 - Jia-Ming Qian - Conceived and designed the study, screened and extracted data, and revised the manuscript.
Author 3 - Jing-Nan Li - Conceived and designed the study, performed the statistical analyses, and revised the manuscript.