

# INPLASY PROTOCOL

To cite: Ma et al. The difference of prognosis between signet ring cell gastric carcinoma and non-signet ring cell gastric carcinoma in different clinical stages: a meta-analysis. Inplasy protocol 2020110011. doi: 10.37766/inplasy2020.11.0011

Received: 02 November 2020

Published: 03 November 2020

**Corresponding author:**  
Wei Fu

fuwei@bjmu.edu.cn

**Author Affiliation:**  
Peking University Third  
Hospital.

**Support:** None.

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

**Conflicts of interest:**  
The authors have declared that no conflicts of interest exists.

## INTRODUCTION

**Review question / Objective:** The aim of this study is to analyze the clinicopathologic characteristics and prognosis of signet ring cell carcinoma (SRC) and non-signet ring cell carcinoma(NSRC) according

## The difference of prognosis between signet ring cell gastric carcinoma and non-signet ring cell gastric carcinoma in different clinical stages: a meta-analysis

Ma, J<sup>1</sup>; Meng, Y<sup>2</sup>; Zhou, X<sup>3</sup>; Fu, W<sup>4</sup>.

**Review question / Objective:** The aim of this study is to analyze the clinicopathologic characteristics and prognosis of signet ring cell carcinoma (SRC) and non-signet ring cell carcinoma(NSRC) according to disease status (early vs advanced gastric cancer) in gastric cancer patients.

**Condition being studied:** SRC and non-SRC are thought to be distinct biologic entities originating from different sources of carcinogenesis. Some studies reported that the SRC has unique and distinct clinicopathological characteristics with NSRC. Worse prognosis of SRC has been suggested by early Western studies. However, several comparative studies have suggested that the prognostic impact of SRC may be dependent on disease stage, although this remains controversial. Therefore, for better understanding of the prognostic impact of SRC, a comparative analysis with non-SRC patients according to tumor grade.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 November 2020 and was last updated on 03 November 2020 (registration number INPLASY2020110011).

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## METHODS

**Search strategy:** A systematic literature search was performed independently by two authors (Junren Ma and Yan Meng). We will search, with no time restrictions, the following databases for relevant English and Chinese language literature: PubMed (MEDLINE), Embase databases, Web of Science, the Cochrane Central Register of Controlled Trials (CENTRAL) and Clinical Trials. The electronic database search will be supplemented by a manual search of the reference lists of included articles.

**Participant or population:** Patients with gastric cancer and treated by gastrectomy will be included.

**Intervention:** Patients with signet ring cell carcinoma (SRC).

**Comparator:** Patients with non-signet ring cell carcinoma (NSRC).

**Study designs to be included:** No study restrictions.

**Eligibility criteria:** Newcastle-Ottawa Quality Assessment Scale (NOS) was used as a methodological quality assessment. Studies with a score equal to or higher than six were considered as high-quality studies.

**Information sources:** All intended information will come from electronic databases.

**Main outcome(s):** Overall survival of SRC and NSRC patients in 5 years.

**Additional outcome(s):** Clinicopathological characteristics of SRC and NSRC.

**Data management:** The data were independently extracted by two authors (Junren Ma, and Yan Meng) from the included studies. For each study, we recorded the name of first author, year of publication, country, study design, the time period of the included patients, the definition of SRC, sample size of SRC and NSRC, the definition of early gastric carcinoma(EGC). The following clinicopathological characteristics were also extracted: age, gender, tumor location, tumor size (cm), depth of tumor invasive (T stage), status of lymph nodes metastasis (N stage), distal metastasis (M stage), TNM stage and postoperative 5-year overall survival. For those with more than one articles and with duplicated data, only the article has the most complete data were included for analysis.

**Quality assessment / Risk of bias analysis:** Two reviewers will be involved in the quality assessment. Any disagreements between reviewers will be resolved by a third reviewer. The publication bias was tested by Begg's funnel plot and Egger's test of the intercept.

**Strategy of data synthesis:** Meta-analysis conducted according to guidelines from preferred reporting items for systematic reviews and meta-analysis (PRISMA) group. Hazard ratio is the summary statistic for survival outcomes, odds ratio for all other dichotomous outcomes and weighted mean difference for continuous variables such as patient age and tumor size. Meta-analysis to be performed using random effect models and between-study heterogeneity to be assessed. The point estimate of HR or OR considered statistically significant at the  $p < 0.05$  level if the 95% confidence interval did not include the value one. Software programme Revman 5 will be used to perform the meta-analysis and create forest plots. A minimum of 10-12 studies is required to perform the meta-analysis. Data synthesised will include survival, and other

clinicopathologic characteristics between SRC and NSRC.

**Subgroup analysis:** Studies were divided into "early gastric cancer" and "advanced gastric cancer" subgroups, and also divided into "stage I", "stage II", "stage III" and "stage IV" subgroups.

**Sensibility analysis:** Sensitivity analysis was conducted mainly by changing the inclusion criteria (especially the controversial studies), and compared with the results of meta-analysis before exclusion to explore the degree of influence of this study on the combined effect size and the robustness of the results.

**Language:** Relevant English and Chinese language literature will be limited.

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

**Keywords:** gastric cancer, prognosis, signet ring cell carcinoma.

#### **Contributions of each author:**

**Author 1 - Junren Ma -** The author retrieving documentation, extracting data, analyzing statistics and drafting manuscripts.

**Author 2 - Yan Meng -** Author 2 retrieving documentation and provided statistical expertise.

**Author 3 - Xin Zhou -** The author provided feedback and approved the final manuscript.

**Author 4 - Wei Fu -** The author is responsible for the design of the study and for the final results.