

# INPLASY PROTOCOL

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**Review Stage at time of this submission:** The review has not yet started.

**Conflicts of interest:**  
None declared.

## Metastatic patterns in patients with colon cancer: protocol for a systematic review and meta-analysis

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**Review question / Objective:** This study will conduct a systematic review and meta-analysis to determine the risk of site-specific metastasis, giving a complete profiling of distant metastasis of colon cancer.

**Information sources:** Searches will be performed using both Mesh terms and free-text terms. The following terms will be combined to generate the search strategy and will be adopted accordingly for each database: colon cancer, colon carcinoma, colon adenocarcinoma, colon neoplasm, metastases, metastasis, metastatic, pattern, incidence, proportion, prevalence, rate, frequency. No filters will be applied on publication types in the initial searches. We will check the bibliography of eligible studies to identify any potential literature missed in the searches of the electronic database. In addition, Google scholar will be used to search any grey studies.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 March 2023 and was last updated on 28 March 2023 (registration number INPLASY202330113).

### INTRODUCTION

**Review question / Objective:** This study will conduct a systematic review and meta-analysis to determine the risk of site-specific metastasis, giving a complete profiling of distant metastasis of colon cancer.

**Condition being studied:** Metastasis of colon cancer.

### METHODS

**Participant or population:** Patients diagnosed as colon cancer are eligible for

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this review no matter what stages or grades the cancer is.

**Intervention:** There are no restrictions on the interventions in this review.

**Comparator:** Controls will not be required for this review as the non-interventive nature of this review.

**Study designs to be included:** We will include reports on the proportions of different target metastasis from either clinical trials, or follow-up studies, or cross-sectional surveys.

**Eligibility criteria:** We will include studies reporting metastatic patterns of colon cancer, which is defined as the proportions of patients with different-sites metastasis among patients with primary colon cancer.

**Information sources:** Searches will be performed using both Mesh terms and free-text terms. The following terms will be combined to generate the search strategy and will be adopted accordingly for each database: colon cancer, colon carcinoma, colon adenocarcinoma, colon neoplasm, metastases, metastasis, metastatic, pattern, incidence, proportion, prevalence, rate, frequency. No filters will be applied on publication types in the initial searches. We will check the bibliography of eligible studies to identify any potential literature missed in the searches of the electronic database. In addition, Google scholar will be used to search any grey studies.

**Main outcome(s):** Studies should report the number of patients who develop different distant metastases out of all patients with colon cancer or patients with different metastases out of patients with IV colon cancer, which can be used to compute the incidence of site-specific metastases and component proportion, respectively.

**Quality assessment / Risk of bias analysis:** As different study types will be included, three different quality assessment tools will be applied, including the tool developed by Hoy et al for prevalence studies, the Newcastle–Ottawa scale for non-

randomised studies and the Cochrane's bias assessment tool for randomized studies.

**Strategy of data synthesis:** The overall pooled estimate for the proportion will be calculated and displayed with 95% CIs. The numerators and denominators for each reported proportion will be extracted or recalculated from the individual studies. The study-specific proportions will be pooled using the random effect meta model. The Freeman-Tukey double arcsine transformation will be used during meta-analysis to stabilize the variance of study-specific proportions. We will perform separate meta-analyses on the incidence and component proportion of metastases due to their differed nature of outcomes. Heterogeneity will be assessed qualitatively by Cochrane's Q test and quantitatively by I<sup>2</sup> statistics. I<sup>2</sup> >50% is defined as substantial heterogeneity. Subgroup and sensitivity analyses will be performed to explore the sources of heterogeneity. If substantial heterogeneity persists after adjusting models based on the sources of heterogeneity, a narrative statistic will be used. The proportions of metastasis in different sites (such as liver, lung, bone, brain, and peritoneum metastases) will be compared and ranked. The significant level of  $\alpha$  is set as 0.05, and p value below 0.05 is considered statistically significant.

**Subgroup analysis:** The proportions of metastasis in different sites (such as liver, lung, bone, brain, and peritoneum metastases) will be compared and ranked.

**Sensitivity analysis:** Subgroup and sensitivity analyses will be performed to explore the sources of heterogeneity.

**Language restriction:** English.

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

**Keywords:** colon cancer; metastasis; systematic review; meta-analysis; proportion.

**Contributions of each author:**  
Author 1 - Yonghua Hu.

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