

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** The purpose of this study is to evaluate the impact of CRS + HIPEC on survival and provide reference for the treatment of colorectal cancer patients with peritoneal metastasis.

## Effect of hyperthermic intraperitoneal chemotherapy(HIPEC) combined with cytoreductive surgery(CRS) on prognosis in colorectal cancer patients with peritoneal metastasis: a systematic review and meta-analysis

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**Review question / Objective:** The purpose of this study is to evaluate the impact of CRS + HIPEC on survival and provide reference for the treatment of colorectal cancer patients with peritoneal metastasis

**Condition being studied:** Peritoneal metastasis often occurs in colorectal cancer patients with peritoneal metastasis and the prognosis is poor. A large body of evidence highlights the beneficial effects of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) on survival, but to date there is little consensus on the optimal treatment strategy for colorectal cancer patients with peritoneal metastasis. The purpose of this study is to evaluate the impact of CRS + HIPEC on survival and provide reference for the treatment of colorectal cancer patients with peritoneal metastasis.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 March 2022 and was last updated on 19 March 2022 (registration number INPLASY202230093).

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little consensus on the optimal treatment strategy for colorectal cancer patients with peritoneal metastasis. The purpose of this study is to evaluate the impact of CRS + HIPEC on survival and provide reference for the treatment of colorectal cancer patients with peritoneal metastasis.

## METHODS

**Participant or population:** Colorectal cancer patients with peritoneal metastases.

**Intervention:** Complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy.

**Comparator:** Patients undergoing surgery or any other systemic palliative treatment.

**Study designs to be included:** Randomised controlled trials, case-control studies or cohort studies.

**Eligibility criteria:** A specific population (P), intervention (I), comparator (C), outcome (O), and study design (S) (PICOS) framework was specified to define study eligibility, as recommended. In particular, the following criteria were outlined:- Population (P): colorectal cancer patients with peritoneal metastases.- Intervention (I): complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy ;- Comparison (C): patients undergoing surgery or any other systemic palliative treatment;- Outcomes (O): patient Survival Outcomes- Study design (S): Randomised controlled trials, case-control studies or cohort studies.

**Information sources:** The PubMed, Embase, Cochrane, Web of Knowledge, and ClinicalTrials.gov databases were screened inception of the review to March 11, 2022 , We applied no language restrictions.

**Main outcome(s):** A total of 3200 patients were enrolled in the study, including 788 patients in the CRS and HIPEC groups and 2412 patients in the control group, of which 3 were randomized controlled trials and 7

were cohort studies. The 3 randomized controlled studies were of high quality and the quality scores of the 7 cohort studies were all 7 or above, indicating high quality. The results showed that the OS of CRS + HIPEC group was higher than that of control group (HR: 0.53, 95%CI: 0.38 - 0.73; P<0.00001, I<sup>2</sup>=82.9%), the heterogeneity of the studies was large. The subgroup analysis showed that the OS of CRS and HIPEC group was higher than that of PC group (HR: 0.37, 95%CI: 0.30 - 0.47; P=0.215, I<sup>2</sup>=31%), and higher than that in CRS group (HR: 0.73, 95%CI: 0.49 - 1.07; P=0.163, I<sup>2</sup>=44.8%), the heterogeneity of the studies was low.

**Quality assessment / Risk of bias analysis:** For randomized controlled studies, the quality of the selected literature was evaluated by the quality evaluation of RCTs' Jadad method. of these, 1–3 score indicated that the test was of inferior quality, and 4–7 score indicated that the test was of high quality. The results showed that the three randomized controlled studies were of high quality. For case-control studies and cohort studies, the Newcastle-Ottawa scale was used for quality assessment. of these, 5-9 as high-quality studies. The quality scores of the seven cohort studies were all 7 or above, indicating high quality.

**Strategy of data synthesis:** HR and 95% CI of both groups were pooled and analyzed. If HR and its 95% confidence interval could not be extracted, data were extracted from survival curves using Engauge Digitizer software and converted. Heterogeneity between studies was quantified by I<sup>2</sup> statistic and Cochran's Q test. When there was no significant heterogeneity, the fixed effect model was used for combined analysis; otherwise, the random effect model was used for combined analysis, and subgroup analysis was performed to find the source of heterogeneity.

**Subgroup analysis:** The results showed that the OS of CRS and HIPEC group was higher than that of PC group , and higher than that in CRS group, the heterogeneity of each subgroup was low. After that, We

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divided the experimental groups into OPEN group and CLOSE group according to the different HIPEC devices. In the OPEN group, The results showed that the OS of THE CRS and HIPEC groups was higher than that in the control group; In the CLOSE group, the experimental group OS was higher. OPEN group showed lower heterogeneity. Divided into different subgroups according to the duration of HIPEC treatment, 30min group and 60-100min group showed that the OS of CRS and HIPEC groups was higher than that of the control group, and there was low heterogeneity in the 60-100min group.

**Sensitivity analysis:** Sensitivity analysis showed that there was no significant difference in the results of the combined analysis after each study was deleted, indicating that the results of the combined analysis were more reliable.

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

**Keywords:** colorectal cancer, peritoneal metastasis, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, meta-analysis.

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