

# INPLASY PROTOCOL

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**Support:** NNSFC.

**Review Stage at time of this submission:** Data extraction.

**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** To evaluate the potential effect of perineural invasion on survival outcomes of all stages colorectal cancer patients undergoing adjuvant chemotherapy

## Effect of perineural invasion on survival outcomes of colorectal cancer patients undergoing adjuvant chemotherapy: A systematic review and meta-analysis

He, Y<sup>1</sup>; Shu, C<sup>2</sup>; Liu, J<sup>3</sup>; Huang, J<sup>4</sup>; Wang, Z<sup>5</sup>; Jin, S<sup>6</sup>.

**Review question / Objective:** To evaluate the potential effect of perineural invasion on survival outcomes of all stages colorectal cancer patients undergoing adjuvant chemotherapy.

**Condition being studied:** Controversies have been aroused regarding the effect of adjuvant chemotherapy on colorectal cancer patients with perineural invasion, questioning that whether these patients will benefit from ACT after surgery. Recent studies reported that ACT had no significant among patients with PNI.

**Information sources:** Patients with colorectal cancer who underwent adjuvant chemotherapy after surgery will be included. Patients who only underwent neoadjuvant chemotherapy or radiotherapy will be excluded.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 April 2022 and was last updated on 18 April 2022 (registration number INPLASY202240106).

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studies reported that ACT had no significant among patients with PNI.

## METHODS

**Participant or population:** Patients with colorectal cancer who underwent adjuvant chemotherapy after surgery will be included. Patients who only underwent neoadjuvant chemotherapy or radiotherapy will be excluded.

**Intervention:** Perineural invasion is the main exposure, and adjuvant chemotherapy is the main intervention.

**Comparator:** Colorectal cancer patients without perineural invasion who underwent adjuvant chemotherapy will be considered as the control group.

**Study designs to be included:** RCTs and observational studies.

**Eligibility criteria:** Patients with colorectal cancer who underwent adjuvant chemotherapy after surgery will be included. Patients who only underwent neoadjuvant chemotherapy or radiotherapy will be excluded.

**Information sources:** Databases including MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials were systematically searched (last update on 13 April 2022).

**Main outcome(s):** Overall survival.

**Quality assessment / Risk of bias analysis:** All data will be extracted by 2 reviewers. Newcastle–Ottawa Scale(NOS) was performed for all included studies. Articles with NOS > 6 were considered as high quality. Begg and Egger test will be used to assess the publication bias.

**Strategy of data synthesis:** We extracted hazard ratios (HRs) from the included trials. Logarithm-transformed HRs were pooled using the DerSimonian and Laird random-effects model along with the corresponding 95% CIs due to the anticipated substantial heterogeneity in terms of the enrolled

populations. For studies that did not provide HRs for the association between PNI and adjuvant chemotherapy, we tried to estimate indirectly from data or curves using the methods described by Parmar. Between-study heterogeneity was calculated by the  $I^2$  statistic with an  $I^2 \geq 50\%$  considering significant heterogeneity. To explore the sources of heterogeneity, we carried out a series of subgroup analyses based on different stages and sites of the cancer.

**Subgroup analysis:** Subgroup analyses will be performed based on tumor stages and location (colon vs. rectal).

**Sensitivity analysis:** A sensitivity analysis will be performed to decide whether to exclude low-quality studies.

**Language:** English.

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

**Keywords:** colorectal cancer; perineural invasion; adjuvant chemotherapy; survival outcomes.

### Contributions of each author:

Author 1 - Yazhou He conceived of the study and approved publication of this study.

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