# INPLASY PROTOCOL

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**None declared.**

# Direct oral anticoagulants versus low-molecular-weight heparin for acute treatment of venous thromboembolism in patients with gastrointestinal cancer: A systematic review and meta-analysis

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**Review question / Objective:** **P: Patients who were diagnosed with gastrointestinal malignancies with cancer-associated thrombosis; I: Direct oral anti-coagulants; C: Low molecular weight heparins; O: Bleeding events.**
**Condition being studied:** **The association between gastrointestinal (GI) cancer and a high incidence of venous thromboembolism (VTE) is well known. Previous randomized controlled studies demonstrated that direct oral anticoagulants (DOACs) effectively treat cancer-associated VTE (CAT). However, some DOACs appeared to increase the risk of bleeding, particularly in patients with GI malignancies. So, we plan to conduct a systematic review and meta-analysis to evaluate the safety and efficacy of DOACs in GI cancer-associated thrombosis.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 August 2021 and was last updated on 30 August 2021 (registration number INPLASY202180113).

## INTRODUCTION

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## METHODS

**Search strategy:** Two investigators separately examined the included articles from the search terms 'DOACs', 'anticoagulants', and 'GI cancer' from two databases (EMBASE and MEDLINE).

**Participant or population:** Adults with gastrointestinal malignancies with cancer-associated thrombosis.

**Intervention:** Direct oral anti-coagulants.

**Comparator:** Low molecular weight heparins.

**Study designs to be included:** Both randomized controlled trial and cohort study (retrospective or prospective).

**Eligibility criteria:** 1) the type of study must have been a randomized controlled trial (RCT) or a cohort studies (either retrospective or prospective); 2) the study must have compared the efficacy between at least one DOAC and at least one LWMH in GI cancer-associated venous thromboembolism; 3) the study must have included the primary outcome of the study; and, 4) the study must have defined the definition of major bleeding according to the criteria of the International Society on Thrombosis and Haemostasis (ISTH).

**Information sources:** Electronic databases including MEDLINE and EMBASE.

**Main outcome(s):** The primary outcome was either recurrent VTE or major bleeding after anticoagulant therapy according to the ISTHcriteria.

**Quality assessment / Risk of bias analysis:** The Jadad Quality Assessment Scale and the Newcastle-Ottawa Scale were used to evaluate the quality of the included randomized controlled trials and the non-randomized studies, respectively.

**Strategy of data synthesis:** Review Manager 5.3 software from the Cochrane Collaboration (London, UK) was used to analyze all data. Two investigators extracted all data from the selected studies using a standardized data extraction form. The effect was estimated and combined with 95% confidence intervals (CIs) using the Mantel-Haenszel method. Cochran's Q test was calculated, and the statistical heterogeneity among the studies was estimated using the I2 statistic. A p-value less than 0.05 was considered statistically significant.

**Subgroup analysis:** The subgroup analysis in this study including major, clinically relevant non-major bleeding, and recurrent thrombosis according to the type of DOACs and type of GI cancers (luminal vs non-luminal).

**Sensitivity analysis:** No sensitivity analysis is planned to perform in this systematic review and meta-analysis.

**Language:** English.

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

**Keywords:** Acute treatment, venous thromboembolism, Direct oral anticoagulants, Gastrointestinal cancer, Low-molecular-weight heparin, Patients.

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