INPLASY PROTOCOL

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None declared.

Cost and clinical outcomes in the use of new oral anticoagulants versus warfarin in deep vein thrombosis: A systematic review protocol

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Review question / Objective: **What are the benefits of using new oral anticoagulants compared to warfarin in terms of efficacy, bleeding, and cost among people with deep vein thrombosis? This study aimed to compare the effectiveness, bleeding incidence, and cost between NOAC and warfarin in DVT patients.**
Condition being studied: **The patient confirmed DVT with the results of the Wells' score and D-dimer test stating "possible DVT" and followed by an ultrasound examination which stated "DVT positive". Patients are taking oral anticoagulants to treat DVT or to prevent a recurrence. Oral anticoagulants consist of apixaban, rivaroxaban, edoxaban, dabigatran, and warfarin.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 December 2022 and was last updated on 27 December 2022 (registration number INPLASY2022120106).

INTRODUCTION

Review question / Objective: **What are the benefits of using new oral anticoagulants compared to warfarin in terms of efficacy, bleeding, and cost among people with deep vein thrombosis? This study aimed to compare the effectiveness, bleeding incidence, and cost between NOAC and warfarin in DVT patients.**

Rationale: **Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third-order vascular disease with the highest morbidity and mortality rates in the world. DVT patients have a high probability of**

recurrence and bleeding. Thus this could have implications for an increase in the economic burden.

Condition being studied: The patient confirmed DVT with the results of the Wells' score and D-dimer test stating "possible DVT" and followed by an ultrasound examination which stated "DVT positive". Patients are taking oral anticoagulants to treat DVT or to prevent a recurrence. Oral anticoagulants consist of apixaban, rivaroxaban, edoxaban, dabigatran, and warfarin.

METHODS

Search strategy: The search strategy will use PubMed and Embase databases. Searches will be conducted using a combination of text words and the relevant Medical Subject Heading (MeSH) terms. We will use the keywords “deep vein thrombosis”, “new oral anticoagulants”, “direct oral anticoagulants”, “novel oral anticoagulants”, “rivaroxaban”, “apixaban”, edoxaban”, “dabigatran”, “warfarin”, "coumarin" “recurrence”, “relapse”, “bleeding”, “hemorrhages”, “cost”, “cost analysis” and “cost-effectiveness”.

Participant or population: Patients with deep vein thrombosis (DVT).

Intervention: New oral anticoagulants including apixaban, rivaroxaban, edoxaban, dabigatran.

Comparator: Old anticoagulants, warfarin, coumarins.

Study designs to be included: All clinical studies which provide the outcomes of clinical efficacy, bleeding, and the cost will be included. All economic evaluations from trial studies or model studies will be analyzed.

Eligibility criteria: We will include economic evaluation studies, including cost minimization, cost-effectiveness analysis, cost-benefit analysis, and cost-utility. We will exclude non-research studies such as book chapters, reports, conference proceedings, and review articles.

Information sources: The search strategy will use PubMed and Embase databases. We will review the published article from January 2005 to July 2021.

Main outcome(s): The rate of DVT recurrence.

Additional outcome(s): The risk of bleeding and the cost.

Data management: The title and abstract of each article will be screened based on inclusion and exclusion criteria. The selected articles will be downloaded for the full-text version. For extracting data, we will present the data in the table, including general information on articles, such as author, year of publication, study design, type of intervention, controls, results, and others. Two independent reviewers will carry out the assessments. If there is a difference of opinion between the two parties, we will discuss it with the third person to make a final decision.

Quality assessment / Risk of bias analysis: We will use the Consensus on Health Economic Criteria (CHEC) to assess the quality assessments and the risk of bias. In analyzing cost-effectiveness analysis (CEA), the instrument used is CHEC.

Strategy of data synthesis: The data that has been collected in the extraction table will then be analyzed and synthesized descriptively. The results of the processing will be displayed in a table. The discussion of the results will be adjusted and discussed with the theories listed in the literature review to answer the problem formulation and produce a conclusion.

Subgroup analysis: The cost outcome will be assessed according to World Bank classification in terms of high-income countries and low- and middle-income countries (LMICs).

Sensitivity analysis: Sensitivity analysis will be performed using deterministic and probabilistic sensitivity analysis.

Language restriction: There will be restricted to English-language in original full-text only.

Country(ies) involved: Indonesia and The Netherlands.

Other relevant information: The study is supported by Universitas Airlangga, Indonesia.

Keywords: anticoagulants, warfarin, recurrence, bleeding, cost.

Dissemination plans: The study's findings will be disseminated in a peer-review journal.

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