INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Bleeding outcomes associated with dabigatran and rivaroxaban used in patients with non-valvular atrial fibrillation: a meta-analysis of random control trials

Zheng, X[1]; Zhang, L[2]; Zhang, J[3].

Review question / Objective: **The patients of this study are non-valvular atrial fibrillation and they are randomly included in the dabigatran group and the rivaroxaban group. The outcome of this study is bleeding events and the type of studies included is randomized controlled trial. In a word, the study is aim to assess bleeding risk of dabigatran and rivaroxaban used in patients with non-valvular atrial fibrillation.**
Information sources: **All information will be collected from the PubMed, Cochrane Central Register of Controlled Trials, Embase, and Clinical Trials.gov.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 December 2021 and was last updated on 01 December 2021 (registration number INPLASY2021120002).

INTRODUCTION

Review question / Objective: **The patients of this study are non-valvular atrial fibrillation and they are randomly included in the dabigatran group and the rivaroxaban group. The outcome of this study is bleeding events and the type of studies included is randomized controlled trial. In a word, the study is aim to assess bleeding risk of dabigatran and rivaroxaban used in patients with non-valvular atrial fibrillation.**

Condition being studied: **Bleeding outcomes associated with dabigatran and rivaroxaban used in patients with non-valvular atrial fibrillation. At this stage, we**

are concentrating on using the search database resource to formulate search strategies.

METHODS

Search strategy: PubMed, EMBASE, and the Cochrane Central Registry of Controlled Trials can be used to searching for literatures on comparing dabigatran with rivaroxaban using the terms 'dabigatran, rivaroxaban, anticoagulants, atrial fibrillation'. Taking PubMed for an example, the search strategy is shown as ((((Dabigatran[MeSH Terms]) OR ((Dabigatran[Title/Abstract] OR Pradaxa[Title/Abstract] OR Rendix[Title/Abstract]) OR (BIBR 953*[Title/Abstract] OR BIBR 1048[Title/Abstract])))) AND ((Rivaroxaban[MeSH Terms]) OR ((rivaroxaban[Title/Abstract] OR Xarelto[Title/Abstract]) OR (Bay 597939[Title/Abstract]))))) OR (((Anticoagulants[MeSH Terms]) OR (((new[Title/Abstract] OR novel[Title/Abstract] OR direct[Title/Abstract]) AND (oral[Title/Abstract])) AND (anticoagulant*[Title/Abstract])))) OR ((NOAC[Title/Abstract]) OR (DOAC[Title/Abstract])))) AND (((((Atrial Fibrillation[MeSH Terms]) OR (Atrial Flutter[MeSH Terms])) OR ((atrial[Title/Abstract] OR atrium[Title/Abstract] OR auricular[Title/Abstract]) AND (fibrillation*[Title/Abstract] OR arrhythmia*[Title/Abstract] OR flutter*[Title/Abstract])))) OR (non-valvular atrial fibrillation[Title/Abstract])) OR (NVAF[Title/Abstract])).

Participant or population: Patients with non-valvular atrial fibrillation.

Intervention: Dabigatran group.

Comparator: Rivaroxaban group.

Study designs to be included: Randomized controlled trial.

Eligibility criteria: XStudies met the following inclusion criteria were included: (1) patients with non-valvular atrial fibrillation;(2) full-text articles of clinical trials examining dabigatran versus rivaroxaban;(3) randomized controlled trials conducted by human;(4) the incidence of bleeding event reported were clinical outcomes of this analysis. Among all bleeding events, major bleeding is defined as symptomatic bleeding in a critical organ or area, like intracranial, retroperitoneal, intraspinal, intraocular, intraarticular or pericardial and so on. Major bleeding was defined based on the International Society on Thrombosis and Haemostasis (ISTH) criteria which included symptomatic bleeding, fatal bleeding, and bleeding causing a fall in the hemoglobin level of 20g/l or contributing to transfusion of ≥ 2 units of red blood cells or whole blood9. Minor bleeding was defined as clinically relevant bleeding that could not meet the criteria of major bleeding.Studies met the following exclusion criteria were excluded: (1) there were duplicate studies from the same trial.(2) there was incomplete outcome data in the studies or they did not report bleeding outcomes among their clinical endpoints;(3) it were not possible to assess the full text or lacked a control group ,such as reviews, meta-analyses, editorials, comment, observational studies and so on.

Information sources: All information will be collected from the PubMed, Cochrane Central Register of Controlled Trials, Embase, and Clinical Trials.gov.

Main outcome(s): 2206 potentially relative publications have been searched using Embase so far. 1369 potentially relative publications had been searchedby using Cochrane Central Register of Controlled Trials by Oct, 6th, 2021.

Quality assessment / Risk of bias analysis: Because the type of the included literature were randomized controlled trials, the quality assessment performed by Cochrane ROB table including random sequence generation, allocation concealment, blinding of the participants and personnel, blinding of outcome assessment, attrition bias, reporting bias and other bias were collected to make the

quality evaluation of the included investigations.

Strategy of data synthesis: #1 (Dabigatran OR Pradaxa OR Rendix):ti,ab,kw OR (BIBR 953* OR BIBR 1048):ti,ab,kw (Word variations have been searched) #2 MeSH descriptor: [Dabigatran] explode all trees #3 (rivaroxaban OR Xarelto):ti,ab,kw OR (Bay 597939):ti,ab,kw (Word variations have been searched) #4 MeSH descriptor: [Rivaroxaban] explode all trees #5 MeSH descriptor: [Anticoagulants] explode all trees #6 (new AND anticoagulant*):ti,ab,kw #7 MeSH descriptor: [Atrial Fibrillation] explode all trees #8 MeSH descriptor: [Atrial Flutter] explode all trees #9 (atrial OR atrium OR auricular):ti,ab,kw AND (fibrillation* OR arrhythmia* OR flutter*):ti,ab,kw | #10 (AF):ti,ab,kw | #11 #1 OR #2 | #12 #3 OR #4 | #13 #11 AND #12 | #14 #5 OR #6 | #15 #7 OR #8 OR #9 OR #10 | #16 #13 OR #14 AND #15.

Subgroup analysis: Not yet.

Sensitivity analysis: Not yet.

Language: We use English mainly.

Country(ies) involved: China.

Keywords: dabigatran; rivaroxaban; atrial fibrillation.

Contributions of each author:

Author 1 - Xu-ya Zheng collects the data related to the studies and approves the final draft.
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Author 3 - Junfeng Zhang analyzes the data and reviews the study.
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