# DSEN ABSTRACT

# Direct oral anticoagulants and the risk of major bleeding in patients with non-valvular atrial fibrillation: Health Canada and European Medicines Agency collaboration (Q17-01)

*A study conducted by the Canadian Network for Observational Drug Effect Studies (CNODES)*


## Summary

- This international, multi-center, retrospective cohort, confirmed that the risk of major bleeding associated with DOACs as a class is not increased compared to VKAs. Furthermore, the study observed a modest increased risk of major bleeding with rivaroxaban, and a lower risk with apixaban and dabigatran.


## Key messages

- This is the largest cohort study that confirms that there is no clinically relevant difference in major bleeding risk between VKAs and DOACs as a class of drugs.

## Project Lead & Team

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- Team members available here

## Link to publication

- Van den Ham et al. PDS. 2021. DOI : 10.1002/pds.5317

## What is the issue?

- Vitamin K antagonists (VKAs) were the first line of anticoagulation therapy; however, the treatments options have broadened with the introduction of the direct oral anticoagulants (DOACs).
- According to the Canadian and European guidelines, DOACs are the preferred treatment over VKAs for first time users of oral anticoagulants in the prevention of embolic stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF).
- Further evidence on the real world safety and effectiveness of DOACs is needed in Canada and Europe.

## What was the aim of the study?

- The aim of this international collaboration with the European Medicines Agency (EMA) is to evaluate the risk of major bleeding in DOAC users compared with VKA users across multiple Canadian provinces and European countries.

## How was the study conducted?

- We undertook a retrospective cohort study, using four European health care databases (Denmark, Germany, Spain, United Kingdom) and six Canadian provincial administrative health databases (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Nova Scotia).
- 421,523 first-time users of VKA or DOACs with a NVAF diagnosis were included.
- The main outcome was any major bleeding. Secondary outcomes were gastrointestinal (GI) bleeding and intracranial hemorrhage (ICH). Incidence rates of the events, hazard ratios (HR) and 95% confidence intervals (CI) were calculated. The risk estimates were pooled across sites using a random effects meta-analysis.

## What did the study find?

- Compared to VKA use, the risk of any major bleeding for:
  - DOACs overall had showed a pooled HR of 0.94 (95% CI: 0.87-1.02),
  - Rivaroxaban showed a modestly increased risk (HR 1.11, 95% CI: 1.06–1.16),
  - Apixaban showed a decreased risk (HR: 0.76, 95% CI: 0.69–0.84),
  - Dabigatran showed a decreased risk (HR 0.85, 95% CI: 0.75–0.96).
- Rivaroxaban and dabigatran increased the risk of GI bleeding by approximately 20%
- Every DOAC reduced the risk for ICH (consistent with the clinical trials results)


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CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

CNODES CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES


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