

# Effectiveness and safety of non-vitamin K anticoagulants (NOACs) versus warfarin in frail patients with nonvalvular atrial fibrillation (AF): a nationwide cohort study

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Study

Ongoing

## Administrative details

### EU PAS number

EUPAS39592

### Study ID

41003

### DARWIN EU® study

No

### Study countries

Denmark

### Study description

Growing evidence suggests that frail patients with AF are less likely to receive adequate oral anticoagulant therapy (OAC), although frail patients present higher thrombotic risk and mortality. Part of this care gap may be explained by the scarce data on the safety and effectiveness of NOACs versus warfarin in frail AF patients. Therefore, this study aimed (1) to present population characteristics and rates of effectiveness and safety outcomes among frail patients with non-valvular AF in Denmark according to OAC treatment regimen (no OAC, warfarin, or NOAC) and (2) to investigate the comparative effectiveness and safety of NOACs (Dabigatran, Rivaroxaban, and Apixaban, as a class) versus warfarin in a Danish nationwide cohort of frail patients with non-valvular AF. Non-interventional, observational cohort studies based on secondary data collection from Danish nationwide administrative databases will be used for the investigations. The source population comprise all residents of Denmark between 2013-2018. The study population will comprise all frail patients with an inpatient or outpatient primary or secondary discharge diagnosis of non-valvular AF. Frail patients will be identified using the ICD-10 based Hospital Frailty Risk Score (HFRS).

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### **Study status**

Ongoing

## Research institutions and networks

### Institutions

[Aalborg University Hospital](#)

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Institution

## Thrombosis and Drug Research Unit

### Contact details

#### **Study institution contact**

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**Study contact**

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#### **Primary lead investigator**

Anette Arbjerg Højen

**Primary lead investigator**

### Study timelines

#### **Date when funding contract was signed**

Planned: 01/02/2021

Actual: 19/04/2021

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#### **Study start date**

Planned: 22/02/2021

Actual: 20/04/2021

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**Data analysis start date**

Actual: 07/05/2021

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**Date of final study report**

Planned: 30/09/2021

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Bayer AG, Berlin, Germany

## Regulatory

**Was the study required by a regulatory body?**

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

#### Study type list

**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Effectiveness study (incl. comparative)

**Main study objective:**

(1) To present population characteristics and rates of effectiveness and safety outcomes among frail patients with non-valvular atrial fibrillation in Denmark according to OAC treatment regimen (no OAC, warfarin, or NOAC). (2) To investigate the comparative effectiveness and safety of NOACs versus warfarin in a Danish nationwide cohort of frail patients with non-valvular atrial fibrillation.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(B01AA03) warfarin

warfarin

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

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### **Medical condition to be studied**

Atrial fibrillation

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### **Additional medical condition(s)**

All frail patients with an inpatient or outpatient primary or secondary discharge diagnosis of non-valvular atrial fibrillation. Frail patients will be identified using the Hospital Frailty Risk Score (HFRS). HFRS, a score utilizing ICD-codes, was developed to identify patients at low (HFRS <5), intermediate (HFRS 5-15) and high risk (HFRS >15) of frailty.

## Population studied

### **Age groups**

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

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### **Estimated number of subjects**

30000

## Study design details

## **Outcomes**

The primary effectiveness outcome is a diagnosis of stroke or systemic embolism. The primary safety outcome is major bleeding recorded as intracranial, gastro-intestinal, and major bleeding in various anatomical positions and reported in total as 'any bleeding'. All-cause death was also included as an outcome.

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## **Data analysis plan**

Substudy 1: Patient baseline characteristics will be described for the overall study population and according to age ( $\geq 80$  or  $< 80$ ). Cumulative incidence functions will be used to visualize how risk of outcomes evolve over time since AF diagnosis according to OAC regimen and age group using the Aalen-Johansen estimator assuming death as competing risk. The absolute risk of each study outcome according to OAC regimen and age group will be calculated at 1 year after AF diagnosis. Substudy 2: Patient baseline characteristics will be described for the study population according to baseline treatment group. To compare the risk of each endpoint among NOAC users with warfarin users reference), pooled logistic regression models will be used to estimate treatment effects by means of hazard ratios for the effectiveness and safety outcomes (both an ITT and PP approach). To allow an unbiased comparison of the treatment groups, we plan to use inverse probability of treatment weighting (IPTW).

## **Data management**

### **ENCePP Seal**

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### **Data source(s)**

Danish registries (access/analysis)

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### **Data source(s), other**

Danish Registries (access/analysis)

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### **Data sources (types)**

Administrative healthcare records (e.g., claims)

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

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### **Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No