### Methods

**Study design**
Cohort study in the SNDS nationwide French claims database including all new users of dabigatran or VKA for NVAF aged ≥ 80 years in 2013, with three-year history and one-year follow-up in the database.

**Data source**
The SNDS database contains individual pseudonymised information from 66 million persons on:
- Gender, date of birth, area of residence, date of death;
- Long-term disease registration with associated ICD-10 codes for full insurance coverage (with start and end dates);
- Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgical hospitalisations, with the date and duration of hospitalisation, medical procedures.

**NVAF population**
Patients with long-term disease registration, hospitalisation or procedure for atrial fibrillation without valvular disease history and nor other probable indication (three-year database history).

**Outcomes: during anticoagulant exposure period (on treatment)**
- Clinical events: hospital admission with main diagnosis of clinically relevant bleeding (CRB), major bleeding, stroke and systemic embolism (SSE) and acute coronary syndrome (ACS);
- Death (all-cause);
- Composite criterion: first event among CRB, SSE, ACS or death.

**Data analysis**
- 1:1 matched analysis on gender, age (±1 year), date of the first drug dispensing (±14 days), and high-dimensional propensity (hdPS) (± 0.05).
- Cumulative incidence of outcomes using Kaplan-Meier estimate (death, composite) or cumulative incidence function (other outcomes).
- Hazard ratios (HR) [95% confidence interval] of outcomes during first prescribed anticoagulant exposure, using Cox proportional hazard risk (death, composite) or Fine and Gray models (other outcomes).

*Probability to be treated by dabigatran versus VKA using a logistic regression model with 500 variables including gender, age, stroke risk factors, bleeding risk factors.

### Results

#### Benefit-risk profile of dabigatran compared with vitamin-K antagonists in elderly patients with non-valvular atrial fibrillation:
- Of 371,539 new users of dabigatran, rivaroxaban or VKA in 2013 in France:
  - 9,257 patients aged ≥ 80 years were treated with dabigatran,
  - 44,853 with VKA for NVAF.
- For dabigatran versus VKA, 8,569 patients were matched per treatment group (93% of dabigatran group).
- Patient characteristics and hdPS distribution showed differences between treatment groups, and were normalized after matching (Figure 1, Table 1). After matching, standardized differences were < 10% for all variables, even ≤ 2% for most variables (Figure 2).

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### Conclusion
- Different dabigatran and VKA prescription patterns in the elderly patients, but same population characteristics after hdPS matching.
- Analysis of this nationwide cohort study of more than 50,000 new anticoagulant users for NVAF aged ≥ 80 years shows a significantly better benefit-risk profile for dabigatran versus VKA in elderly patients with 16% fewer major outcomes of clinically relevant bleedings, stroke and systemic embolism or death.

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**Declaration of interest:** This study was funded by an unrestricted grant from Boehringer Ingelheim France. It was designed, conducted, and analysed independently by the Bordeaux PharmacoEpi of the Bordeaux University. It was overseen by independent experts.

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**Table 1. Main patients characteristics in all NVAF populations**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Dabigatran ≥ 80 years</th>
<th>VKA n = 44,853</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>3704 (41.0)</td>
<td>22065 (51.2)</td>
</tr>
<tr>
<td>Age at index date (in years), mean ± SD</td>
<td>85.7 (3.9)</td>
<td>77.9 (11.1)</td>
</tr>
<tr>
<td>Age at index date (in categories), n (%)</td>
<td>80 years</td>
<td>n (0.0)</td>
</tr>
<tr>
<td>≥ 80 years</td>
<td>9257 (100.0)</td>
<td>23357 (52.3)</td>
</tr>
<tr>
<td>Stroke risk factors (score), n (%)</td>
<td>2151 (23.2)</td>
<td>13720 (30.7)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>4481 (48.1)</td>
<td>32832 (73.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1602 (18.3)</td>
<td>11707 (26.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1383 (14.9)</td>
<td>7018 (15.0)</td>
</tr>
<tr>
<td>Stroke or transient ischaemic attack (TIA) history</td>
<td>1315 (14.2)</td>
<td>5904 (13.0)</td>
</tr>
<tr>
<td>Vascular disease history</td>
<td>85-74 years</td>
<td>n (0.0)</td>
</tr>
<tr>
<td>Age 85-74 years</td>
<td>9257 (100.0)</td>
<td>3904 (88.5)</td>
</tr>
<tr>
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</table>

*Based on general characteristics of patients, long-term disease with full insurance coverage, as well as three-year history of hospital discharge summary diagnosis, and drugs reimbursed.

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**Table 2. One-year cumulative incidence of outcomes during the drug exposure period for matched NVAF populations**

<table>
<thead>
<tr>
<th>Event</th>
<th>Dabigatran ≥ 80 years</th>
<th>VKA n = 8,569</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (all-cause)</td>
<td>329 (3.7 [3.2; 4.3])</td>
<td>345 (3.2 [2.9; 3.5])</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>110 (2.0 [1.6; 2.4])</td>
<td>150 (2.0 [1.6; 2.4])</td>
</tr>
<tr>
<td>Stroke and systemic embolism (SSE)</td>
<td>114 (2.1 [1.7; 2.6])</td>
<td>170 (2.6 [2.2; 3.0])</td>
</tr>
<tr>
<td>Acute coronary syndrome (ACS)</td>
<td>91 (1.7 [1.4; 2.0])</td>
<td>182 (2.3 [2.0; 2.6])</td>
</tr>
<tr>
<td>Death (all-cause)</td>
<td>496 (84.9)</td>
<td>674 (80.6)</td>
</tr>
<tr>
<td>Composite criterion (CRB, SSE, ACS, death)</td>
<td>449 (14.3 [13.4; 15.3])</td>
<td>1128 (17.1 [16.2; 18.1])</td>
</tr>
</tbody>
</table>

*95% CI: 80 years versus VKA

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**Figure 1. hdPS distribution in all and matched populations: dabigatran ≥ 80 years versus VKA**

**Figure 2. Standardized differences for all and matched populations: dabigatran ≥ 80 years versus VKA**

**Figure 3. Hazard ratios and 95% CI of outcomes: dabigatran ≥ 80 years versus VKA**

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**Conclusions**
- Different dabigatran and VKA prescription patterns in the elderly patients, but same population characteristics after hdPS matching.
- Analysis of this nationwide cohort study of more than 50,000 new anticoagulant users for NVAF aged ≥ 80 years shows a significantly better benefit-risk profile for dabigatran versus VKA in elderly patients with 16% fewer major outcomes of clinically relevant bleedings, stroke and systemic embolism or death.