# Reduction in ischemic stroke rates in patients with non-valvular atrial fibrillation during the period 2013-2020: a real-life study in Spain

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## Introduction

- AF is a disabling condition and causes up to 30% of strokes[1]. The prevalence of AF in Spain is 4.4% in people aged >40 years, and most of them suffer non-valvular AF (NVAF)[1-3].
- Antithrombotic treatments such as vitamin K antagonists (VKA) and the new direct-acting oral anticoagulants (NOAC) are effective in preventing cardioembolic complication[1,4–6], other antithrombotic treatments commonly used are antiplatelet drugs.
- The management of stroke in patients with AF constitutes a considerable burden for healthcare systems, being hospitalizations the major cost component[7,8]

## Objective

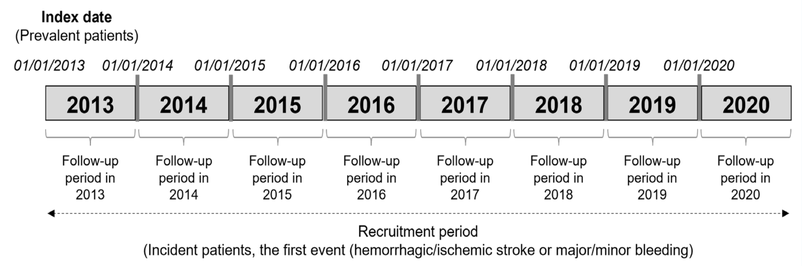
- This study aims to analyze the variations in the incidence of cardiovascular events and mortality rates in patients with NVAF receiving antithrombotic treatment (VKA, NOAC or antiplatelet drugs) between 2013 and 2020, and estimates the impact of these variations in the use of healthcare resources and costs in Spain.

## Methods

### Design of the study

- This is an observational, retrospective study based on the electronic medical records (EMRs) of the BIG-PAC database[13].
- EMRs undergo rigorous anonymization in the centers of origin, in compliance with Spanish regulations.
- The study considered patients diagnosed with AF, who were on treatment with antithrombotic therapies (VKA, NOAC or antiplatelet drugs) between 2013 and 2020 (Figure 1).
  - Prevalent patients were those on treatment with oral anticoagulant treatment with antithrombotic therapies and were followed until December 31st of the same year, the first event (hemorrhagic/ischemic stroke or major/minor bleeding), the discontinuation of treatment, or death, whichever occurred first.

**Figure 1. Study design**




### Study variables

- Demographic characteristics, comorbidities, effectiveness, treatment patterns and healthcare resources utilization were analyzed. The results in prevalent patients were compared between the antithrombotic therapies between 2013 and 2020 that led to their inclusion in the study.

## Results

### Characteristics of prevalent patients

- On average, age of the prevalent patient groups varied from 76.6 years (SD: 10.4) to 78.1 years (SD: 10.3), whereas the percentage of males ranged between 42.2% and 43.8% (p≤0.005) (Table 1).
- Regarding the prevalence of comorbidities, increased during the period of the study from an average of 1.5 comorbidities (SD: 1.3) to 3.2 comorbidities (SD: 1.7) (p<0.001) (Table 1). In 2020, the most frequent comorbidities were hypertension (68.5%), followed by hypercholesterolemia (49.1%) and diabetes (32.1%).
- The average Charlson comorbidity index increased in the different cohorts, up to 2.5 (SD: 2.1) in 2020 (p<0.001). The CHA2D2S-VASc varied from 3.3 (SD: 1.5) to 3.9 (SD: 1.8), whereas HAS-BLED ranged between 2.6 (SD: 0.7) and 2.7 (SD: 0.8) (p<0.001 in both comparisons) (Table 1). Therefore, the study population had a high risk of stroke and thromboembolism, and bleedings.
- The use of VKA decreased from 73.4% in 2013 to 59.4% in 2020 (decrease: 19.1%; p<0.001). On the other hand, there was an 79.2%-increase in the use of NOAC from 18.8% to 33.7% in those years, respectively (p≤0.014). There was a slight decrease in the prescription of antiplatelet drugs, from 7.8% to 7.0% (decrease: 10.3%; p≤0.012) (Table 1).

**Table 1. Characteristics of prevalent patients**

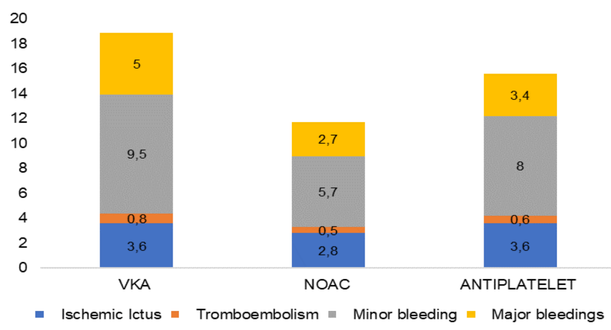
| Study groups | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | p |
|---|---|---|---|---|---|---|---|---|---|
| **Number of patients, n (%)** | 10062 (6.1) | 14031 (8.5) | 16868 (10.2) | 19369 (11.7) | 22509 (13.6) | 24536 (14.8) | 27277 (16.5) | 30878 (18.7) | |
| **Age, years, mean (SD)** | 76.6 (10.4) | 76.8 (10.5) | 77.0 (10.4) | 77.2 (10.5) | 77.4 (10.4) | 77.5 (10.3) | 77.8 (10.3) | 78.1 (10.3) | <0.001 |
| **Gender male, (%)** | 43.5 | 43.3 | 43.8 | 43.3 | 42.7 | 42.3 | 42.6 | 42.2 | 0.005 |
| **Comorbidities per patient, mean (SD)** | 1.5 (1.3) | 2 (1.4) | 2.3 (1.5) | 2.5 (1.5) | 2.7 (1.6) | 2.9 (1.6) | 3.1 (1.7) | 3.2 (1.7) | <0.001 |
| **Scales** | | | | | | | | | |
| **CCI, mean (SD)** | 1.4 (1.5) | 1.6 (1.7) | 1.8 (1.8) | 2 (1.8) | 2.1 (1.9) | 2.3 (2.0) | 2.4 (2.1) | 2.5 (2.1) | <0.001 |
| **$CHA_2DS_2$-VASc, mean (SD)** | 3.3 (1.5) | 3.4 (1.6) | 3.5 (1.6) | 3.6 (1.7) | 3.7 (1.7) | 3.8 (1.7) | 3.8 (1.8) | 3.9 (1.8) | <0.001 |
| **HAS-BLED, mean (SD)** | 2.6 (0.7) | 2.6 (0.7) | 2.6 (0.8) | 2.6 (0.8) | 2.6 (0.8) | 2.7 (0.8) | 2.7 (0.8) | 2.7 (0.8) | <0.001 |
| **Antithrombotic treatments** | | | | | | | | | |
| **VKA, n (%)** | 7384 (73.4) | 9835 (70.1) | 11512 (68.2) | 13039 (67.3) | 15019 (66.7) | 15987 (65.2) | 17094 (62.7) | 18328 (59.4) | |
| **NOAC, n (%)** | 1892 (18.8) | 3191 (22.7) | 3933 (23.3) | 4784 (24.7) | 5847 (26) | 7114 (29) | 8424 (30.9) | 10394 (33.7) | |
| **Antiplatelet drugs, n (%)** | 786 (7.8) | 1005 (7.2) | 1423 (8.4) | 1546 (8) | 1643 (7.3) | 1435 (5.8) | 1759 (6.4) | 2156 (7.0) | |

CCI: Charlson comorbidity index; NOAC: new direct-acting oral anticoagulants; SD: standard deviation; VKA: vitamin K antagonists.

### Cardiovascular events and deaths

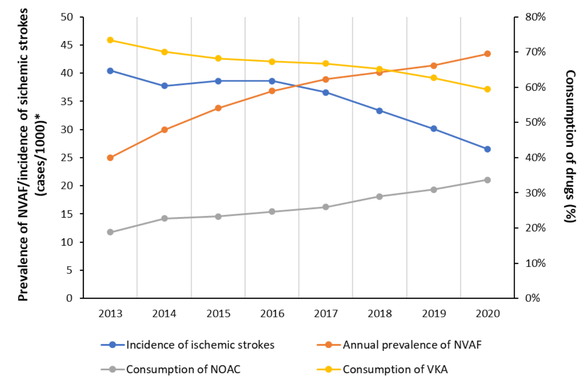
- There were no differences in the number of patients with cardiovascular events during the years (between 15.1% and 16.3%; p=0.053)
- The most frequent events were minor bleedings, followed by major bleedings and ischemic strokes (Figure 2).
- During the follow-up period of the study, patients on treatment with NOAC had fewer cardiovascular events (Figure 2).
- The mortality rate ranged between 4.5% and 5.1% (p=0.028).

**Figure 2. Incidence of cardiovascular events and deaths**




NOAC: Non-vitamin K antagonist oral anticoagulants; VKA: vitamin K antagonists.

**Figure 3. Relationship between NOAC consumption, ischemic stroke incidence rate, prevalence NVAF according to the time period analyzed.**



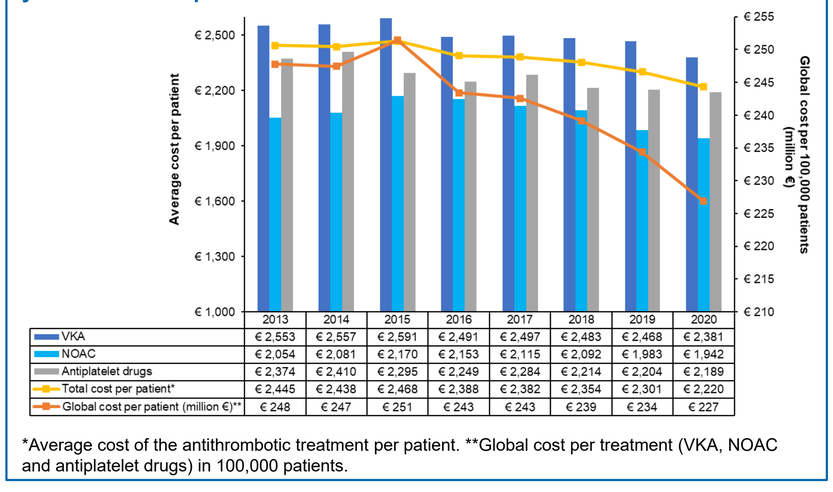

*The prevalence of NVAF was estimated as the number of cases per 1,000 inhabitants ≥ 40 years registered in BIG-PAC. The incidence of ischemic strokes was estimated as the number of cases per 1,000 patients with NVAF in the corresponding cohorts.

- It was estimated that the consumption of NOAC increased whereas the incidence of ischemic strokes and the prevalence of NVAF decreased during the study period (Figure 3).

### Use of healthcare resources and costs: overall results per year

- The most frequent resources required by NVAF patients with antithrombotic therapies were primary care, nursing and specialist visits and laboratory tests.
- In addition, the average length of hospital stays decreased from 1.8 days (SD: 7.3) to 1.2 days (SD: 5.6). It should be noted that the decrease in the number of visits may be more pronounced in 2020 due to the COVID-19 pandemic.
- The decrease in the use of healthcare resources led to a reduction in healthcare costs, from €2,445 (SD: 3,945) to €2,220 (SD: 3,042) in 2013 and 2020, respectively (reduction 9.2%; p<0.001) (Figure 4).
- There were also substantial costs savings between 2013 and 2020, due to reductions in primary care, nursing and specialist visits.

**Figure 4. Distribution of the total healthcare cost (EUR) according to the years of follow-up and the treatment administered.**




*Average cost of the antithrombotic treatment per patient. **Global cost per treatment (VKA, NOAC and antiplatelet drugs) in 100,000 patients.

### Use of healthcare resources and costs: results per antithrombotic treatment

- NOAC patients required fewer healthcare resources than the other groups (p<0.001 for all comparisons), for this reason, the management costs of NOAC patients were lower (€2,051 [SD: 1,997]) than those on treatment with VKA (€2,489 [SD: 4,019]) and antiplatelet drugs (€2,260 [SD: 3,531]; p<0.001).
- The annual management costs per antithrombotic therapy decreased during the study period (Figure 4).

**Table 2. Distribution of the total healthcare cost (EUR) according to the years of follow-up and the treatment administered.**

| Study groups | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|---|---|---|---|---|---|---|---|---|
| **Number of patients, n (%)** | 10062 (6.1) | 14031 (8.5) | 16868 (10.2) | 19369 (11.7) | 22509 (13.6) | 24536 (14.8) | 27277 (16.5) | 30878 (18.7) |
| **VKA** | € 2.553 | € 2.557 | € 2.591 | € 2.491 | € 2.497 | € 2.483 | € 2.468 | € 2.381 |
| **NOAC** | € 2.054 | € 2.081 | € 2.170 | € 2.153 | € 2.115 | € 2.092 | € 1.983 | € 1.942 |
| **Antiplatelet drugs** | € 2.374 | € 2.410 | € 2.295 | € 2.249 | € 2.284 | € 2.214 | € 2.204 | € 2.189 |
| **Total** | € 2.445 | € 2.438 | € 2.468 | € 2.388 | € 2.382 | € 2.354 | € 2.301 | € 2.220 |

## Conclusions

Between 2013 and 2020, the treatment pattern of patients with NVAF in Spain significantly changed. In clinical practice, there was a decrease in the prescription of VKA and a substantial increase in the use of NOAC. Our results showed a decrease in the incidence of ischemic strokes, along with a reduction in the use of healthcare resources (particularly, primary care, nursing and specialist visits) and costs.

## References

1, Heidenreich PA, Estes NAM, Fonarow GC, Jurgens CY, Kittleson MM, Marine JE, et al. 2020 Update to the 2016 ACC/AHA Clinical Performance and Quality Measures for Adults With Atrial Fibrillation or Atrial Flutter: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. Circ: Cardiovascular Quality and Outcomes [Internet]. 2021 [cited 2021 Apr 8];14(1). 2. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur J Cardiothorac Surg. 2016;50(5):e1–88. 3. Gómez-Doblas JJ, Muñiz J, Martin JJA, Rodríguez-Roca G, Lobos JM, Awamleh P, et al. Prevalencia de fibrilación auricular en España. Resultados del estudio OFRECE. Revista Española de Cardiología. 2014;67(4):259–69. 4. Schäfer A, Flierl U, Berliner D, Bauersachs J. Anticoagulants for Stroke Prevention in Atrial Fibrillation in Elderly Patients. Cardiovasc Drugs Ther. 2020;34(4):555–68. 5. Lip GYH, Potpara T, Boriani G, Blomström-Lundqvist C. A tailored treatment strategy: a modern approach for stroke prevention in patients with atrial fibrillation. J Intern Med. 2016;279(5):467–76. 6. Escobar C, Borrás X, Freire RB, González-Juanatey C, Morillas M, Muñoz AV, et al. A Delphi consensus on the management of oral anticoagulation in patients with non-valvular atrial fibrillation in Spain: ACOPREFERENCE study. PLOS ONE. 2020;15(6):e0231565. 7. Li X, Tse VC, Au-Doung LW, Wong ICK, Chan EW. The impact of ischaemic stroke on atrial fibrillation-related healthcare cost: a systematic review. Europace. 2017;19(6):937–47. 8. Luengo-Fernandez R, Candio Paolo, Leal J, Violato M. Stroke Alliance for Europe. At what cost [Internet]. 2020 [cited 2022 Apr 21]. Available from: https://www.safestroke.eu/wp-content/uploads/2020/10/02.-At_What_Cost_EIOS_Summary_Report.pdf.

## Disclosures

This study was sponsored by Pfizer Inc./Bristol Myers Squibb. Dr. J. Comín-Colet reports fees as a coordinator investigator of this study by Pfizer and Bristol Myers Squibb. Antoni Sicras is an Atrys Health employee, CRO of the study. Inés Pérez Román is an Atrys Health employee, CRO of the study. Joel Salazar-Mendiguchía reports that he is a Bristol Myers Squibb employee and has BMS stocks. Isabel del Campo reports that she is a Bristol Myers Squibb employee has BMS stocks. Ainara Echeto reports that she is a Bristol Myers Squibb employee has BMS stocks. David Vilanova Larena reports that he is a Bristol Myers Squibb employee has BMS stocks. Dra. Olga Delgado Sánchez reports fees as a coordinator investigator of this study by Pfizer and Bristol Myers Squibb.

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