The use of new oral anticoagulants in patients with atrial fibrillation in Scotland – A population-based drug utilisation study

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Conflicts of Interest
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Background
Atrial fibrillation (AF) is a common arrhythmic disorder and a major risk factor for stroke.¹ Oral anticoagulants (OACs) are used long-term to prevent thromboembolic events; warfarin has been a mainstay in clinical practice for decades, and its utilisation and effects have been widely studied.² Non-adherence to medication – not taking a drug according to prescribing instructions – is a widespread phenomenon among patients treated with warfarin, and can cause a range of problems, including an increased risk of stroke shortly after treatment discontinuation.³ This rebound effect has been reported for some of the direct oral anticoagulants (DOACs) – dabigatran, rivaroxaban, and apixaban – as well,⁴ the short half lives of these new drugs might pose additional problems in non-adherent patients.

Concerns have therefore been raised regarding treatment interruptions with these new drugs. However, information regarding adherence to DOAC treatment is still rare.

Objective
To examine the uptake and use of DOACs in patients with a diagnosis of AF, confirmed in secondary care, in Scotland.

Methods
Study Design
Patients who have been treated with any DOAC between January 2009 and June 2014 have been identified using data from the Scottish Morbidity Records (SMR), linked to the Prescribing Information System (PIS), as shown in figure 1; data linkage was facilitated by using the Community Health Index (CHI), a unique patient identifier assigned to every resident.

Measuring adherence
Drug utilisation has been analysed by calculating discontinuation of and persistence to DOAC treatment, as well as adherence to medication. As adherence measures are not standardised and results from different studies are thus difficult to compare, three distinct measures to describe adherence have been used, as listed in figure 2: medication refill adherence (MRA), compliance rate (CR), and continuous, single-interval measure of medication availability (CSA).⁵

Results
Patient baseline characteristics
Median follow-up time was 230 days; 15.7% of patients received only one prescription for any DOAC, and the median number of DOAC prescriptions was 5 (IQR 2–9). Hypertension was present in approximately half of all patients (50.8%), while 19.7% had a history of prior stroke/transient ischaemic attacks.

Table 1: Patient baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Number patients</td>
<td>5438</td>
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<tr>
<td>Female (%)</td>
<td>2488 (45.8)</td>
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<tr>
<td>Mean age first prescription [years]</td>
<td>74.4 (11.3)</td>
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<tr>
<td>Prior VKA use (%)</td>
<td>3058 (56.2)</td>
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<tr>
<td>Median number different drugs, including OACs (IQR)</td>
<td>13 (9–18)</td>
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<tr>
<td>Mean CHA²-VASc score (SD)</td>
<td>3.3 (1.8)</td>
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<tr>
<td>Mean CHS score (SD)</td>
<td>1.8 (1.8)</td>
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DOAC uptake over time
Even though the majority of patients were still treated with vitamin K antagonists (VKAs), changes in treatment decisions could already be observed; figure 3 highlights the share of previously OAC-naïve patients where OAC treatment was initiated with a DOAC. Among these patients, 67.7% received rivaroxaban as drug of first choice; dabigatran and apixaban accounted for 17.7% and 14.6%, respectively.

Discontinuation & persistence
Applying an admissible gap of 28 days without drug supply after the presumed end of a prescription, 2020 patients (37.1%) discontinued treatment; however, 49.3% of these patients subsequently received at least one additional prescription for any DOAC, potentially indicating re-initiation of treatment.

Persistence declined considerably over time; while 65.3% of patients were still on treatment after 6 months, this was only the case for 47.5% after 12 months. Figure 4 depicts the decline in persistence over time.

Adherence
4585 patients received at least two prescriptions and have been included in calculations of adherence to treatment; median MRA was 102.9%, median CR 1.04, and median CSA 1.00.

The median interval length between prescriptions was 30 days (IQR 25 – 49), and the median days' supply per prescription was 28 (IQR 28 – 56). Supply gaps between prescriptions were uncommon.

Conclusion
In Scotland, prescribing trends indicate that DOACs are increasingly used as an alternative to vitamin K-antagonists for long-term stroke prevention in patients with atrial fibrillation; AF patients being treated with DOACs are in general elderly, have a range of comorbidities, and receive a large number of additional drugs. Overall adherence to treatment seems to be adequate; however, further research is needed in order to understand underlying reasons for treatment discontinuations.

References

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