Review of: "Prescribing of direct oral anticoagulants and warfarin to older people with atrial fibrillation in UK general practice: a cohort study"

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This was a retrospective cohort study to observe how the introduction of DOACs has affected anticoagulant prescription in a cohort comprising 165,596 patients aged ≥ 75 years in UK general practice, using the Clinical Practice Research Datalink (CPRD) between January 1, 2003, and December 27, 2017. The authors raised the following four questions in this study:

1. Did the incidence and prevalence of OAC prescriptions for people aged ≥ 75 years change in the period prior to the introduction of DOACs, between the time DOACs were introduced and the time they were recommended by NICE, and following the NICE recommendation?

The incidence of OAC prescription in the pre-DOAC era (2003– 2007) was 122.6 per 1000 person-years. This increased to 164.2 per 1000 person-years in the era when DOACs were available but not yet recommended by NICE, more than doubling thereafter to 387 per 1000 person-years in the era following the NICE recommendation (2013–2017).

1. How do older people switch between different OACs?

Majority of OAC switches are from warfarin to DOACs, followed by DOACs to DOACs.

1. Which patient characteristics and co-morbidities affect the chance of being prescribed an OAC, and has this changed since the introduction of DOACs?

The likelihood of being prescribed an OAC is lower in patients with a history of dementia, falls, major bleeds and fractures. Stroke risk (as calculated by the CHA_2DS_2-VASc score) had little effect on whether an OAC was prescribed.

1. How does persistence with therapy differ between different OACs?

Persistence with warfarinwas higher than DOACs in the first year, although this trend reversed by the third year of therapy.

Monitoring the prescription is valuable in determining trends in physicians' attitudes, especially for newly introduced drugs, such as DOACs. It is also meaningful to identify changes in prescription patterns after the release of new recommendations or guidelines. From this aspect, this article well reflects the changing

practice pattern in UK after the introduction of DOACs and the release of new guidelines from NICE, especially among the elderly population. Most of the results and interpretations are agreeable and concur with previous reports from other populations or countries.

KH Ho, M van Hove, G Leng. Trends in anticoagulant prescribing: a review of local policies in English primary care. BMC health services research, 2020; 20:2-8

Kato ET, Goto S, Giugliano RP. Overview of oral antithrombotic treatment in elderly patients with atrial fibrillation. Ageing Res Rev 2019;49:115-124.

Indeed, prescription of OACs for older people with AF has increased significantly after the introduction of DOACs, although there are several uncertainties in real-world practice in terms of such prescriptions, as the authors pointed out. They found that stroke risk had little effect on whether an OAC was prescribed. As the risk of stroke usually correlates with the risk of bleeding, this result is not surprising. They also observed substantial disparities in terms of age and other conditions, such as risk of falls and dementia. Although these results do not reflect the national guidance, under-prescription of OACs for patients with certain co-morbidities appears to be related to the practical decisions of each physician with consideration of individual risk-benefit management, which is well understandable and realistic. Detailed reasons and conditions related to the risks and decision-making by each physician would be of interest.
Furthermore, physicians usually decrease the dose of DOACs based on patient age, renal function and body weight, as recommended, although the dose is sometimes determined by the physician’s own decision. Thus, information regarding the actual dose of DOACs prescribed is also valuable from the perspective of new treatment options in future. Indeed, Okumura et al recently conducted a multicenter trial to compare a once-daily dose of 15 mg of edoxaban with placebo in elderly patients with non-valvular AF who were not considered appropriate candidates for OACs at doses approved for stroke prevention. They found that a once-daily 15 mg dose of edoxaban was superior to placebo in preventing stroke and systemic embolism, and did not result in a significantly higher incidence of major bleeding than the placebo.
Okumura K, et al. Low-dose edoxaban in very elderly patients with atrial fibrillation. N Engl J Med 2020; 383:1735-1745
The authors showed the difference in the risk of being started on an OAC in each period. From 2012 to 2017, when both DOACs and warfarin were marketed, the incidence of warfarin prescription decreased and DOAC prescription increased rapidly in this cohort. Since the effect of disease history or risks for each event might be different between warfarin and DOACs, it would be interesting to perform stratified analysis by warfarin and DOAC prescription for each parameter.

Clinical outcomes are also important. As the main purpose of OACs in the treatment of AF is to prevent embolic stroke without significant adverse effects, it will be very valuable to investigate the incidence of stroke, as well as bleeding events and other CV outcomes in this patient population, although that is beyond the scope of this study. Further studies are warranted to provide additional information about this issue.

Nonetheless this cohort study is the first to provide a detailed overview of prescription of anticoagulants in older people with AF in the UK, and how their use has changed since DOACs were recommended by national guidelines. This information would be helpful for physicians, healthcare providers and policy makers to further understand the changing practice pattern of anticoagulation therapy for atrial fibrillation among the elderly in real world clinical practice in the DOAC era.