

A Systematic Review of Observational Studies comparing Direct Oral Anticoagulants with Vitamin K Antagonists for Stroke Prevention in Older People with Atrial Fibrillation

ANNEKA MITCHELL (1, 2) MARGARET C. WATSON (1) TOMAS WELSH (3) AND ANITA MCGROGAN (1)

(1) UNIVERSITY OF BATH; (2) UNIVERSITY HOSPITAL SOUTHAMPTON; (3) THE RESEARCH INSTITUTE FOR THE CARE OF OLDER PEOPLE

Direct oral anticoagulants (DOACs) were introduced in 2009 as an alternative to warfarin. Randomised controlled trials found direct oral anticoagulants to be as safe and effective as warfarin for stroke prevention in atrial fibrillation (AF). However, older people were underrepresented in these studies and there is uncertainty as to which treatment offers the best risk/benefit ratio^{1,2}. The aim of this systematic review was to compare the effectiveness and safety of DOACs to vitamin K antagonists (VKAs) in people ≥ 75 years with AF when treated in routine clinical practice.

Studies were included in the systematic review if they used an observational study design, compared a DOAC to a VKA and presented data for an outcome of interest in participants ≥ 75 years old with AF. An exhaustive search was undertaken: Medline, EMBASE, Scopus, and Web of Science were searched from 01.01.09 to 03.01.18. Pharmaceutical companies were contacted to request unpublished data; reference lists were screened; foreign language articles were translated. Abstracts, editorials and letters were excluded as they did not include sufficient methodology information. The Newcastle-Ottawa scale was used to assess studies for risk of bias. The study protocol was registered with PROSPERO (CRD42018081696). Ethical approval is not required for reviews.

Database searches returned 12,330 original articles. Articles were screened for inclusion and 23 studies were included in the review. The majority ($n = 11$) of studies were conducted in the USA and Canada, Asia ($n = 6$), Europe ($n = 5$), and New Zealand ($n = 1$). No studies were identified from the UK. The most studied DOAC was dabigatran ($n = 21$), followed by rivaroxaban ($n = 12$) and apixaban ($n = 7$). Generally, the included studies were rated highly with over half scoring 7 or above. Seven studies scored 6, one study scored 5 and three studies scored 4 or below.

Effectiveness and safety outcomes:

- Ischaemic stroke: The majority of studies (6/9) found no significant difference between DOACs and VKAs, two found a decreased risk and one an increased risk with DOACs.
- Major bleeding: Most studies (8/12) found no significant difference between the groups, three found a decreased risk and one an increased risk with DOACs.
- Intracranial haemorrhage: Six studies reported that DOACs significantly decreased the risk, whereas five studies reported no significant difference.
- Gastrointestinal bleeding: Seven studies reported an increased risk with DOACs and two found no significant difference.

This review found no difference in effectiveness between DOACs and VKAs but variable safety outcomes in those aged ≥ 75 . However, the findings were limited by the low numbers of older people in the included studies and the low quality scores of those involving only the over 75s. The strength of this study was the broad search strategy; the main limitation was the reliance on published results as access to individual participant data was not available. The majority of studies did not report event rates so effect sizes could not be recalculated. This review has highlighted the need for high quality research investigating the comparative safety and effectiveness of DOACs in older people. It supports further work to examine this question.

Keywords

Anticoagulation, Atrial fibrillation, Older people, Stroke, Bleeding

References

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