Developing a protocol for a systematic review and meta-analysis of observational studies comparing direct oral anticoagulants with vitamin K antagonists for stroke prevention in people aged over 75 with atrial fibrillation

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Introduction: Randomised controlled trials (RCTs) have demonstrated that anticoagulation by direct oral anticoagulants (DOACs) or vitamin-K-antagonists (VKAs) reduces the risk of stroke in people with atrial fibrillation. RCTs of DOACs demonstrated that they were non-inferior to VKAs and had a lower incidence of major bleeding. However, it is uncertain whether these results extrapolate to older people who were under-represented in these trials. This abstract describes the development of a protocol for a systematic review of observational studies to investigate whether the rates of ischaemic stroke and major bleeding differ between older patients treated with DOACs and vitamin-K-antagonists.

Methods: The research question, search, inclusion and exclusion criteria were developed iteratively using the PICOS acronym as the base:

Population– People aged over 75 with atrial fibrillation

Intervention– DOACs

Comparator– Vitamin K antagonists

Outcomes– Stroke and major bleeding

Study design– Observational studies

Results: A systematic review protocol of observational studies was derived and registered with PROSPERO (CRD42018081696). The primary outcomes to be assessed were effectiveness (ischaemic stroke prevention) and safety (bleeding). In outline, Medline, EMBASE, Scopus and Web of Science will be searched from 2009 to present. Reference list searches will be used to identify further relevant studies. Manufacturers of DOACs will be contacted to request unpublished data. Data will be extracted independently by two reviewers using a pre-piloted form. Study data will be quantitatively synthesised and standard meta-analyses will be undertaken for each pair of treatment comparisons. Preliminary database searches have identified 13,623 citations. From abstract and title review it is expected that 400 will be eligible for full text review.

Conclusions: This systematic review of observational data will complement the evidence from RCTs to provide an insight into the effectiveness and safety of these medications in older patients who have historically been be underrepresented in clinical trials. The findings of this review will provide important information for patients and practitioners alike.