**Research Information Sheet for Practices (RISP)**

**Study contacts:**

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| **Study** **Title** | DaRe2THINK |
| **IRAS Number** | 290420 |
| **Sponsor** | University of Birmingham, UK |
| **Funders** | National Institute for Health Research (HTA 19/109 - NIHR130280) |
| **Chief Investigator** | Dipak Kotecha (Chief Investigator), Professor of Cardiology, Institute of Cardiovascular Sciences, University of Birmingham & Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust; Email: d.kotecha@bham.ac.uk David Shukla (Deputy Chief Investigator), General Practitioner & Lead for the West Midlands Primary Care CRN team, Institute of Applied Health Research, University of Birmingham; Email: david.shukla@nihr.ac.uk |
| **Study Design** | DaRe2THINK is an individual-patient, randomised, parallel-group, open-label, event-driven superiority trial with 1:1 allocation to either direct oral anticoagulant (DOAC) or no added therapy.  A staged internal pilot programme is incorporated into the design of this Clinical Trial of an Investigational Medicinal Product (CTIMP). |
| **Primary Study Aim & Objectives** | DaRe2THINK will test the hypothesis that DOACs are effective at reducing thromboembolic events and vascular dementia compared to no treatment, in patients with AF and a low or intermediate expected risk of stroke. Using a healthcare data approach to reduce the burden on both NHS staff and patients. |
| **Total Recruitment Target** | 3000 Nationally |
| **Practice/Site Target** | 5 patients |
| **Recruitment Period** | 01/06/2021 to 01/06/2023. [Study follow up will be conducted through yearly data extraction from the patient's electronic health records by CPRD.  Follow up will continue for 5 years after recruitment] |
| **Eligibility Criteria**  | 1. Diagnosis of AF (previous, current or chronic).
2. Age at enrolment ≥60 years to ≤73 years.
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| **Exclusion Criteria**  | 1. Existing use of an anticoagulant.
2. Another clinical indication for anticoagulation.
3. Hypersensitivity or known intolerance to direct oral anticoagulants.
4. Prior documented stroke, transient ischaemic attack or thromboembolism.
5. Two or more CHA2DS2-VASc one-point risk factors indicating a risk of stroke or thromboembolism: Heart failure\*; Hypertension\*; Age 65 years or older; Diabetes mellitus\*; Previous myocardial infarction, peripheral artery disease or aortic plaque; and/or Female gender†.
6. Active clinically-significant bleeding.
7. Prior major bleeding, defined as any intracranial bleed, or bleeding that resulted in a drop in haemoglobin ≥2g/dL, required hospitalisation or transfusion.
8. Condition that poses a significant risk for bleeding (within 12 months) including gastrointestinal ulceration, brain/spinal/ophthalmic injury or surgery, arteriovenous malformations or vascular aneurysms, major intraspinal or intracerebral vascular abnormalities, hepatic disease associated with coagulopathy, known or suspected oesophageal varices, and cancers with high bleeding risk.
9. Estimated glomerular filtration rate <30 mL/min/1.73m2 measured within the last 12 months.
10. Patients receiving systemic treatment with azole-antimycotics within the last 3 months (ketoconazole, itraconazole, voriconazole and posaconazole).
11. Current diagnosis of dementia.
12. Life expectancy <2 years.
13. Unable or unwilling to provide informed consent for access and linkage of past and future electronic healthcare records.
14. Currently participating in another Clinical Trial
15. For the automated pre-screening via CPRD IRSP, these criteria will be confirmed by the concurrent use of relevant medical therapy: Heart failure (confirmed by use of loop diuretic therapy within the last 3 months); Hypertension (confirmed by use of anti-hypertensive therapy within the last 3 months); Diabetes mellitus (confirmed by use of oral antidiabetic therapy or insulin within the last 3 months).

**†** In the absence of other CHA₂DS₂-VASc risk factors, female gender is not independently associated with a higher risk of stroke or thromboembolism |
| **Core Practice/Site Activities and Requirements** | This trial will recruit participants from GP practices in England that contribute or are willing to contribute to CPRD1. Review a list of pre-screened patients on the CPRD platform.
2. Invite eligible patients to take part, using a letter and text message built-in to your EMIS system, and follow-up by text messages or calls after 7 days.
3. Countersign the remote e-consent form that patients complete on their mobile phone or device.
4. Use EMIS to start a DOAC of your choice if the patient is randomised to the intervention arm (no added therapy in the control arm).
5. Report any protocol-defined Serious Adverse Events (SAEs) during the 5-year length of the trial.
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| **Core Patient Activities** | * Receive the study invite letter/text message
* Review study information
* Complete remote informed consent
* Randomised to either direct oral anticoagulants (DOACs intervention group) or to continue without oral anticoagulation (control; standard of care).
* There is no follow up visits and patient reported cognitive functions will be collected through web-based interface. Similarly, Quality of life is collected every 6 months, a questionnaire will be sent either as text message or to patient’s nominated email address.
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| **Benefits to the Site/Resources provided by the study team and WM CRN** | * Training and general study Q&A session are available for all sites/delegates that have signed up for the study
* Completely remote trail with no need for direct patient contact
* Automated SAE safety net with sites notified of any potential events in their patients
* CRN Nurse Support is also available
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| **Financial Arrangements** | Research Costs (Provide by CPRD)* Site set-up fee - £268.35
* Per patient - £101.43

Study Support Costs (provided by the CRN)* Site set-up fee - £180.00
* Per patient - £15.00
* Extra RSI payment - £1300.00
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# TRIAL FLOW CHART

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