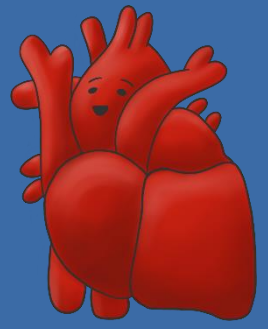

DANCE Trial:

The Direct Oral Anticoagulation versus Warfarin after Cardiac Surgery Trial

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Background Information

- Atrial fibrillation (AF) is associated with higher risks of stroke and arises in 30-60% of patients in the early post-operative period after undergoing cardiac surgery
- Oral anticoagulation (OAC) therapy is the preferred method of thromboembolic prevention in patients however, the balance of benefits and risks of OAC may differ and the most safe and effective OAC therapy is not certain
- Until 2009, **vitamin K antagonists (VKA)** were the only OAC agents available but their use is limited by a narrow therapeutic index to ensure appropriate levels anticoagulation, leading to non-compliance and discontinuation
- **Direct oral anticoagulants (DOACs)** have emerged as a more convenient alternative compared to VKA however no completed randomized control trial (RCT) has evaluated the safety of DOACs to VKA.

Trial Design & Intervention

Study Design	Multi-centre, RCT comparing the safety of DOACs versus VKA in the early period (30 days) after cardiac surgery in patients with an indication for oral anticoagulation
Objectives	*Pilot:* assess the feasibility of conducting a large RCT *Full Trial:* evaluate the safety & efficacy of DOACs vs VKAs after cardiac surgery in patients with AF requiring oral anticoagulation
Sample Size	Pilot: n=200 | Vanguard: n=400 | Full Trial: n=6215
Intervention	*Intervention Group*: will receive a DOAC at doses recommended for atrial fibrillation, adjusted for their renal function. Choice of DOAC will be at the discretion of the treating physician. DOAC may be resumed/initiated at the earliest on the day of discharge or on postoperative day 5, whichever occurs first. *Control Group*: Patients will receive a VKA once daily; the individual dose will be titrated to achieve a guideline-recommended INR range. The first dose of VKA can be resumed/initiated as soon as postoperative day 1.

Trial Outcomes

Pilot/Vanguard

Feasibility Measures:

- average enrolment rate of 5 patients per centre per month
- proportion of participants that crossover OAC arms is < 5%
- ability to achieve follow-up at 30 days in ≥ 95% of enrolled patients

Full Trial

Primary Outcomes Measures:

- Major bleeding at 30 days

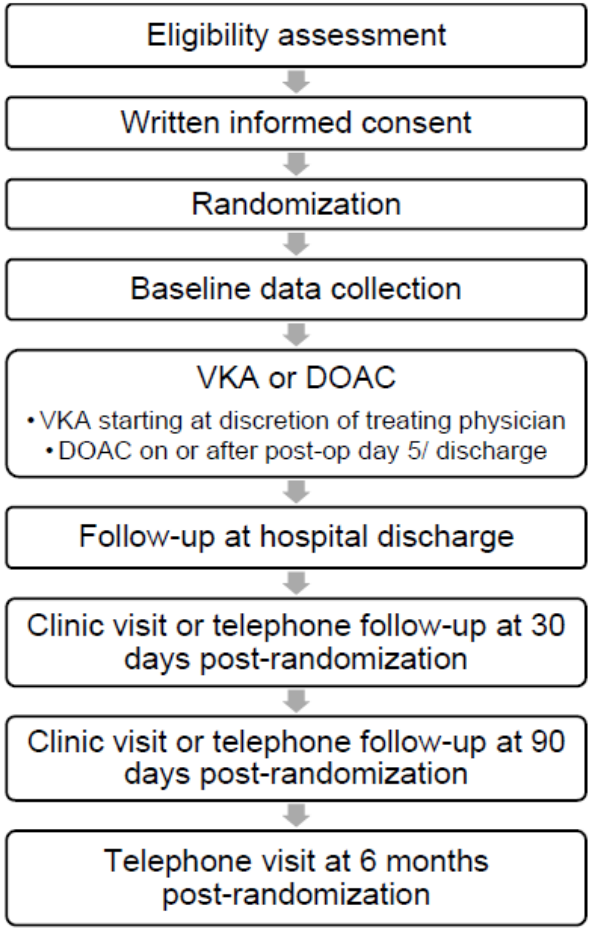
Secondary Outcomes:

- Most important: Composite of stroke and non-central nervous system systemic arterial embolism at 30 and 90 days.
- Major bleeding at 90 days; pleural effusion requiring drainage, pericardial effusion requiring drainage, systemic arterial embolism, ischemic stroke, deep vein thrombosis, pulmonary embolism, all-cause mortality, length of postoperative hospital stay at 30 and 90 days; all-cause mortality at 6 months.

Tertiary Outcomes:

- Minor bleeding, all bleeding (major plus minor), myocardial infarction, valve thrombosis, hemorrhagic stroke, all stroke, all arterial thrombosis/thromboembolism (ischemic stroke, systemic arterial embolism, myocardial infarction, valve thrombosis), quality of life measured by the EQ-5D-5L questionnaire, patient satisfaction with their anticoagulant treatment as assessed by the Perception of Anticoagulant Treatment Questionnaire (PACT-Q) and aggregate costs for both groups at 30 and 90 days

Trial Flow & Follow-up



DANCE

SUNDANCE:

SUbclinical valve thrombosis iN patients with surgical bioprosthetic aortic valve replacement: An imaging substudy of the DANCE trial

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Aortic Valve Replacement

- Only definitive, life-saving treatment for severe aortic stenosis
- >90% of aortic valve replacements are with bioprostheses
  - Do not require lifelong anticoagulation like mechanical valves
  - Susceptible to valve deterioration and failure
- **Subclinical valve thrombosis** occurs in 17-28% of patients at one year
  - May be related to increased risk of clinical valve thrombosis, stroke and thromboembolism, and reduced valve durability
- Anticoagulation reduces the incidence of subclinical valve thrombosis:
  - The effect of **direct oral anticoagulants (DOACs)** versus **vitamin K antagonists (VKAs)** on subclinical valve thrombosis has not been studied in a randomized control trial (RCT)

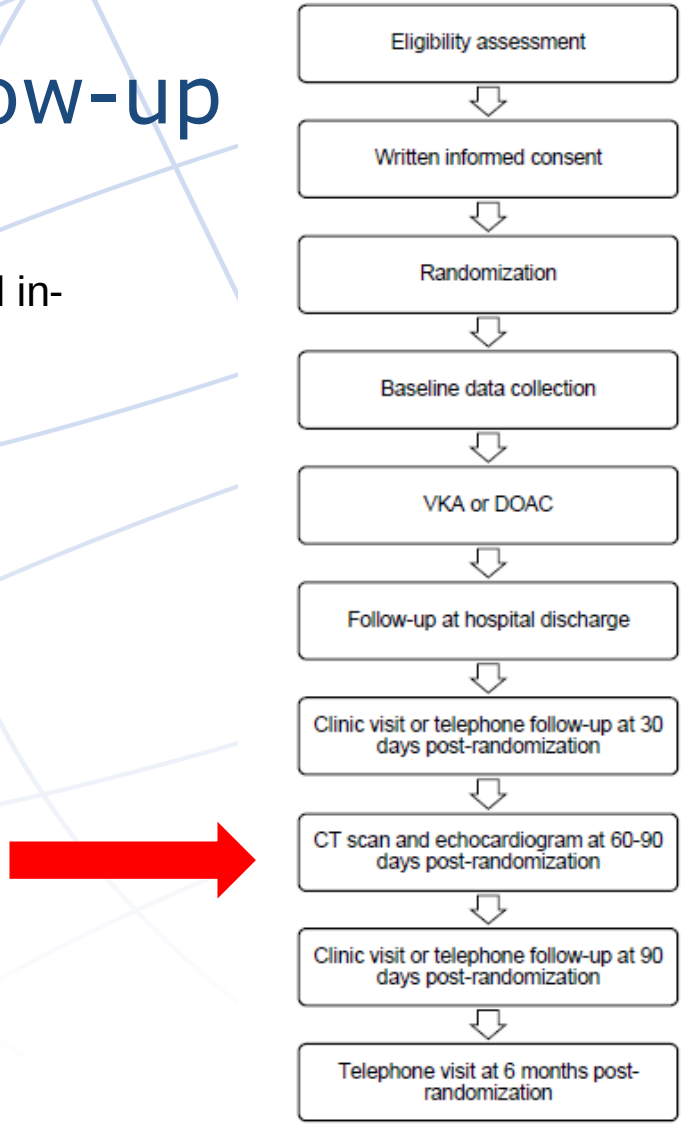
DANCE

SUNDANCE Design

Study Design	Substudy of DANCE
Objectives	**Vanguard:** assess the feasibility of conducting a large RCT **Full Trial:** evaluate the incidence of subclinical valve thrombosis and any effect of DOACs vs VKAs in DANCE patients with a new bioprosthetic aortic valve
Sample Size	**Vanguard**: n=60 | **Full Trial**: n=910
Intervention	As in the overall DANCE trial
Outcomes	*Vanguard (feasibility):* • Recruit ≥ 50% of bioprosthetic AVR patients enrolled in DANCE • Complete 60 to 90-day CT scans and echos in ≥ 90% of patients • At least "good" quality in ≥ 90% of CT scans *Full trial:* Primary outcome: • Incidence of subclinical valve thrombosis on CT scan performed 60-90 days

SUNDANCE Flow & Follow-up

- In addition to standard DANCE trial follow-up, SUNDANCE participants will have one additional in-person follow-up visit at 60-90 days with:
  - Cardiac CT scan
  - Echocardiogram



DANCE