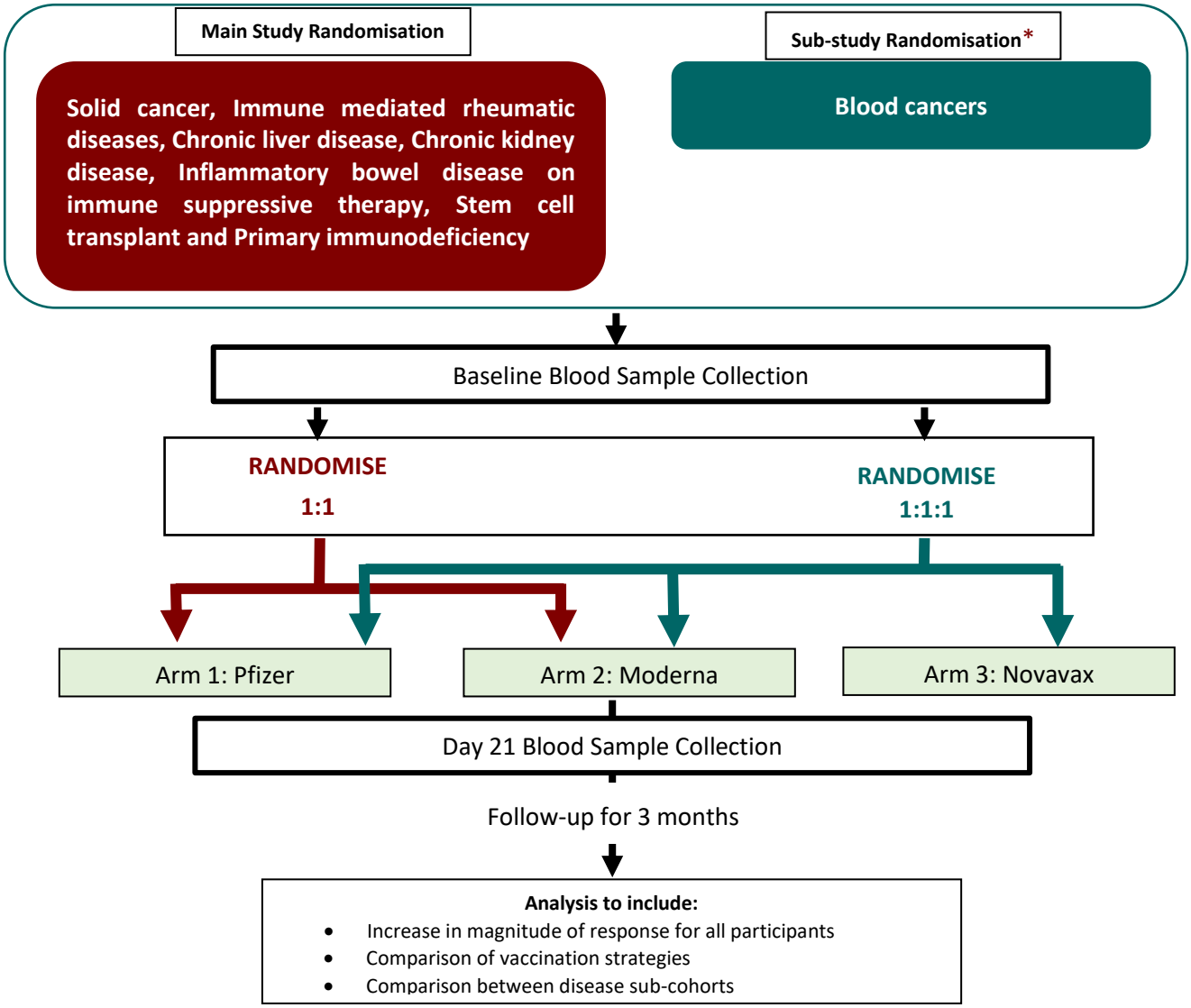
Title	**Randomised Trial Optimising COVID-19 Vaccination in Patients with Chronic Health Conditions and a Poor Response to Standard Vaccination**
Background	To date, more than 43 million people have been fully vaccinated with 2 doses in the UK. Research studies have shown that two doses of vaccine prevent COVID-19 infection in up to 90% of people. However, these vaccines were tested in predominantly healthy people. Recent research in individuals with chronic health problems or cancer, suggest that approximately 40% of patients who are immune compromised, either because of a chronic health condition or the treatment they are receiving, generate low or no detectable antibody or T-cells (a type of white blood cell) after two doses of the Pfizer or AstraZeneca COVID-19 vaccines. This raises the question of the potential benefit of a third primary dose of vaccine (called a top-up) in vulnerable patients with inadequate immune responses. This strategy has been successfully used for other vaccines but the limited research performed to date for COVID-19 has given variable results, so additional research is needed.
Aim	The OCTAVE-DUO trial aims to find out whether a third primary dose of the vaccine for COVID-19 can help generate a better immune response in immune compromised patients with chronic health conditions or cancer.
Trial Entry Criteria	The OCTAVE-DUO trial is for patients aged 18 years or over with one or more of the following health conditions: breast or lung cancer; certain types of blood cancer; immune-mediated rheumatic diseases (e.g. rheumatoid arthritis); chronic kidney disease; chronic liver disease; inflammatory bowel disease on immune suppressive therapy; stem cell transplant; and primary immunodeficiency (a group of disorders characterised by poor or absent immune function). Patients must have no or an inadequate immune response to 2 doses of COVID-19 vaccine and there should be no other reason why the patient cannot receive the vaccine. For the blood-cancer sub-study, pregnant women are excluded and women of childbearing age must agree to use contraceptive measures.
Randomisation and Trial Treatment	**Main Study Randomisation** Participants in the main study are randomised to receive the Pfizer or Moderna COVID-19 vaccines intramuscularly at the approved dose for that vaccine. **Sub-study Randomisation** Participants with blood cancer are randomised to receive Pfizer or Moderna or Novavax (a new vaccine which is not yet authorised for use) COVID-19 vaccines intramuscularly at the approved dose for that vaccine.
Sample and Data Collection	Blood samples are collected prior to and at 21 days after the top-up vaccine. Relevant clinical data will be collected including: type of disease, treatments received, and whether the participant goes onto catch COVID-19.
Follow-up	Participants will be followed up for 3-months after re-vaccination. Long term follow-up is planned by data linkage with national datasets.
Analysis	Samples will be analysed in laboratories around the UK. The results of these laboratory tests and the clinical data will then be analysed and the results published. The analysis will look at the population as a whole A lay summary of the results will be posted on the trials website: www.birmingham.ac.uk/octave

Number of Patients	**Total:** Up to 1200 (recruitment targets vary per disease cohort).
Trial Duration	Patients are expected to be recruited over a 3-month period and followed up for 3 months.
Contacts	**Sponsor:** University of Birmingham **Chief Investigator:** Professor Iain McInnes, University of Glasgow **OCTAVE Trial Office:** Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, Edgbaston, Birmingham, B15 2TT ✉ OCTAVE-DUO@trials.bham.ac.uk

Trial Diagram



* Sub-study participants randomised to Pfizer and Moderna arms will be included in the Main Study comparisons also