Establishing an experimental medicine vaccine research model in older adults; experience from the Lymph nodE single cell Genomics AnCestrY and ageing (LEGACY) Network

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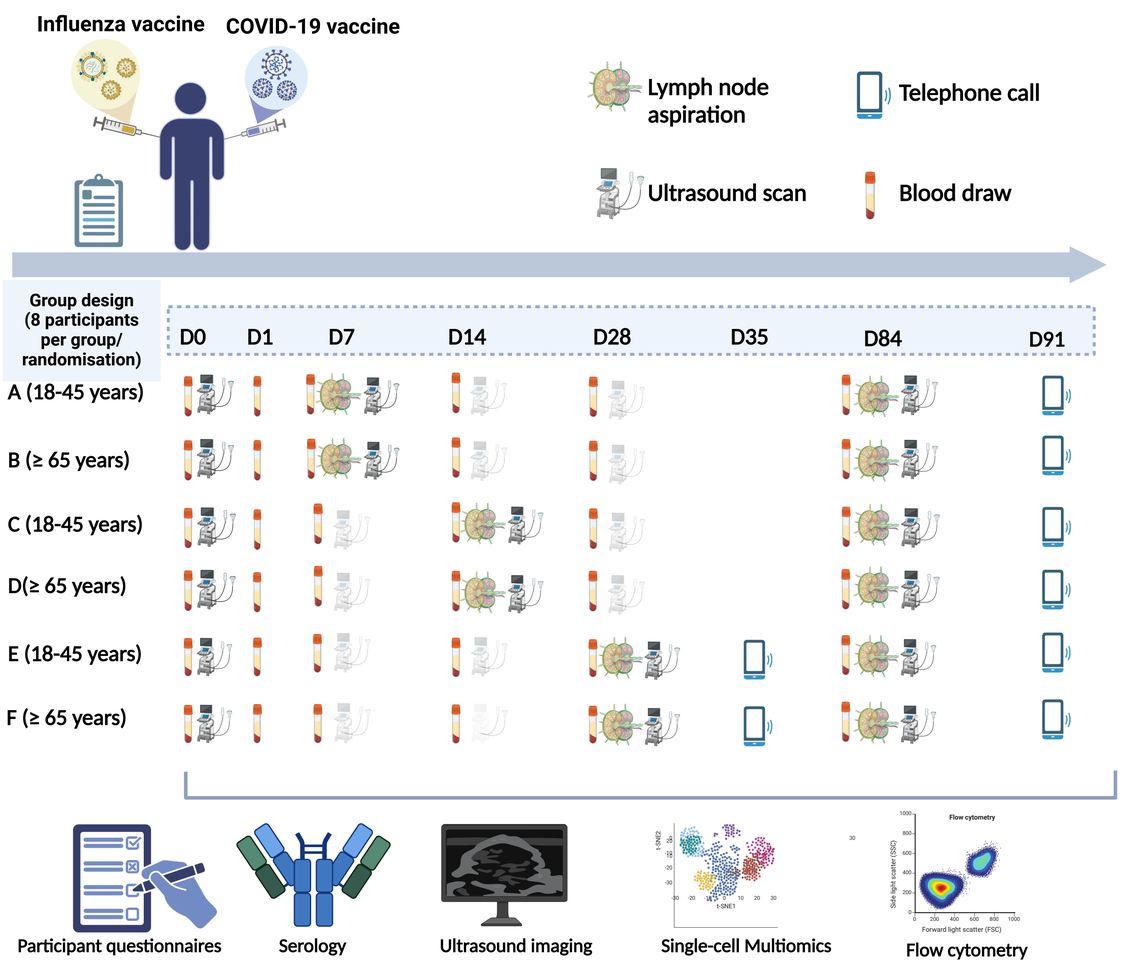
INTRODUCTION

Ageing impacts immune responses to vaccination, leading to reduced efficacy, particularly for influenza vaccines. Despite this, vaccines are rarely designed for older adults, and early-stage clinical research often excludes older adults, limiting actionable data[1-3].

To investigate age-related differences in tissue-based immune responses to vaccination, we established LEGACY03 (ISRCTN12928349) at the Oxford Vaccine Group, University of Oxford, UK, using fine-needle aspirates (FNAs) from axillary lymph nodes to assess immune responses to booster vaccination with recall antigens (SARS-CoV-2 S glycoprotein and influenza haemagglutinin) in younger and older adults. This approach was to enable direct comparison of age-related differences in the magnitude and durability of the lymph node immune response. IgG antibody levels against vaccine antigens were measured at all study timepoints using ELISA.

This study was designed to compare immune responses in lymph nodes and blood between younger and older adults across different timepoints post-vaccination. In this poster, we present cumulative data from an interim analysis of the LEGACY03 study.

STUDY DESIGN



*COVID-19 vaccine: Moderna. Spikevax XBB.1.5 and JN.1 0.1 mg/mL dispersion for injection (MDV)
Influenza vaccine: Adjuvanted Quadrivalent Influenza Vaccine (aQIV), (surface antigen, inactivated), Seqirus suspension for injection in pre-filled syringe

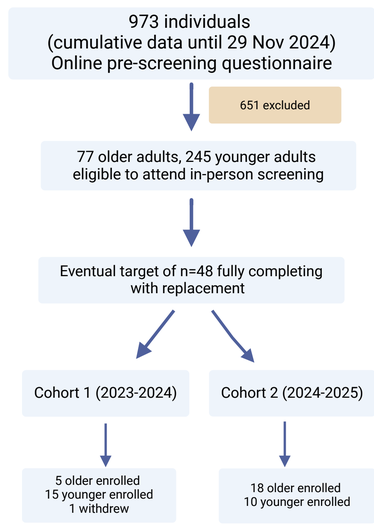
METHODS

This study was an open-label, observational, experimental medicine investigation designed to examine immune responses in lymph node (LN) cells following simultaneous administration of a lipid nanoparticle mRNA COVID-19 vaccine and a seasonally updated adjuvanted quadrivalent influenza vaccine (aQIV)[4]. Both vaccines were given as intramuscular injections into opposite arms during the UK winter seasons of 2023-2024 and 2024-2025. Healthy adults from two age groups (18-45 years and ≥65 years) were recruited if they met all age-specific and health inclusion criteria and provided written informed consent. Participants were block randomised (1:1:1) to determine whether their initial FNA biopsy would take place on day 7, 14, or 28 post-vaccination.

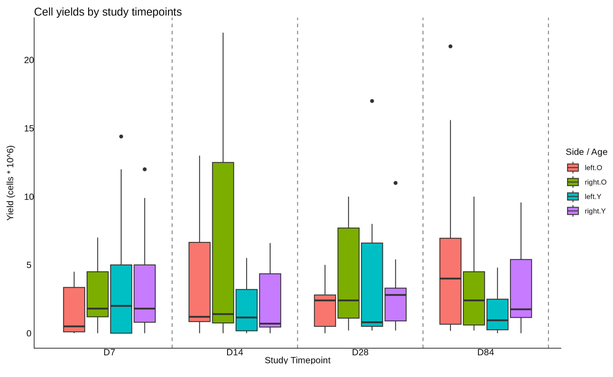
Each participant received a COVID-19 booster vaccine in the left arm and a seasonal influenza vaccine (aQIV) in the right arm. They were then randomly assigned to undergo bilateral LN fine-needle aspiration (FNA) biopsies from both axillae at one of three primary timepoints: day 7, 14, or 28 after vaccination, with a follow-up biopsy at day 84. Additionally, serum and peripheral blood mononuclear cells (PBMCs) were collected at these timepoints. LN cells were obtained via ultrasound (US)-guided FNA, and corresponding LN US images were stored for further analysis.

RESULTS

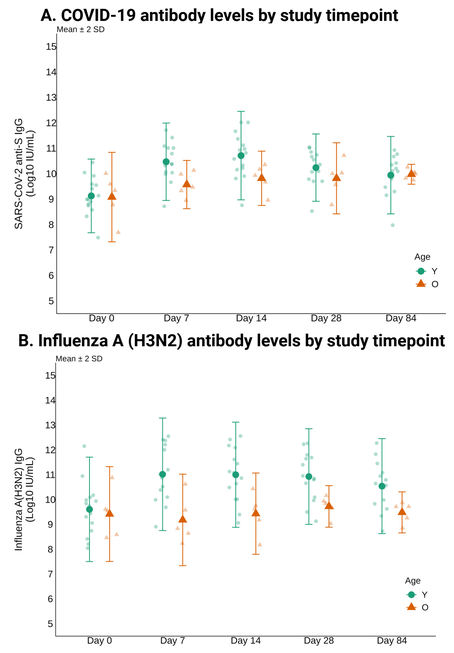
Participant recruitment



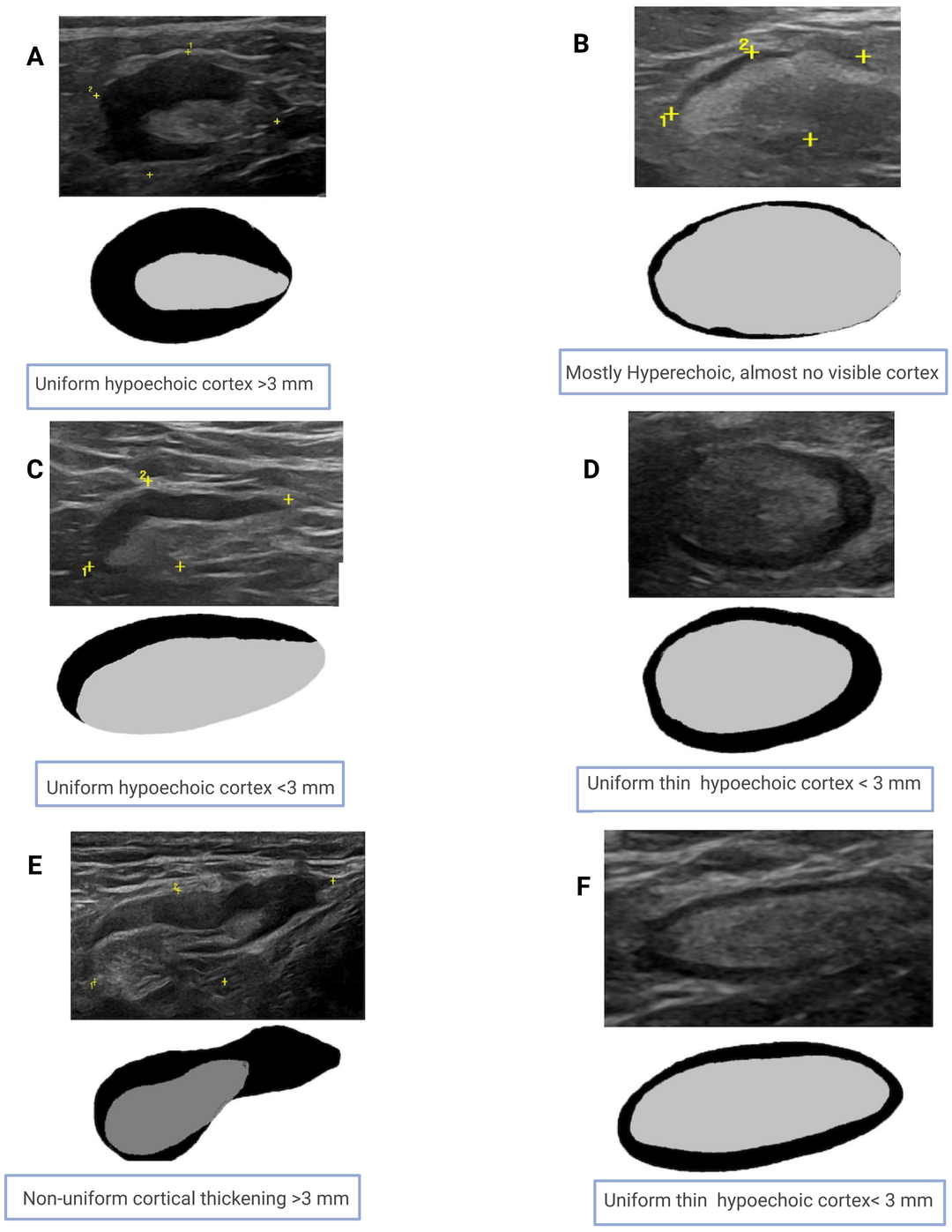
LEGACY03 FNA cell yield



Comparison of IgG responses to vaccinations in younger (18-45 years) and older (≥65) cohort 1



Ultrasound images of lymph node after vaccination



*Left-sided axillary level 1 lymph nodes at D7 post vaccination with COVID-19 vaccine in younger and older cohorts

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CONCLUSION

- Up to 29 November 2024, 973 individuals expressed interest in the study, of whom 651 were excluded; after in-person screening, a total of 48 participants had enrolled.
- Our preliminary ultrasound imaging dataset suggests that younger adults more frequently exhibited increased lymph node cortical thickness at day 7 post-COVID-19 vaccination compared to older adults.
- ELISA data showed that younger adults had higher vaccine induced IgG titres against influenza A/H3N2 and SARS-CoV-2 spike protein, particularly at early time points.