Supplementary Methods.

Study population

This observational clinical trial (ACTRN12621000532808) was conducted on a single centre population of KTR and their CHC commencing in February 2021. Participants were identified by clinical nephrologists and screened. Inclusion criteria were kidney-only transplant over 18 years old with an available CHC without kidney disease. Exclusion criteria were patients with past COVID-19 infection, those who had already received a COVID-19 vaccine prior to enrolment, those who could not provide informed consent, or those who did not have a non-immunosuppressed and unvaccinated CHC. KTR immunosuppressed with a CNI, antimetabolite, and steroid are presented here. Demographics including gender, age, cause of kidney disease, and graft details were collected and presented as percentages for ordinal variables, and mean ± standard deviation for continuous variables. See consort diagram below.

Sample processing and PBMC cryopreservation

Forty to fifty millilitres of whole blood was collected from participants by venepuncture prior to vaccination, three weeks after their first dose, and three weeks after their second dose. PBMCs were isolated by density gradient centrifugation within 18 h and cryopreserved in liquid nitrogen prior to analysis.

Anti-SARS-CoV-2 spike IgG

Spike IgG was quantified with an in-house assay, as previously described (Valtanen et al). Prefusion SARS-CoV-2 Spike ectodomain (isolate WHU1, residues 1-1208) with HexaPro mutations (kindly provided by Dr Adam Wheatley) was produced for ELISA. Recombinant proteins were overexpressed in Expi293 cells (Thermo Fisher) and 72 hrs later purified by Ni-NTA affinity and size-exclusion chromatography. Purified proteins were quantified using the Bradford protein assay (Bio-Rad) and analysed by SDS-PAGE and Western blot before storage at -80°C.

MaxiSorp 96-well plates were coated overnight at 4°C with 5 g/mL of recombinant Spike protein and blocked with 5% w/v skim milk in 0.05% Tween-20/PBS (PBS-T) at room temperature. Heat inactivated patient sera were serially diluted in blocking buffer, added and incubated for 2 h at room temperature, followed by four washes in 0.05% PBST. HRP-conjugated goat anti-human IgG (H+L) (Invitrogen) was diluted 1:30,000 in 5% skim milk in PBST as follows and incubated for 1 hour at room temperature, followed by four washes with PBS-T. Plates were developed with 1-Step™ Ultra TMB Substrate (ThermoFisher Scientific, Waltham, MA) and the reaction stopped with 2M sulphuric acid. Absorbance was measured at 450 nm using Synergy HTX Multi-Mode Microplate Reader. SARS-CoV-2 Spike endpoint titers were calculated for 8 serum dilution (of half log10) and expressed as area under the curve (AUC). The baseline cut-off for seropositivity was defined as 2 standard deviations above the mean pre-vaccination titer for transplant recipients (0.969) and healthy cohabitants (11.63) independently. AUC calculations were performed using GraphPad Prism.

Anti-SARS-CoV-2 receptor binding domain IgG

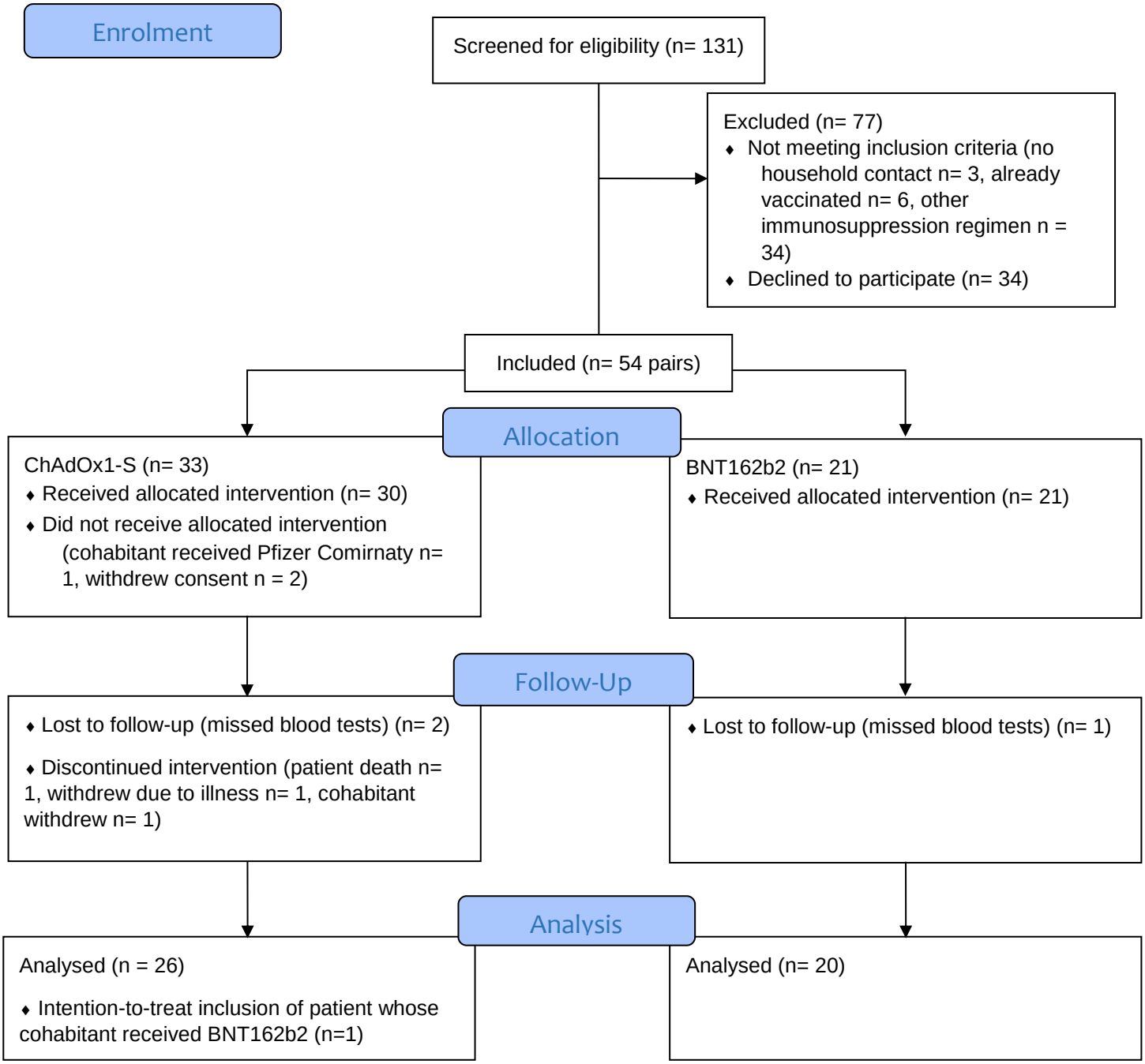
RBD and nucleocapsid IgG was quantified using the 'Elecsys Anti-SARS-CoV-2 S' and 'Elecsys anti-SARS-CoV-2' assays on the Cobas system (Roche, Basel, Switzerland), as per the manufacturer's instructions. The quantitation range for detection of anti-RBD IgG in this assay is 0.4-250 U/mL.

Live virus neutralization

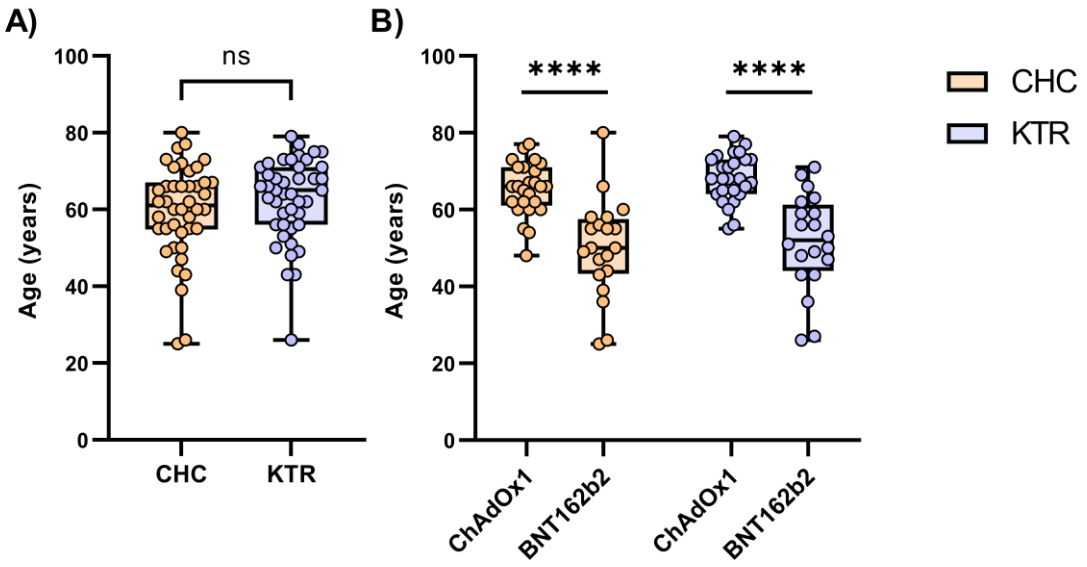
HEK-ACE2/TMPRSS cells (Clone 24; PMID: 34228725) were seeded in 384-well plates at 5×10^3 cells per well in the presence of the live cell nuclear stain Hoechst-33342 dye (NucBlue, Invitrogen, Waltham, MA) at a concentration of 5% v/v. Two-fold dilutions of patient plasma samples were mixed with an equal volume of SARS-CoV-2 (Wuhan clade B.1) virus solution (1.25×10^4 TCID50/ml) and incubated at 37°C for 1 hour before adding 40 µL in duplicate to the cells (final MOI = 0.05). Plates were incubated for 24 hours post infection and entire wells were imaged by high-content fluorescence microscopy, cell counts obtained with automated image analysis software. Neutralization was defined as achieving 50% virus neutralization at serum dilution of 1/20 of greater.

IFNγ ELISpot

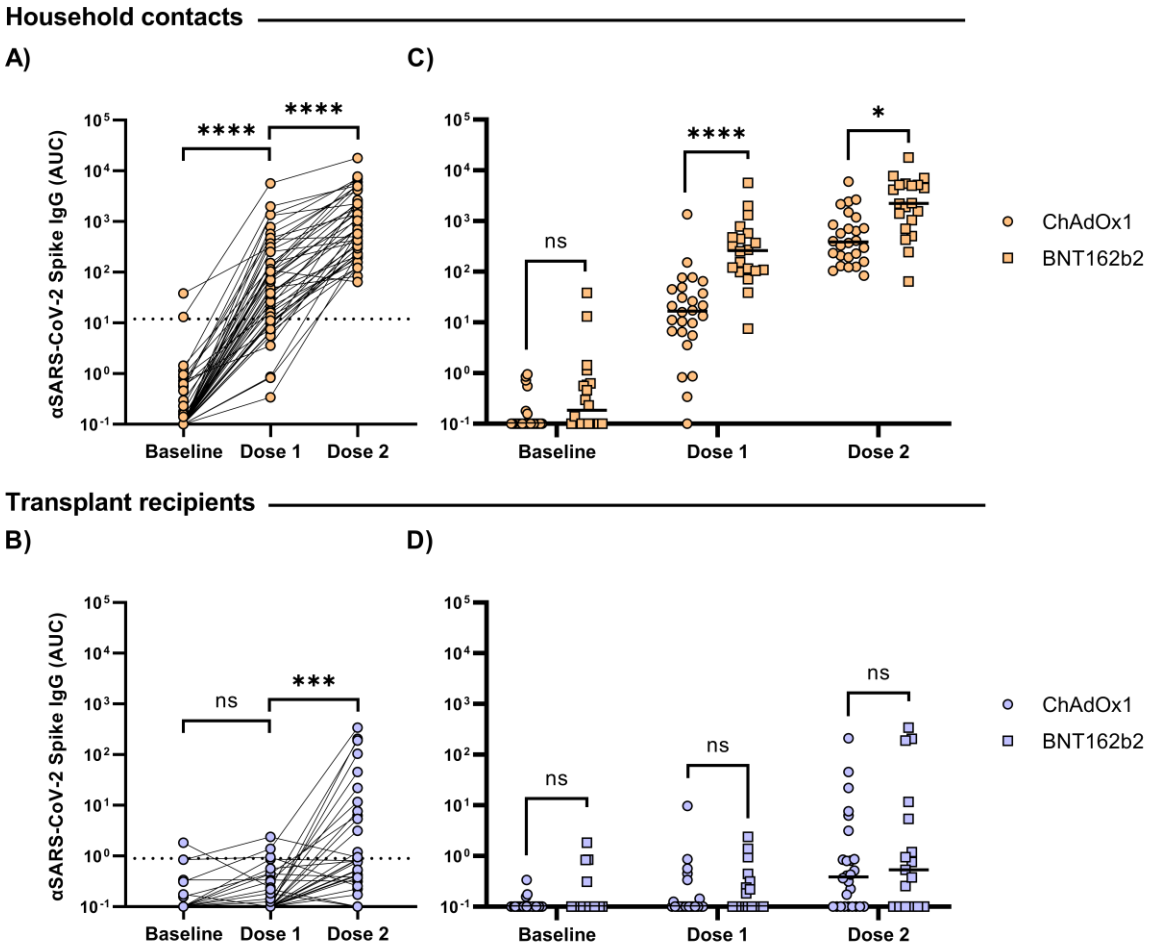
Millipore 96-well plates with nitrocellulose membranes (Merck, Branchburg, NJ) were activated with 35% ethanol for 30 s, before washing twice with PBS. Wells were coated with anti-IFNγ capture antibody (Clone 2G1, ThermoFisher, Cambridge, MA) overnight at 4°C, then washed twice with PBS. PBMCs were thawed by dropwise addition of complete medium (RPMI + 20% FCS, glutamate, penicillin, streptomycin) and benzonase (Merck, Kenilworth, NJ) to prevent aggregation, and rested for 2 h before counting. PBMCs were treated with 4 pools of overlapping peptides spanning the length of the spike protein. PHA (7.5 µg/mL; Merck, Branchburg, NJ, USA) and cytomegalovirus pp65 protein derived peptides (PepTivator® CMV pp65, Miltenyi Biotech, Bergisch Gladbach, Germany) were used as positive controls. After 16 h at 37°C, wells were washed five times with PBS, then ten times with PBS + 0.05% tween-20. Captured IFNγ was detected with a biotinylated anti-IFNγ antibody (Clone B133.5; ThermoFisher, Cambridge, MA) at 4 °C overnight. Unbound detection antibody was removed by washing with PBS + 0.05% tween-20, and a streptavidin:HRP conjugate (BD Biosciences, NJ) was added for four hours at 4 °C. AEC substrate (BD Biosciences, New Jersey, USA) was added for 10 min at room temperature, before rinsing with deionized water and enumeration of spots using an ImmunoSpot analyzer and software (Cellular Technology Ltd., Bonn, Germany). All washing steps were performed using an automated plate washer.


Enrolment
Screened for eligibility (n= 131)
Excluded (n= 77)
♦ Not meeting inclusion criteria (no household contact n= 3, already vaccinated n= 6, other immunosuppression regimen n = 34)
♦ Declined to participate (n= 34)
Included (n= 54 pairs)
Allocation
ChAdOx1-S (n= 33)
♦ Received allocated intervention (n= 30)
♦ Did not receive allocated intervention (cohabitant received Pfizer Comirnaty n= 1, withdrew consent n = 2)
BNT162b2 (n= 21)
♦ Received allocated intervention (n= 21)
Follow-Up
♦ Lost to follow-up (missed blood tests) (n= 2)
♦ Discontinued intervention (patient death n= 1, withdrew due to illness n= 1, cohabitant withdrew n= 1)
♦ Lost to follow-up (missed blood tests) (n= 1)
Analysis
Analysed (n = 26)
♦ Intention-to-treat inclusion of patient whose cohabitant received BNT162b2 (n=1)
Analysed (n= 20)

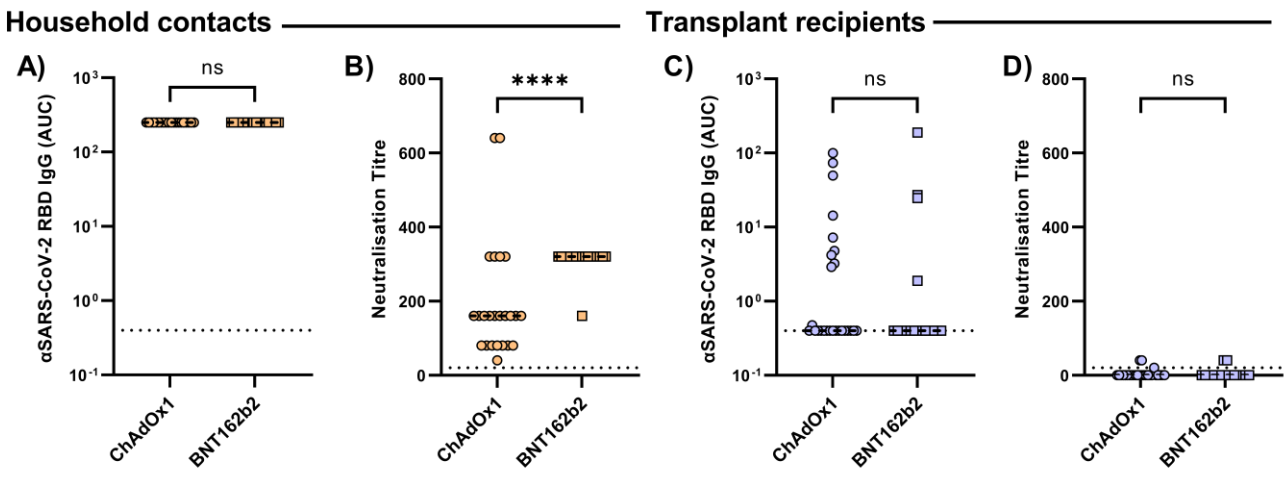
Supplementary Figures.



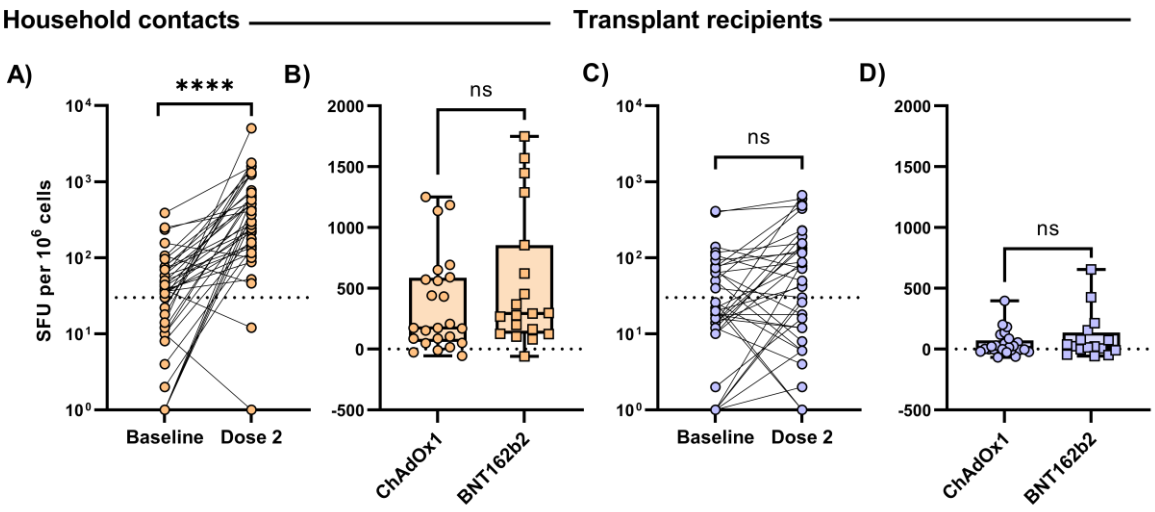
Supplementary Figure 1. Participant age by treatment and vaccine. Differences between groups tested using the 2-tailed Mann-Whitney test. NS, not significant. ****, p<0.0001.



Supplementary Figure 2. Anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike IgG. (**A,B**) Antibody titers in close household contacts and kidney transplant recipients at baseline, 3 weeks after dose 1, and 3 weeks after dose 2. (**C,D**) Antibody titers compared by vaccine received. Differences between groups tested using the 2-tailed Mann-Whitney test. NS, not significant; *, p<0.05; ***, p<0.001; ****, p<0.0001.



Supplementary Figure 3. Anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) humoral immune response by vaccine. (**A,C**) Anti–SARS-CoV-2 receptor-binding domain (RBD) IgG titers in close household contacts (CHCs) and kidney transplant recipients (KTRs) 3 weeks after the second vaccine dose. (**B,D**) Serological live virus neutralization in CHCs and KTRs 3 weeks after the second vaccine dose. Differences between groups tested using the 2-tailed Mann-Whitney test. NS, not significant; ****, p<0.0001.



Supplementary Figure 4. Vaccine-induced antiviral T-cell response. (**A,C**) Spike-reactive interferon-γ (IFN-γ)–secreting T cells in close household contacts (CHCs) and kidney transplant recipients (KTRs) at baseline and 3 weeks after dose 2. (**C,D**) Change in IFN-γ spot-forming units (SFUs) between baseline and 3 weeks after the second vaccine dose in CHCs and KTRs compared by vaccine received. Differences between groups tested using the 2-tailed Mann-Whitney test. NS, not significant; ****, p<0.0001.

Supplementary References.

S1. M. Shen, Z. Peng, Y. Guo, et al., Assessing the effects of metropolitan-wide quarantine on the spread of COVID-19 in public space and households, *Int J Infect Dis*, 96, 2020, 503–505.