COV-BOOST

Evaluating COVID-19 vaccine boosters

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Chief Investigator:	Prof Saul Faust
Sponsor:	University Hospital Southampton NHS Foundation Trust
Objectives:	Evaluation of COVID vaccine platform combinations for administration of 3rd dose to people immunised with two doses of Pfizer or ChAdOx vaccines in the UK schedule.

Key COV-BOOST partners

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- Laboratory Oversight
- Logistic Support
- Communications Support

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Medicines & Healthcare products Regulatory Agency

MHRA

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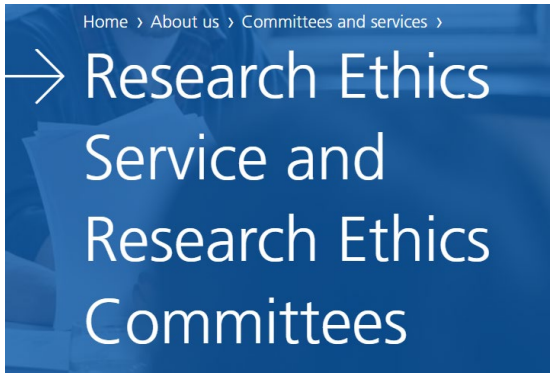

COV-BOOST data

- Data was presented to MHRA and JCVI in real time during 2021 and 2022
- Analysis ongoing as of January 2024.

THE LANCET

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial

Alasdair P S Munro, Leila Janani*, Victoria Cornelius*, Parvinder K Aley, Gavin Babbage, David Baxter, Marcin Bula, Katrina Cathie, Krishna Chatterjee, Kate Dodd, Yvanne Enever, Karishma Gokani, Anna L Goodman, Christopher A Green, Linda Harndahl, John Haughney, Alexander Hicks, Agatha A van der Klaauw, Jonathan Kwok, Vincenzo Libri, Martin J Llewelyn, Alastair C McGregor, Angela M Minassian, Patrick Moore, Mehmood Mughal, Yama F Mujadidi, Jennifer Murira, Orod Osanlou, Rostam Osanlou, Daniel R Owens, Mihaela Pacurar, Adrian Palfreeman, Daniel Pan, Tommy Rampling, Karen Regan, Stephen Saich, Jo Salkeld, Dinesh Saralaya, Sunil Sharma, Ray Sheridan, Ann Sturdy, Emma C Thomson, Shirley Todd, Chris Twelves, Robert C Read, Sue Charlton, Bassam Hallis, Mary Ramsay, Nick Andrews, Jonathan S Nguyen-Van-Tam, Matthew D Snape†, Xinxue Liu†, Saul N Faust†, on behalf of the COV-BOOST study group‡*

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S0140-6736(21)02717-3

COV-BOOST Stage 1 design- 3 groups of 6 sites

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Group A: 888 participants (including 444 vaccinated previously with 2 doses of BNT162b2 and 444 vaccinated previously with 2 doses of ChAdOx1-nCov19) randomised 1:1:1:1 to receive a booster dose of either **ChAdOx1-nCov19, Novavax, Novavax half dose**, or MenACWY (control group).

Bournemouth, Bradford, Portsmouth, Leicester, University College London, Wrexham (Wales).

Group B: 1110 participants (including 555 vaccinated previously with 2 doses of BNT162b2 and 555 vaccinated previously with 2 doses of ChAdOx1-nCov19) randomised 1:1:1:1:1 to receive a booster dose of either **BNT162b2, Valneva, Valneva half dose, Janssen** or MenACWY (control group).

Cambridge, Guys London, Glasgow (Scotland), Leeds, Oxford, Southampton.

Group C: 888 participants (including 444 vaccinated previously with 2 doses of BNT162b2 and 444 vaccinated previously with 2 doses of ChAdOx1-nCov19) randomised 1:1:1:1 to receive a booster dose of either **mRNA-1273 (Moderna), CureVac, BNT162b2 half dose**, or MenACWY (control group).

Birmingham, Exeter, Liverpool, Northwick Park London, Stockport, Sussex

Study Design: April 2021

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Stage1

Eligible population

= 2,886

General cohort

= 2,236

Immunology cohort

= 650

25

Comprising 25 participants from each group

6 sites

Group A = 888

- Pfz-BNT/Pfz-BNT = 444
  - Oxford-AZ = 111
  - Novavax = 111
  - Novavax-half = 111
  - Control = 111
- Oxford-AZ = 444
  - Oxford-AZ = 111
  - Novavax = 111
  - Novavax-half = 111
  - Control = 111

6 sites

Group B = 1,110

- Pfz-BNT/Pfz-BNT = 555
  - Pfz-BNT/Pfz-BNT= 111
  - Valneva = 111
  - Valneva-half = 111
  - Janssen = 111
  - Control = 111
- Oxford-AZ = 555
  - Pfz-BNT/Pfz-BNT = 111
  - Valneva = 111
  - Valneva-half = 111
  - Janssen = 111
  - Control = 111

6 sites

Group C = 888

- Pfz-BNT/Pfz-BNT = 444
  - Moderna = 111
  - CureVac = 111
  - Pfz-BNT half = 111
  - Control = 111
- Oxford-AZ = 444
  - Moderna = 111
  - CureVac = 111
  - Pfz-BNT half = 111
  - Control = 111

Baseline characteristics

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- Enrolled people 10-12 weeks after their 2nd dose of Pfizer of AstraZeneca vaccines
- Good age spread in 2 age groups 30-69 and >70s
- Included people with cardiovascular disorders, diabetes and respiratory conditions.
- Did not include people with immune problems

Summary of Results

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- The initial trial demonstrated the potential of all vaccines tested (AZ, Pfizer-BNT, Moderna, Novavax, Janssen, CureVac and Valneva) to boost immunity following AZ/AZ initial course and of 6 vaccines (AZ, Pfizer-BNT, Moderna, Novavax, Janssen, CureVac) to boost following Pfizer-BNT/Pfizer-BNT initial course.
- Heterologous schedules (mix and match) were safe and immunogenic despite the short interval between dose 2 and dose 3.
- The 100mcg dose of Moderna mRNA vaccine was the most reactogenic vaccine following 2 doses of AstraZeneca or Pfizer vaccines.
- Maximum mRNA antibody 3rd dose antibody responses were achieved by day 7 after 3rd dose following 2 doses of AstraZeneca or Pfizer vaccines.

Policy decisions supported by COV-BOOST

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- Pfizer and half dose Moderna as vaccines for UK 3rd dose booster programme
- Heterologous schedules (mix and match) safe and immunogenic
- 3 month interval decision to speed up programme
- Communication that maximum antibody response by day 7 after 3rd dose
- Global health: incorporated into WHO guidelines, supported further studies of fractional doses (including in COV-BOOST)

3 month analysis of main study

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Participants enrolled and had telephone pre-screening

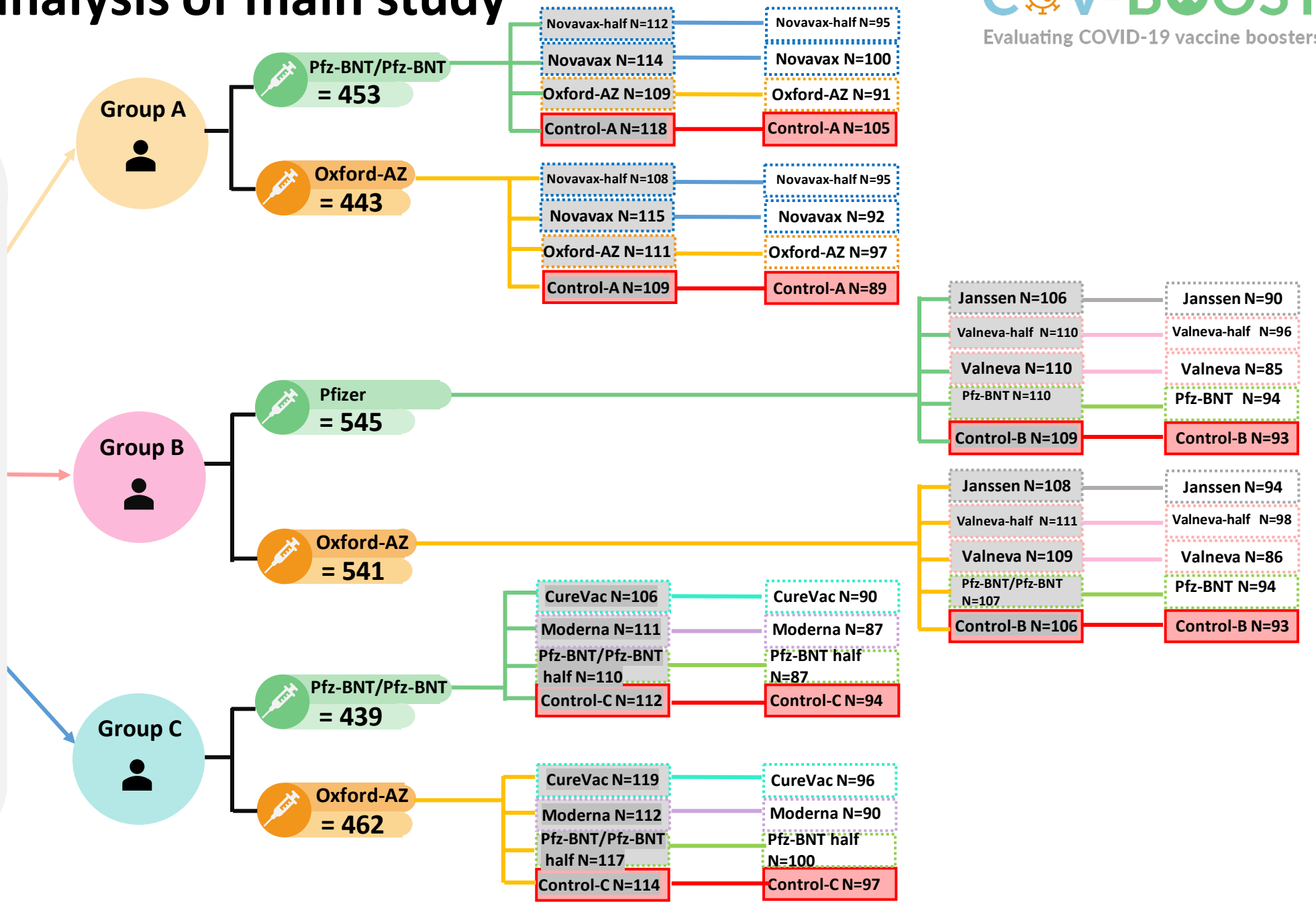
= 3,498

Participants screened for eligibility

= 3,054

Participants randomised

= 2,883



3 month analysis of main study

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FULL LENGTH ARTICLE | VOLUME 84, ISSUE 6, P795-813, JUNE 01, 2022

PDF [6 MB] Figures

Persistence of immunogenicity after seven COVID-19 vaccines given as third dose boosters following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK: Three month analyses of the COV-BOOST trial.

Xinxue Liu #, † • Alasdair P S Munro # • Shuo Feng # • Leila Janani # • Parvinder K Aley • Gavin Babbage • David Baxter • Marcin Bula • Katrina Cathie • Krishna Chatterjee • Wanwisa Dejnirattisai • Kate Dodd • Yvanne Enever • Ehsaan Qureshi • Anna L. Goodman • Christopher A Green • Linda Harndahl • John Haughney • Alexander Hicks • Agatha A. van der Klaauw • Jonathan Kwok • Vincenzo Libri • Martin J Llewelyn • Alastair C McGregor • Angela M. Minassian • Patrick Moore • Mehmood Mughal • Yama F Mujadidi • Kyra Holliday • Orod Osanlou • Rostam Osanlou • Daniel R Owens • Mihaela Pacurar • Adrian Palfreeman • Daniel Pan • Tommy Rampling • Karen Regan • Stephen Saich • Teona Serafimova • Dinesh Saralaya • Gavin R Screaton • Sunil Sharma • Ray Sheridan • Ann Sturdy • Piyada Supasa • Emma C Thomson • Shirley Todd • Chris Twelves • Robert C. Read • Sue Charlton • Bassam Hallis • Mary Ramsay • Nick Andrews • Teresa Lambe • Jonathan S Nguyen-Van-Tam • Victoria Cornelius # • Matthew D Snape # • Saul N Faust #, † • the COV-BOOST study group ‡ • Show less • Show footnotes

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3 month analysis

- The persistence of antibody responses were different between vaccines
- After 2 doses of AstraZeneca, mRNA vaccines still have the highest antibody response at day 84.
- **After 2 doses of Pfizer, viral-vector vaccines (Janssen and AstraZeneca) have comparable or even higher antibody response at D84 compared with people who received 3 doses of Pfizer.**
- Mix and match (heterologous) and same vaccine (homologous) schedules have different kinetics of antibody level decline by day 84 which appears to depend both on vaccine class and the order of administration.
- Half dose Pfizer induced comparable levels of humoral and cellular responses at day 84 compared with full dose full dose Pfizer.

8 month analysis of main study

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RESEARCH ARTICLE | VOLUME 87, ISSUE 1, P18-26, JULY 2023 Download Full Issue

Persistence of immune responses after heterologous and homologous third COVID-19 vaccine dose schedules in the UK: eight-month analyses of the COV-BOOST trial

Xinxue Liu [1] • Alasdair P S Munro [1] • Annie Wright [1] • Shuo Feng • Leila Janani • Parvinder K Aley • Gavin Babbage • Jonathan Baker • David Baxter • Tanveer Bawa • Marcin Bula • Katrina Cathie • Krishna Chatterjee • Kate Dodd • Yvanne Enever • Lauren Fox • Ehsaan Qureshi • Anna L. Goodman • Christopher A Green • John Haughney • Alexander Hicks • Christine E Jones • Nasir Kanji • Agatha A. van der Klaauw • Vincenzo Libri • Martin J Llewelyn • Rebecca Mansfield • Mina Maallah • Alastair C McGregor • Angela M. Minassian • Patrick Moore • Mehmood Mughal • Yama F Mujadidi • Hanane Trari Belhadef • Kyra Holliday • Orod Osanlou • Rostam Osanlou • Daniel R Owens • Mihaela Pacurar • Adrian Palfreeman • Daniel Pan • Tommy Rampling • Karen Regan • Stephen Saich • Dinesh Saralaya • Sunil Sharma • Ray Sheridan • Matthew Stokes • Emma C Thomson • Shirley Todd • Chris Twelves • Robert C. Read • Sue Charlton • Bassam Hallis • Mary Ramsay • Nick Andrews • Teresa Lambe • Jonathan S Nguyen-Van-Tam • Victoria Cornelius [2] • Matthew D Snape [2] • Saul N Faust [2] • the COV-BOOST study group [3] • Show less • Show footnotes

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8 month analysis

- The persistence of antibody responses remained different between vaccines
- Humoral responses following booster doses of adenoviral vector vaccines decay slower than following booster doses of mRNA vaccines.
- Lower doses of mRNA vaccines as boosters may be equally as effective.

4th dose substudy Study Design

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Stage1

Eligible population

= 2,886

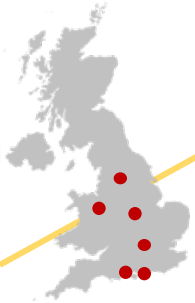
General cohort = 2,236

Immunology cohort = 650

25

Comprising 25 participants from each group

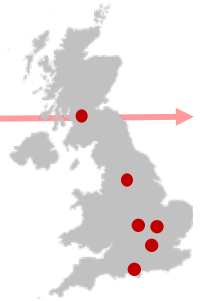
6 sites



Group A = 888

- Pfz-BNT/Pfz-BNT = 444
  - Oxford-AZ
  - Novavax
  - Novavax-half
  - Men ACWY
- Oxford-AZ = 444
  - Oxford-AZ
  - Novavax
  - Novavax-half
  - Men ACWY

6 sites



Group B = 1,110

- Pfz-BNT/Pfz-BNT = 555
- Oxford-AZ = 555

6 sites

Group C = 888

- Pfz-BNT/Pfz-BNT = 444
  - Moderna
  - CureVac
  - Pfz-BNT half
  - Men ACWY
- Oxford-AZ = 444
  - Moderna
  - CureVac
  - Pfz-BNT half
  - Men ACWY

4th dose population

- Pfz-BNT N=88
  - Valneva
  - Valneva-half
  - Janssen
  - Men ACWY
- Pfz-BNT N=78
  - Valneva
  - Valneva-half
  - Janssen
  - Men ACWY

Pfz-BNT N = 44 → Pfz-BNT N=35

Moderna 50mcg N = 44 → Moderna 50mcg N= 34

Pfz-BNT N = 39 → Pfz-BNT N=31

Moderna 50mcg N = 39 → Moderna 50mcg N= 33

- The sub-study is nested within the main COV-BOOST trial
- No formal sample size calculation
- To compare the immune response at D14 post 4th dose with that at D28 post 3rd dose

THE LANCET
Infectious Diseases

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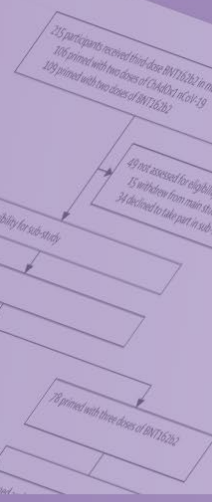
ARTICLES | ONLINE FIRST

Safety, immunogenicity, and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters following two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose of BNT162b2 (COV-BOOST): a multicentre, blinded, phase 2, randomised trial



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Sue Charlton, PhD • Bassam Hallis, PhD • Prof Mary Ramsay, FFPH • Prof Nick Andrews, PhD •
Prof Teresa Lambe, PhD • Prof Jonathan S Nguyen-Van-Tam, DM • Prof Matthew D Snape, MD † • Xinxue Liu, PhD † •
Prof Saul N Faust, PhD † • on behalf of the COV-BOOST study group ‡ • Show less • Show footnotes

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4th dose substudy

- After a period of approximately 7 months following third-dose boosters with BNT162b2, an additional dose of a COVID-19 mRNA vaccine can boost humoral anti-spike protein IgG titres and cellular responses to, or higher than, levels seen at 28 days after a third dose.

- Some participants with high levels of humoral and cellular responses before the fourth dose had limited boosting from the fourth dose, indicating that there could be a vaccine-specific ceiling effect.

Ongoing substudy analysis

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- JCVI have seen initial results as generated, no time to present today

- **Late boosted control substudy** analysis being finalised
  - Pfizer 30 mcg and 15 mcg, Moderna 50 mcg

- **Novavax substudy (Novavax/Novavax/Pfizer)** – analysis being finalised after laboratory inconsistencies noted that resulted in repeat testing prior to data lock

- **Young person's fractional dose substudy** (CEPI funded)
  - Pfizer 30 mcg and 15 mcg, Moderna 50 mcg and 25 mcg
  - Laboratory and statistical analysis ongoing

- **Moderna bivalent (WT and omicron) compared to Pfizer WT substudy**
  - Analysis in process of completion

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