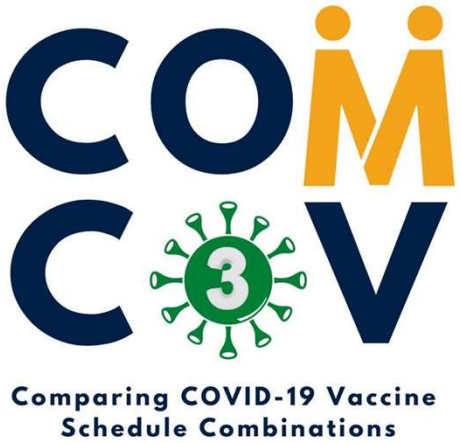

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Com-COV3 Study

Comparing COVID-19 Vaccine Schedule Combinations in Adolescents

Cohort A study design

Participants:
Healthy 12-to - 16-year-olds

1st dose:
BNT162b2
30 mcg

Randomised 1:1:1 to either:

- **BNT162b2 30 mcg (full dose)**
- **BNT162b2 10 mcg (1/3 dose)**
- ~~NVX-CoV2373~~

Sept 2021 — **Nov 2021**

Recruitment

Outcomes

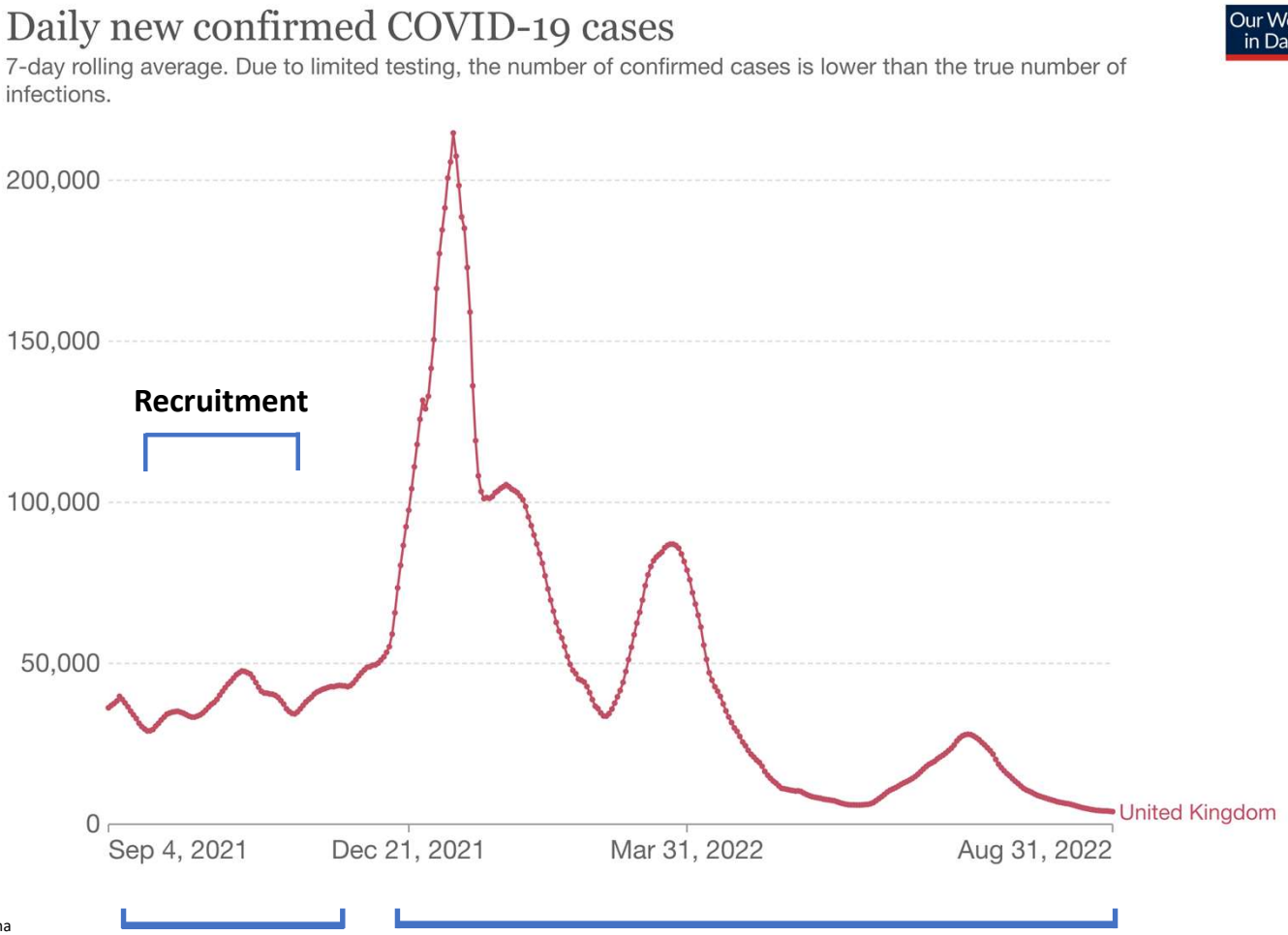
Primary:
Reactogenicity

Secondary:
Immunogenicity
Safety

Exploratory:
Neutralising antibodies, 'Breakthrough infections'

Recruitment across 7 UK sites. Cohort A completed Sept 2022.

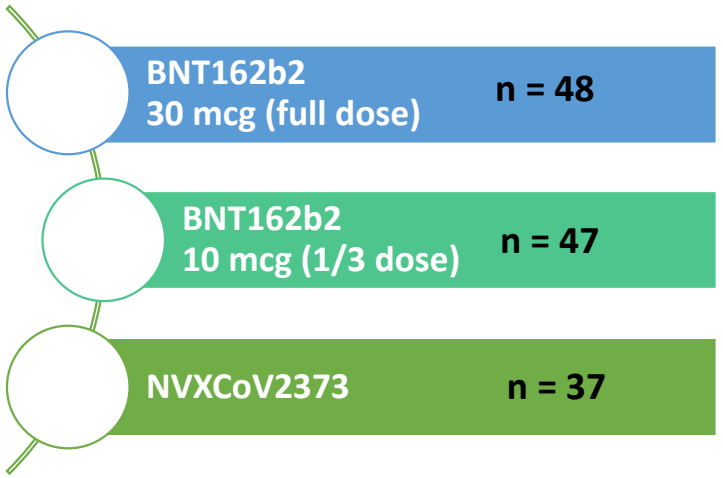
UK infection rates during Cohort A study



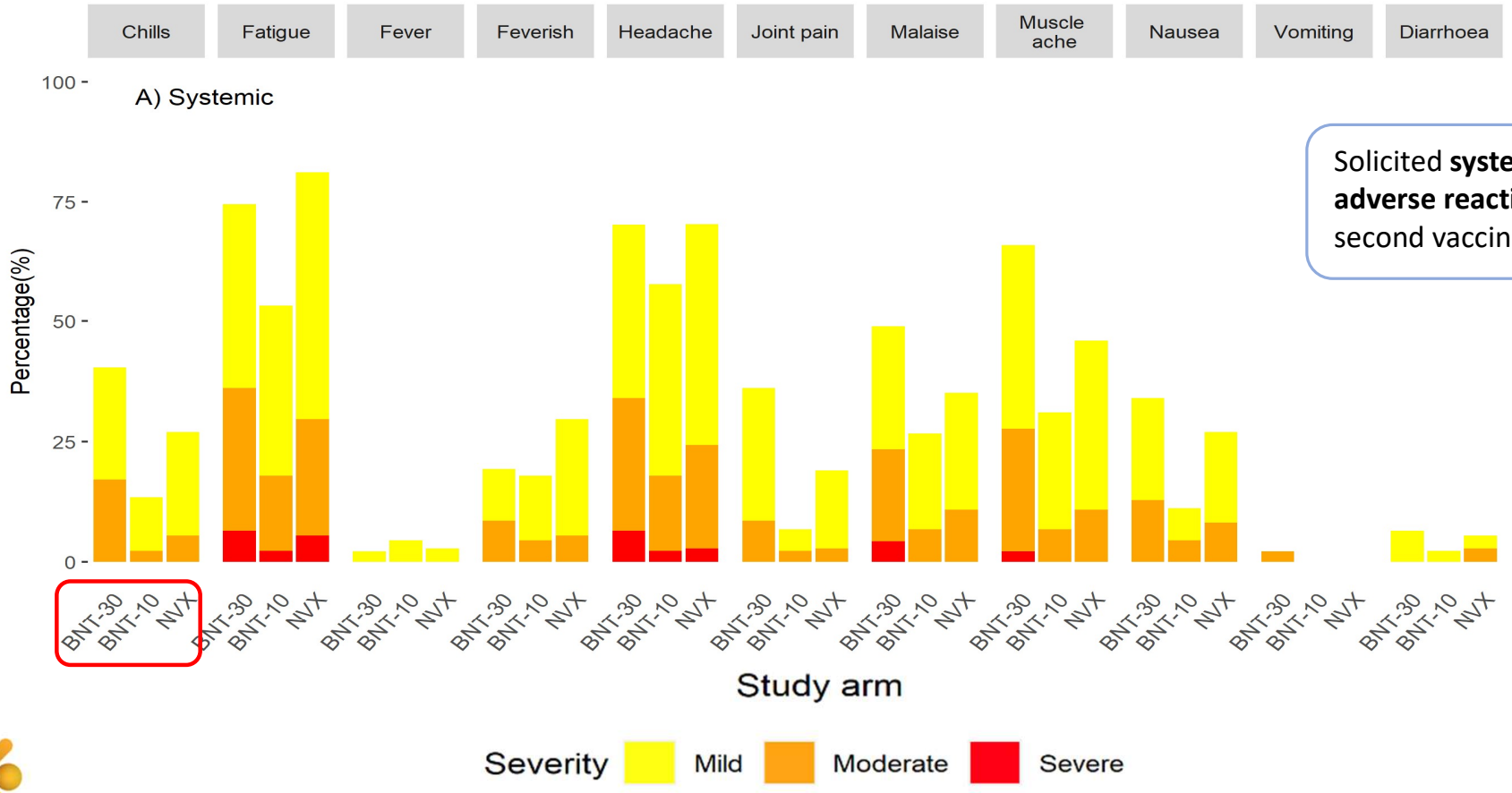
Max Roser and Esteban Ortiz-Ospina (2019) – "UK: Daily new confirmed COVID-19 cases". Published online at OurWorldInData.org.

Cohort A Demographics

- **148** participants enrolled and 132 randomised to receive second dose
- Median age **14 years old**
- **61%** female
- **96%** Caucasian
- **30%** anti-nucleocapsid positive at time of second dose
  (previously infected with SARS-CoV-2)
- Inter-dose interval median **59 days** (range 56, 109)

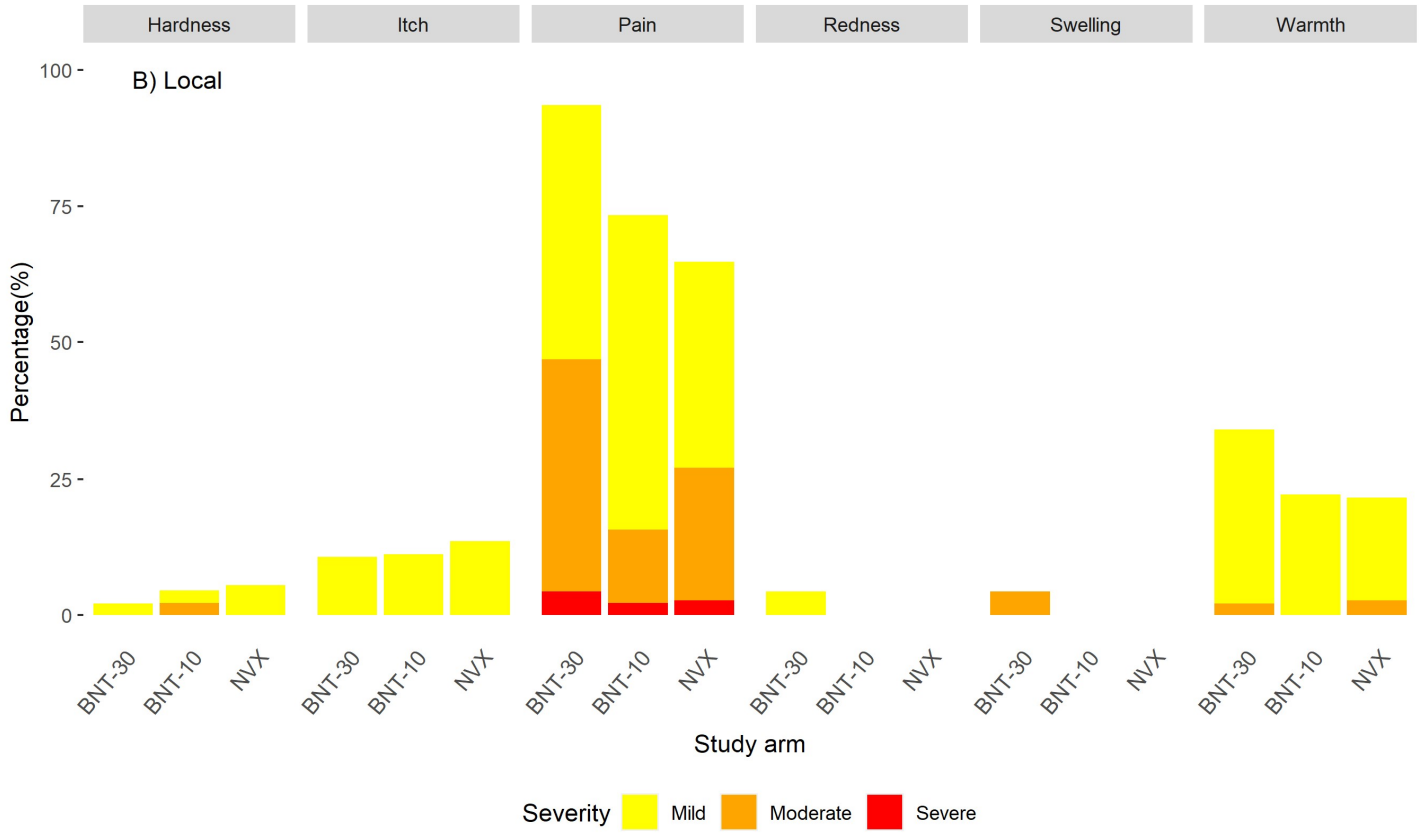


Cohort A Primary outcome: Reactogenicity



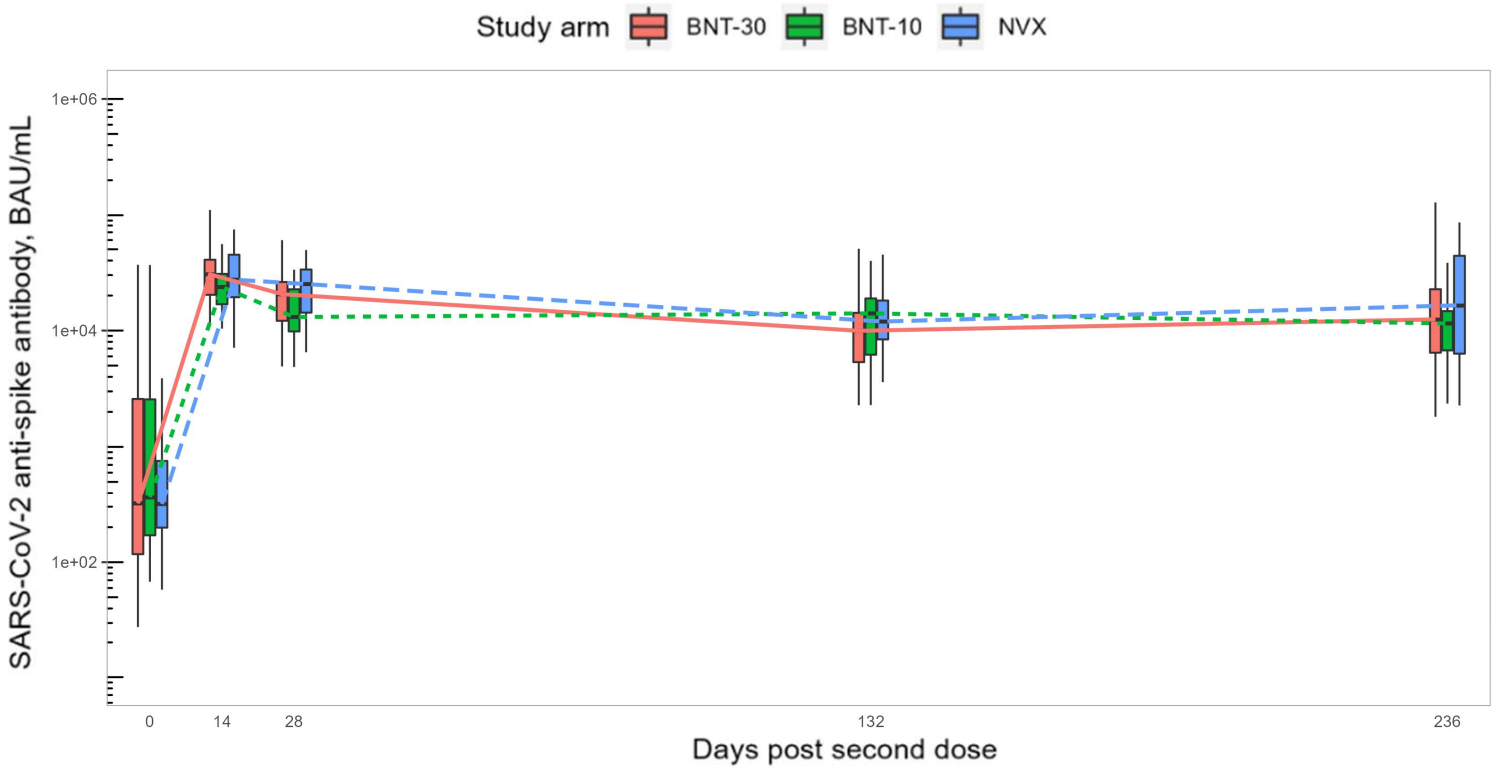
Solicited **systemic adverse reactions** post second vaccination

Solicited local adverse reactions post second vaccination



Anti-spike antibody response (Victoria)

All participants, day 236 mITT population



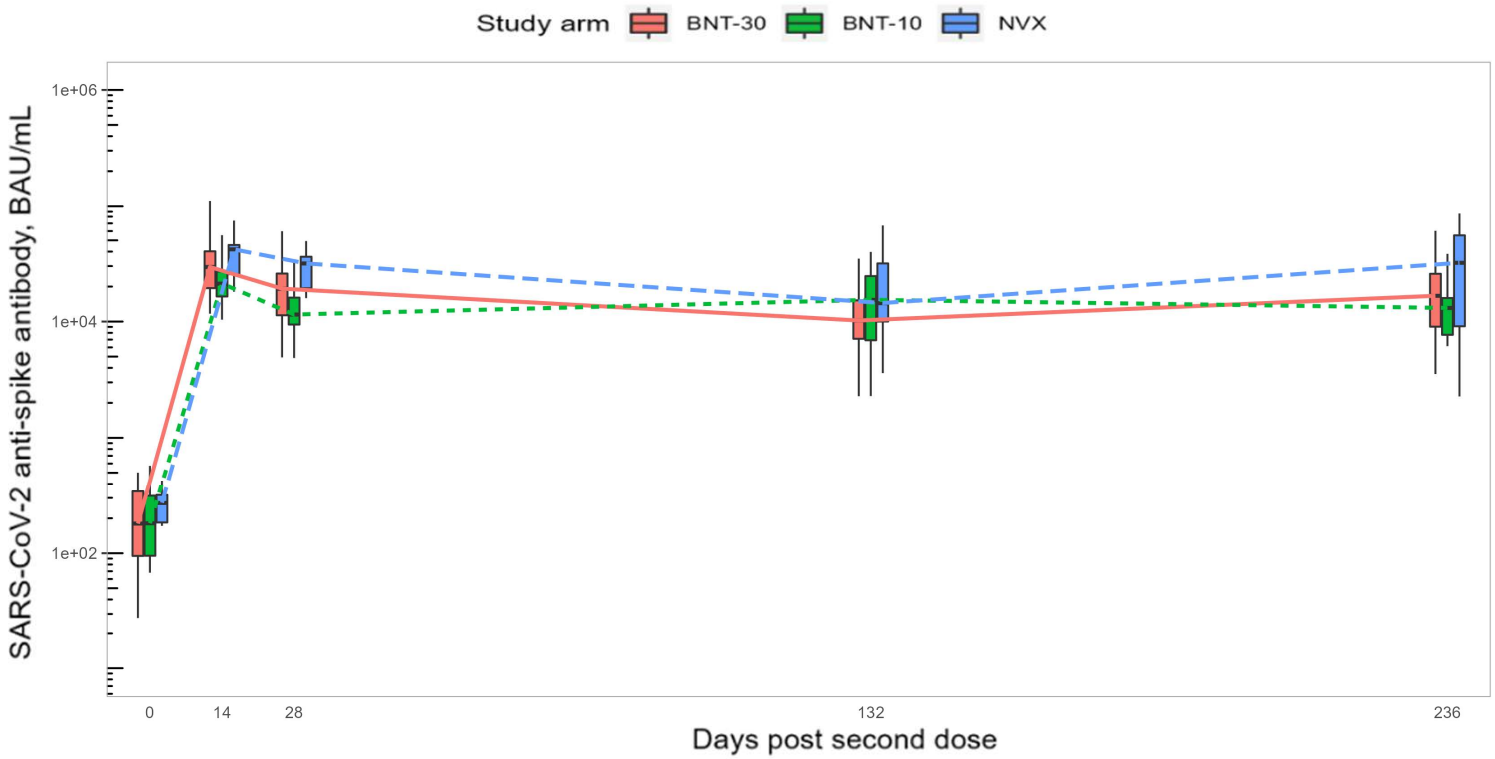
Participant numbers:
Total =103
BNT-30: 42
BNT-10: 35
NVX: 26

Modified intention-to-treat (mITT) population excludes participants who withdrew, had no blood sample at visit, self-reported a COVID-19 infection within 14 days of second dose, or received a third dose before 236 visit.

Anti-spike antibody response

Seronegative pre-second dose participants, mITT population

B

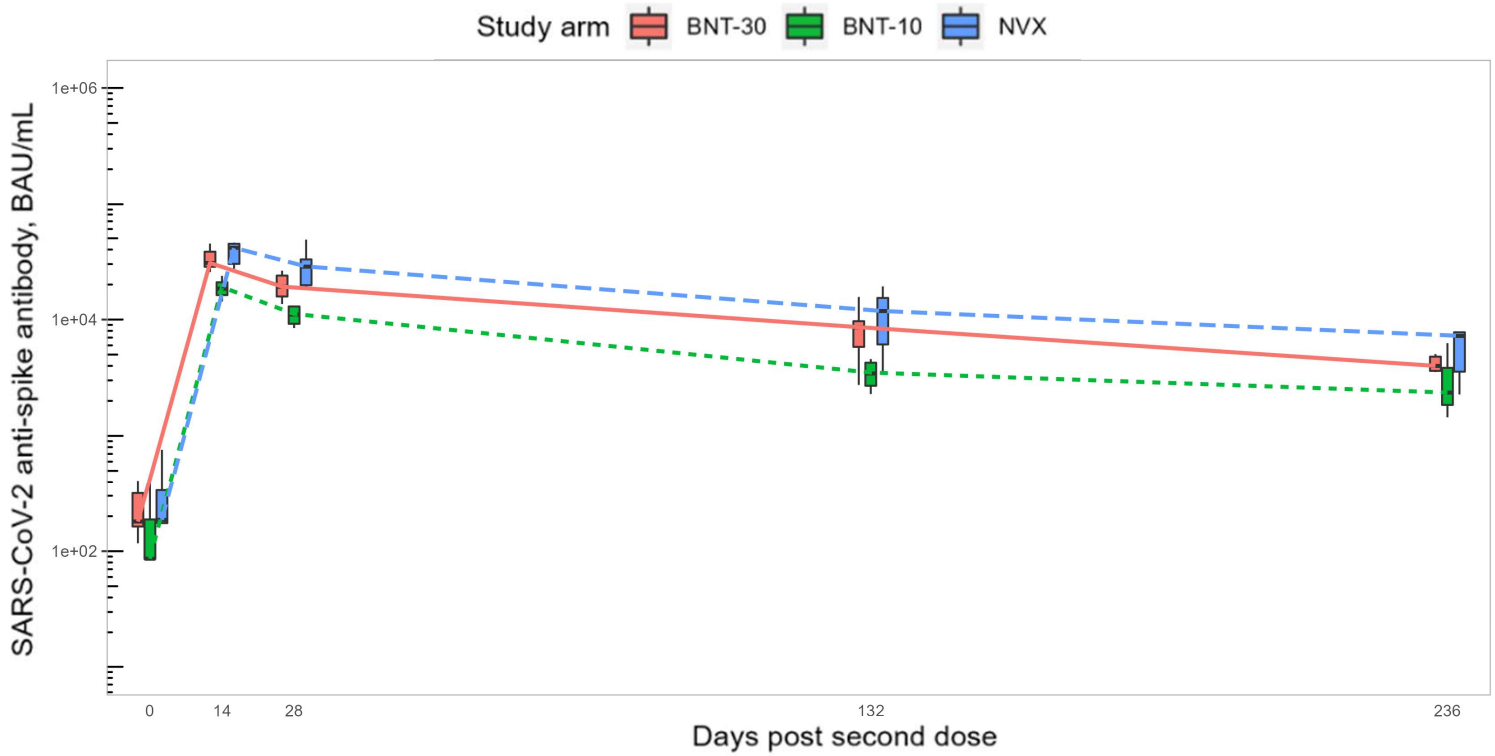


Participant numbers:
Total = 68
BNT-30: 28
BNT-10: 22
NVX: 18

Anti-spike antibody response

Seronegative pre-second dose participants with no infection during follow-up, mITT population

D



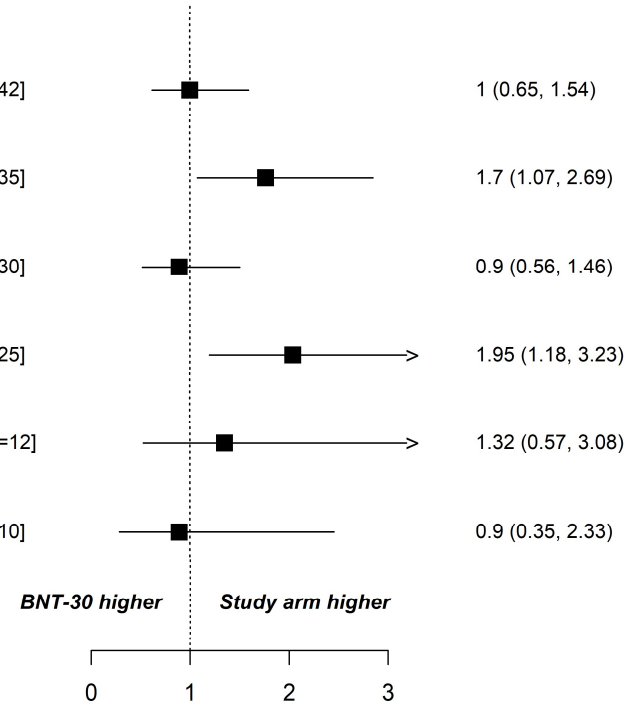
Participant numbers:
Total = 38
BNT-30: 16
BNT-10: 9
NVX: 13

COVID-19 infections from 28 to 236 days post second dose are excluded

BA.1 live virus neutralising antibody response

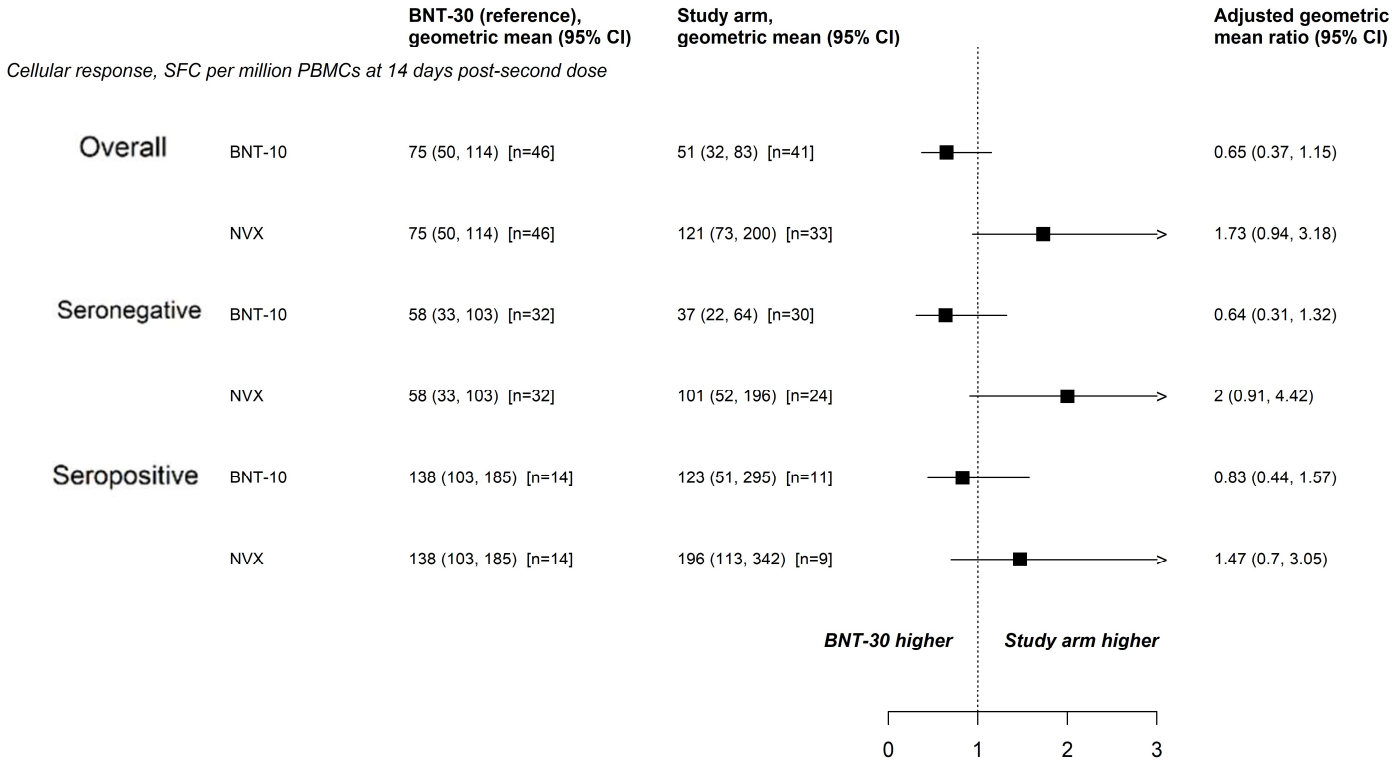
Day 28 modified intention-to-treat population

		BNT-30 (reference), geometric mean (95% CI)	Study arm, geometric mean (95% CI)	Adjusted geometric mean ratio (95% CI)
BA.1 live virus neutralising antibody, normalised NT50 at 28 days post-second dose				
Overall	BNT-10	361 (263, 497) [n=45]	333 (233, 476) [n=42]	1 (0.65, 1.54)
	NVX	361 (263, 497) [n=45]	556 (414, 748) [n=35]	1.7 (1.07, 2.69)
Seronegative	BNT-10	293 (202, 427) [n=31]	242 (165, 354) [n=30]	0.9 (0.56, 1.46)
	NVX	293 (202, 427) [n=31]	604 (441, 827) [n=25]	1.95 (1.18, 3.23)
Seropositive	BNT-10	573 (316, 1036) [n=14]	738 (370, 1474) [n=12]	1.32 (0.57, 3.08)
	NVX	573 (316, 1036) [n=14]	451 (207, 986) [n=10]	0.9 (0.35, 2.33)



Cellular response

Day 14 modified intention-to-treat population

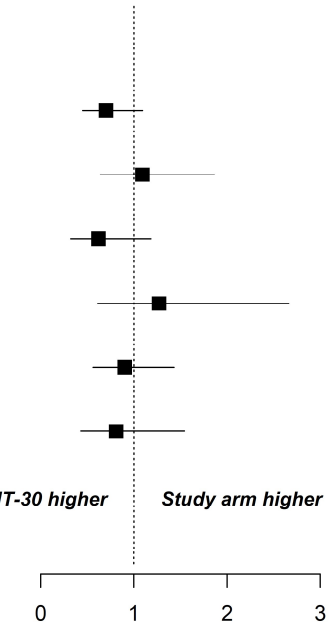


mITT population excludes participants who withdrew, had no blood sample at visit, self-reported a COVID-19 infection within 14 days of second dose.

Cellular response

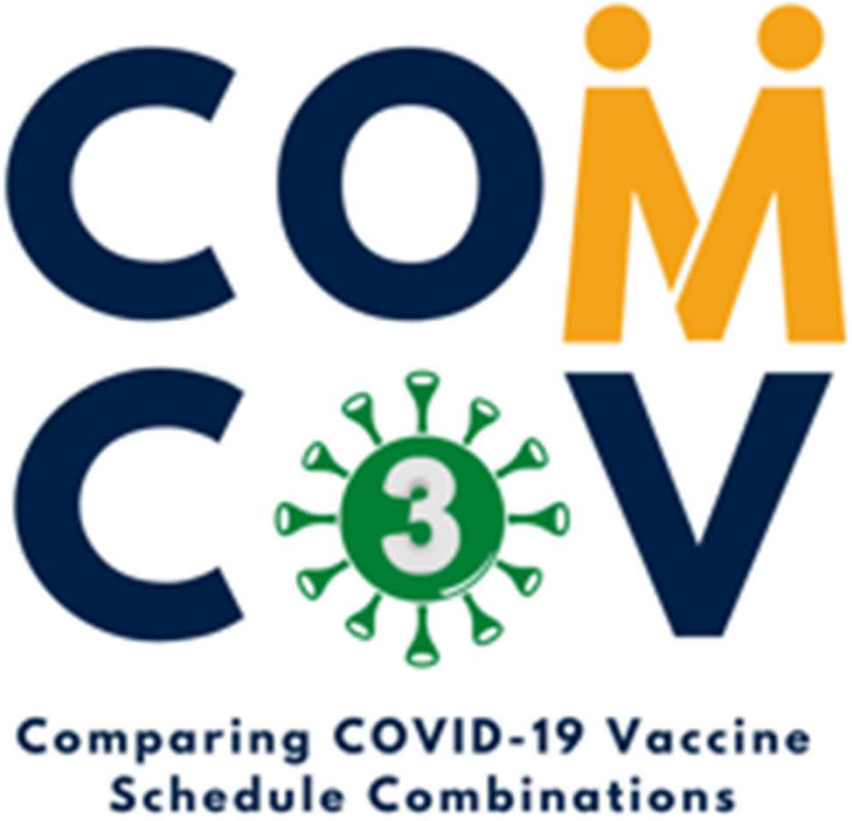
Day 236 modified intention-to-treat population

		BNT-30 (reference), geometric mean (95% CI)	Study arm, geometric mean (95% CI)	Adjusted geometric mean ratio (95% CI)
Cellular response, SFC per million PBMCs at 236 days post-second dose				
Overall	BNT-10	66 (50, 87) [n=41]	45 (30, 66) [n=35]	0.7 (0.45, 1.09)
	NVX	66 (50, 87) [n=41]	75 (49, 114) [n=21]	1.09 (0.64, 1.86)
Seronegative	BNT-10	60 (42, 87) [n=27]	34 (19, 61) [n=22]	0.62 (0.32, 1.18)
	NVX	60 (42, 87) [n=27]	75 (39, 146) [n=14]	1.27 (0.61, 2.66)
Seropositive	BNT-10	80 (52, 122) [n=14]	70 (50, 96) [n=13]	0.9 (0.56, 1.43)
	NVX	80 (52, 122) [n=14]	73 (59, 91) [n=7]	0.81 (0.43, 1.54)



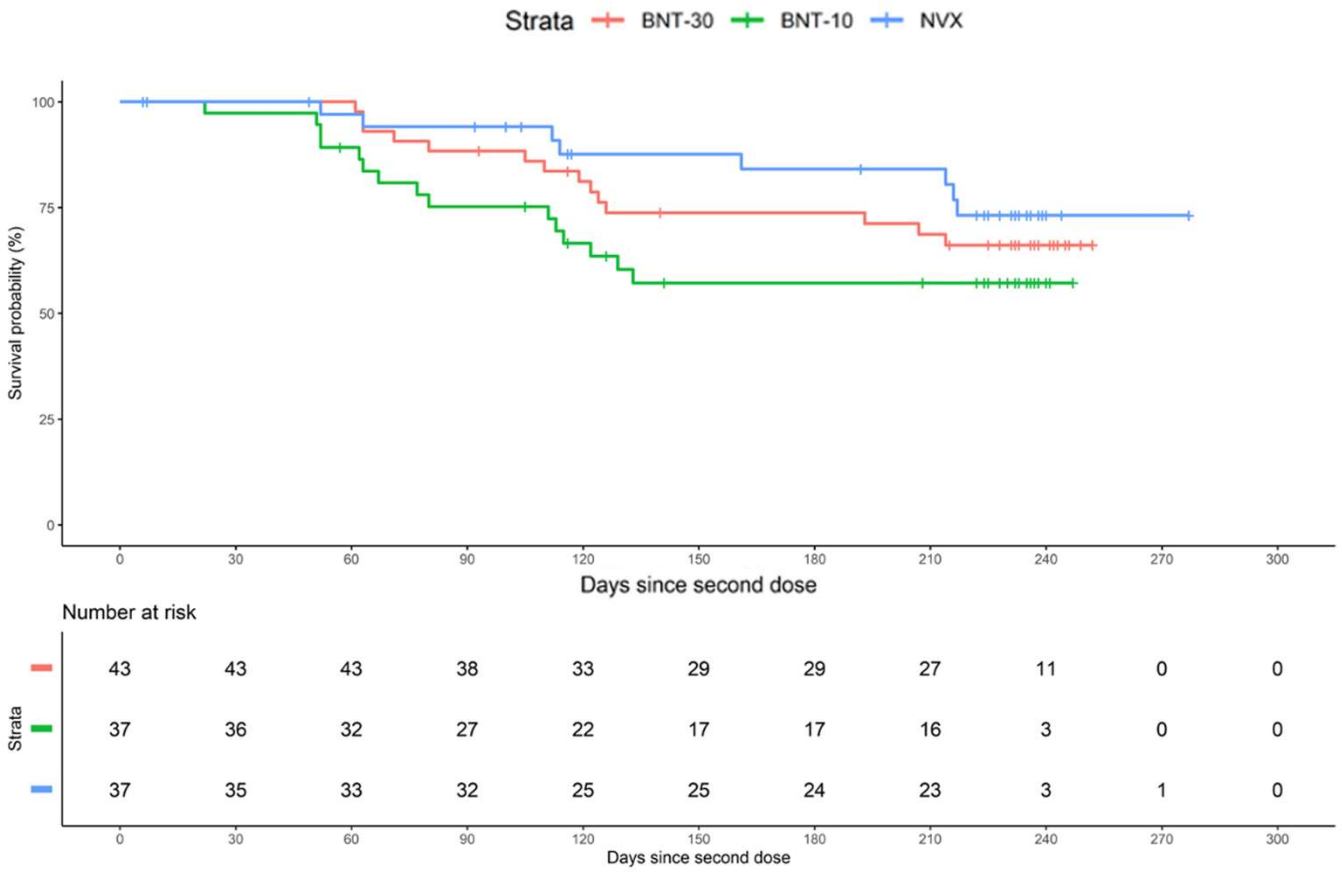
mITT population excludes participants who withdrew, had no blood sample at visit, self-reported a COVID-19 infection within 14 days of second dose, or received a third dose before visit.

COVID-19 ‘Breakthrough Infections’ during follow up



Time-to-event analysis: Self-reported COVID-19 infections during follow-up

All participants



Summary

- Heterologous and fractional dose COVID-19 vaccine schedules were well tolerated, no safety concerns

Anti-spike antibodies:

- Similar anti-spike Ig responses across the three study arms
- Highest response in seronegative NVX participants
- Steady decline in responses across the study arms for participants with no infection during follow-up

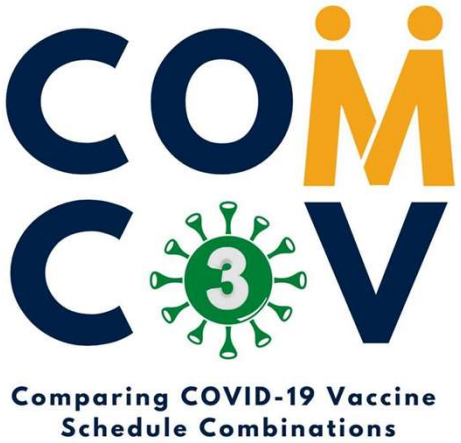
Breakthrough infections:

- Highest rate in BNT-10 group; lowest in NVX group

Support for heterologous COVID-19 vaccine schedules

- Implications for schedule flexibility and vaccine access globally

Kelly E, Greenland M, de Whalley PCS et al. Reactogenicity, immunogenicity and breakthrough infections following heterologous or fractional second dose COVID-19 vaccination in adolescents (Com-COV3): A randomised controlled trial. J Infect. 2023 Sep;87(3):230-241. doi: 10.1016/j.jinf.2023.06.007.



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CEPI | New vaccines for a safer world

Com-COV3 Cohort B Study

Reactogenicity and Immunogenicity following Heterologous and Homologous Third Dose COVID-19 vaccination in Adolescents

Cohort B study design

Study arm*	Dose 1 + 2 (Received in community/ Cohort A)	Dose 3 given at Study D0: (3 months after dose 2)	3 months (Day 84)	6 months (Day 182)
1 (n= up to 62)	BNT162b2 30 µg x 2	**BNT162b2 30 µg**	-	-
2 (n= up to 62)	BNT162b2 30 µg x 2	**BNT162b2 10µg (adult) 1/3 dose 0.1 ml**	-	-
3 (n= up to 62)	BNT162b2 30 µg x 2	**BNT162b2 10µg (paediatric) 0.2 ml**	-	-
4 (n= up to 62)	BNT162b2 30 µg x 2	**NVXCoV2373**	-	-
5 (n= up to 62)	BNT162b2 30 µg x 2	**4CMenB CONTROL**	4CMenB CONTROL	**Comirnaty Original/ Omicron BA.1 15/15µg**

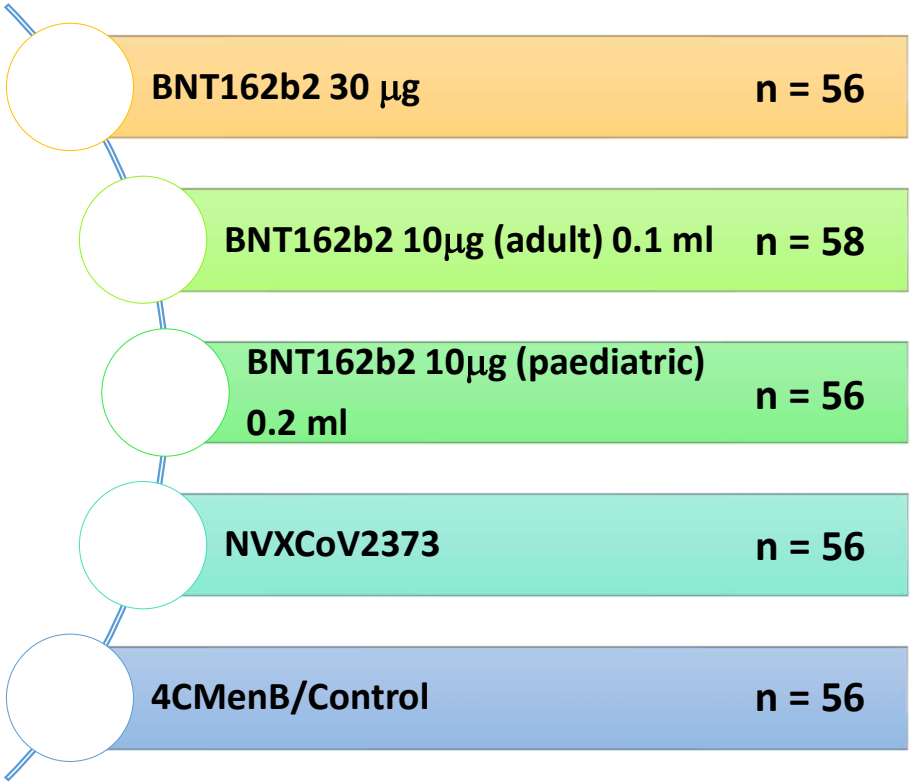
* Target n = up to 310 based on non-inferiority power calculation

Cohort B: Outcomes

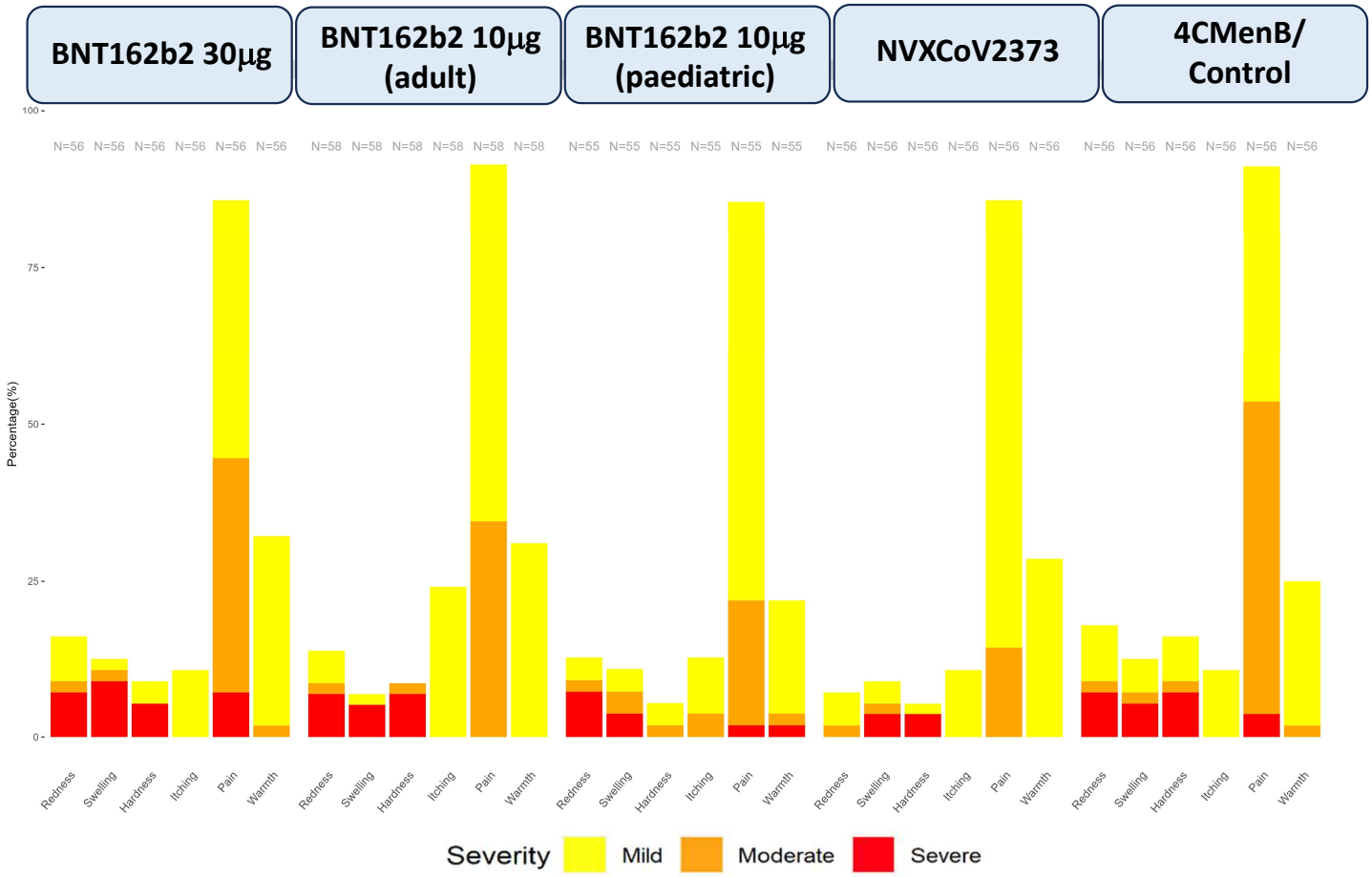
- **Primary**:
  - Reactogenicity
  - To determine if immunogenicity following 10µg adult formulation BNT162b2 is non-inferior to 10µg paediatric formulation BNT162b2
- **Secondary**:
  - Immunogenicity
  - Safety
- **Exploratory**
  - Neutralising Ab (Victoria, BA.5, XBB.1.5)
  - Breakthrough infection

Demographics

- **281** participants enrolled
- Mean age **14 years old**
- **56%** female
- **89%** Caucasian
- **65%** previous history of SARS-CoV-2 infection
- 2nd & 3rd Inter-dose interval:
  - mean **244.8** days (SD 91.3)



Cohort B Co-Primary outcome: Local Reactogenicity



Study Team

- Chief investigator
  - Dr. Angela Minassian
  - Prof. Matthew Snape
- Site Principal Investigators
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- Lead Fellow
  - Dr Eimear Kelly
  - Dr Philip De Whalley
- Senior Research Nurse
  - Stanislava Koleva
- Senior Clinical Trials Project Manager
  - Dr Grace Macaulay
- Programme and Regulatory Affairs Director: Emma Plested
- Statisticians
  - Prof. Xinxue Liu
  - Melanie Greenland
  - Liberty Cantrell
- Laboratory leads
  - Elizabeth Clutterbuck
  - Rachel Anslow
- Data Managers
  - Yama Mujadidi
  - Hanane Trari Belhadef
  - Ankana Singha
- Digital Projects Lead
  - Robert Aley
- Project Managers
  - Sharon Toner
  - Mia Johnson
  - Juliette Cotton
  - Jasmin Kinch
- Director of Global Operations
  - Parvinder Aley

Comparing COVID-19 Vaccine Schedule Combinations

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