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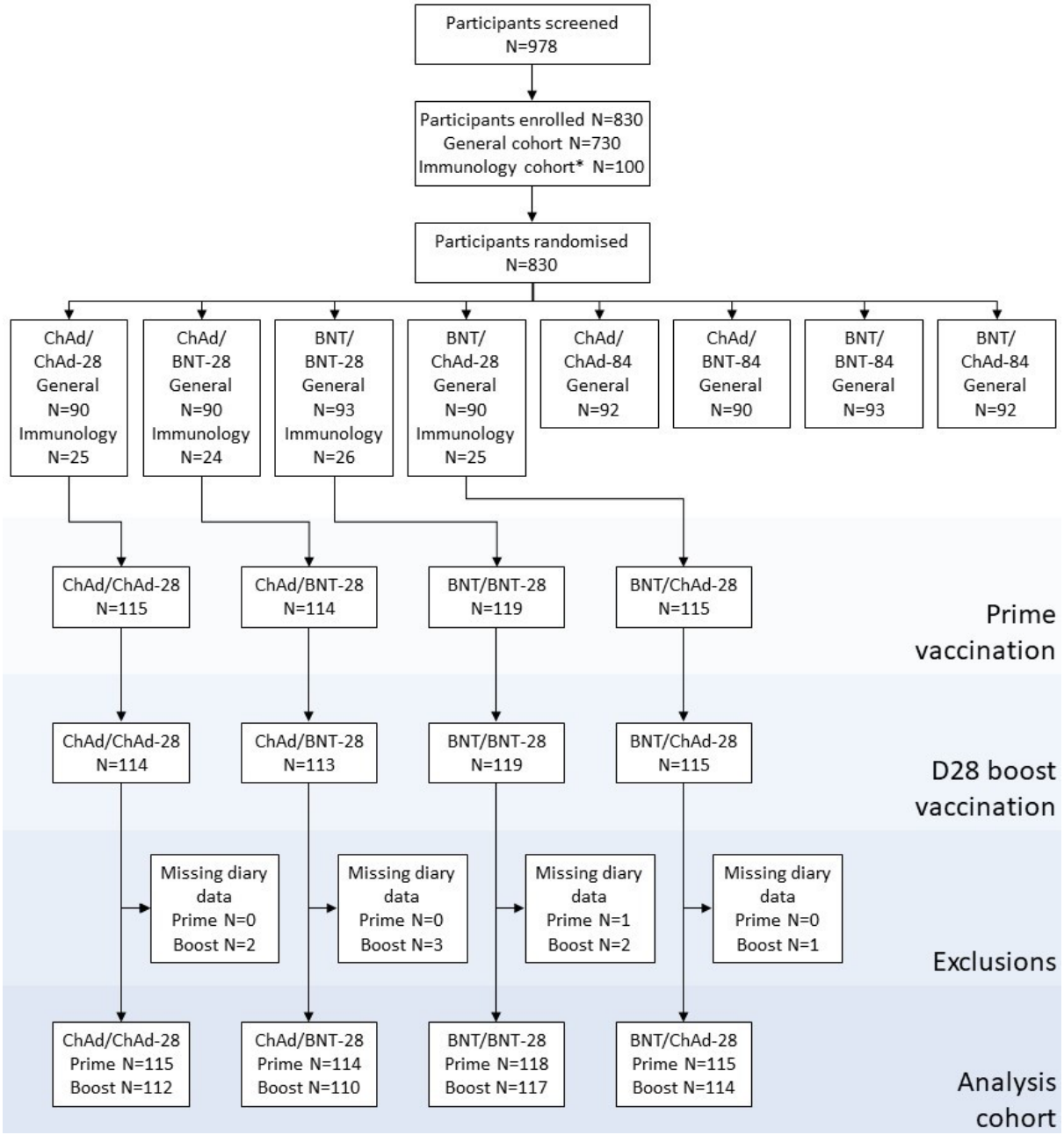
Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

This online publication has been corrected. The corrected version first appeared at thelancet.com on May 18, 2021.

Supplement to: Shaw RH, Stuart A, Greenland M, et al. Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data. *Lancet* 2021; published online May 12. http://dx.doi.org/10.1016/S0140-6736(21)01115-6.

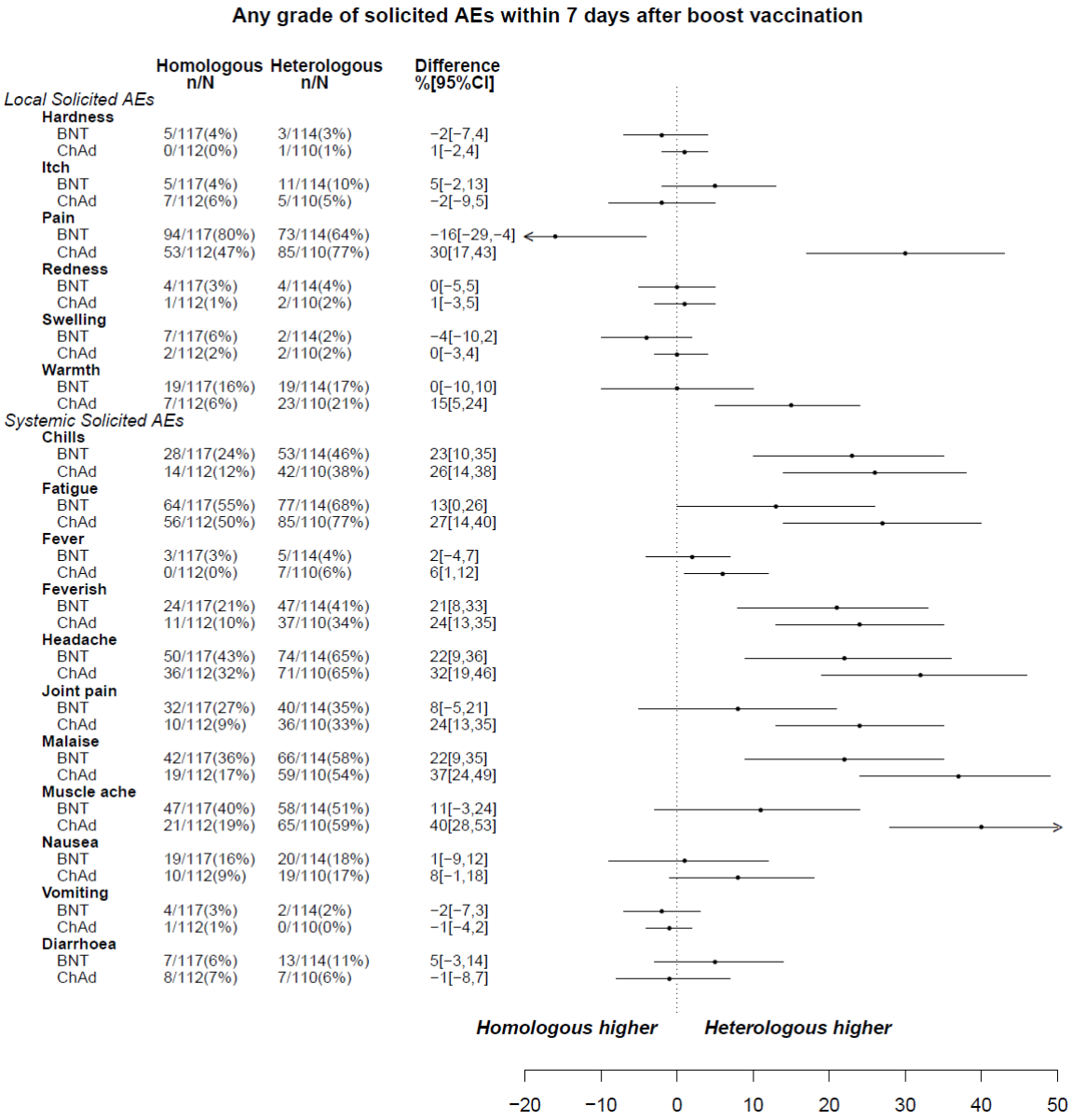
Supplementary Figure 1: CONSORT flow diagram of participants



* The immunology cohort was only randomised to the four arms with 28 days prime-boost interval.

Participants were recruited at eight sites: University College London Hospitals NHS Foundation Trust; St Georges University Hospitals NHS Foundation trust; University Hospitals Birmingham NHS Foundation Trust; North Bristol NHS trust; Oxford Vaccine Group, University of Oxford; The University of Nottingham Health Services; University Hospital Southampton NHS Foundation Trust and Liverpool School of Tropical Medicine.

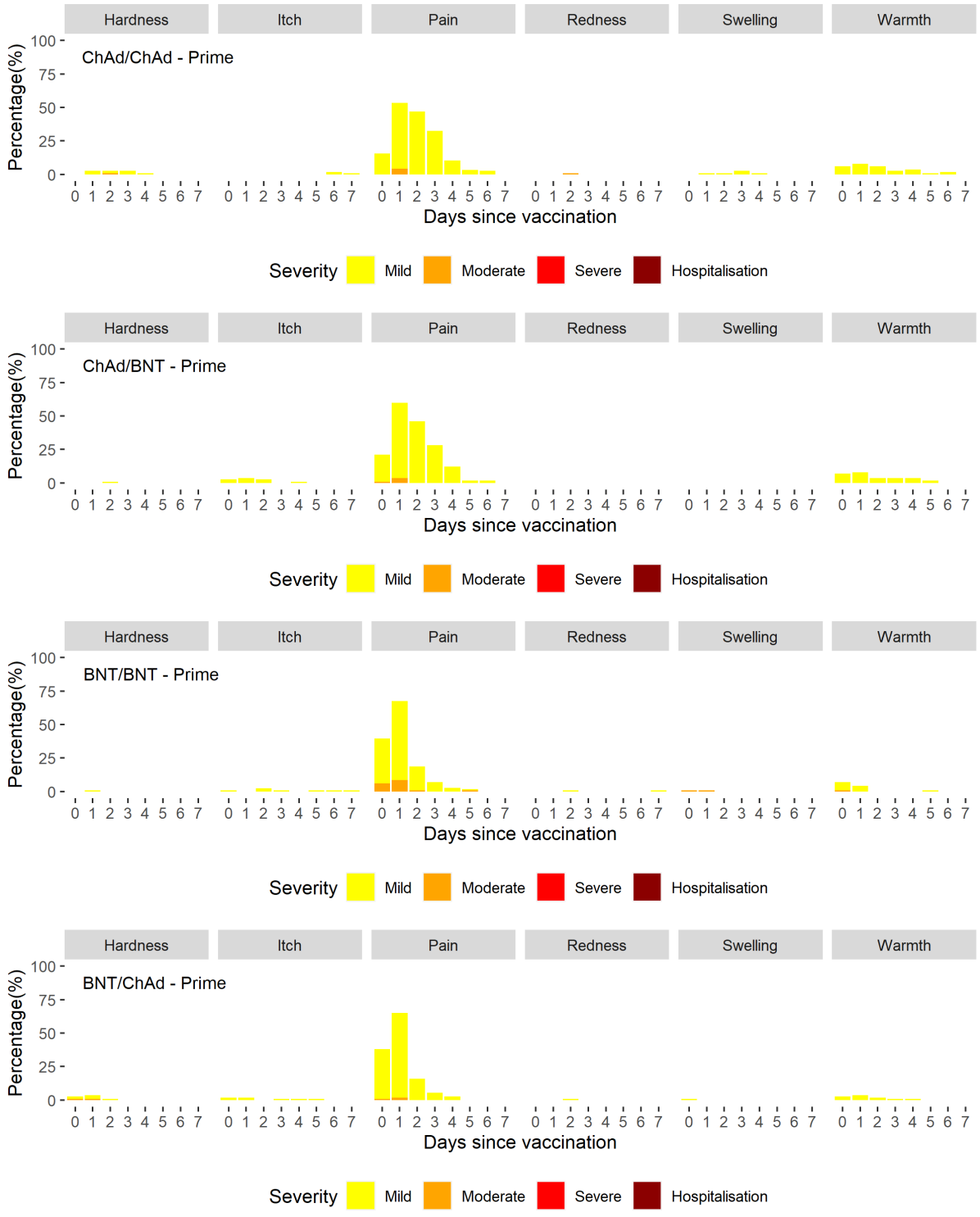
Supplementary Figure 2: Forest plot



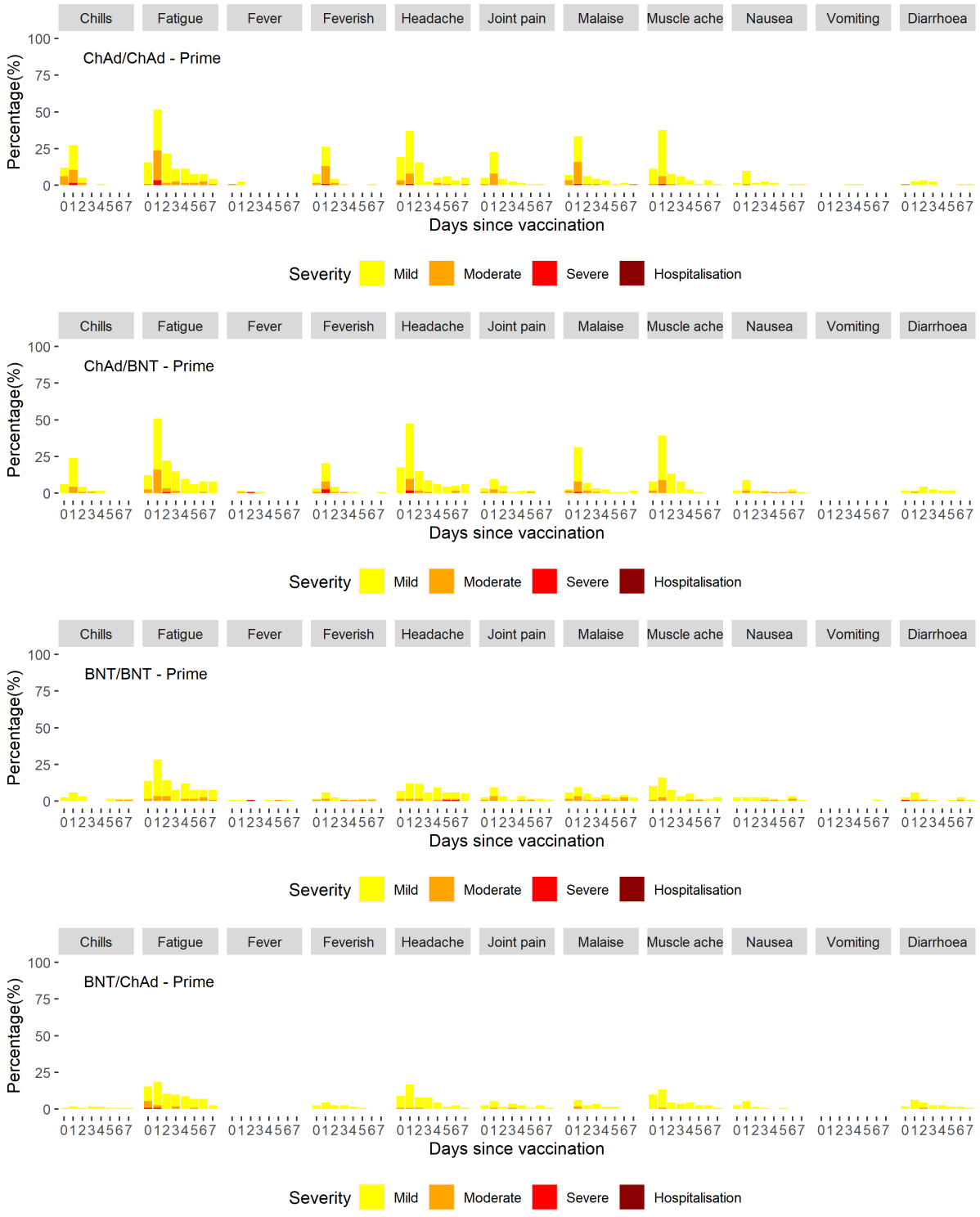
BNT and ChAd refer to the prime vaccination. Forest plot presents the absolute differences in the proportion of participants with any grade solicited AEs (across 7 days post boost vaccination) with 95% confidence intervals (Yates's correction for continuity) between the heterologous and homologous arms.

Supplementary Figure 3: Solicited local and systemic reactions across the first 7 days following vaccination as self-reported in participant electronic diaries by prime/boost vaccination and study arm, A) local following prime; B) systemic following prime; C) local following boost; D) systemic following boost.

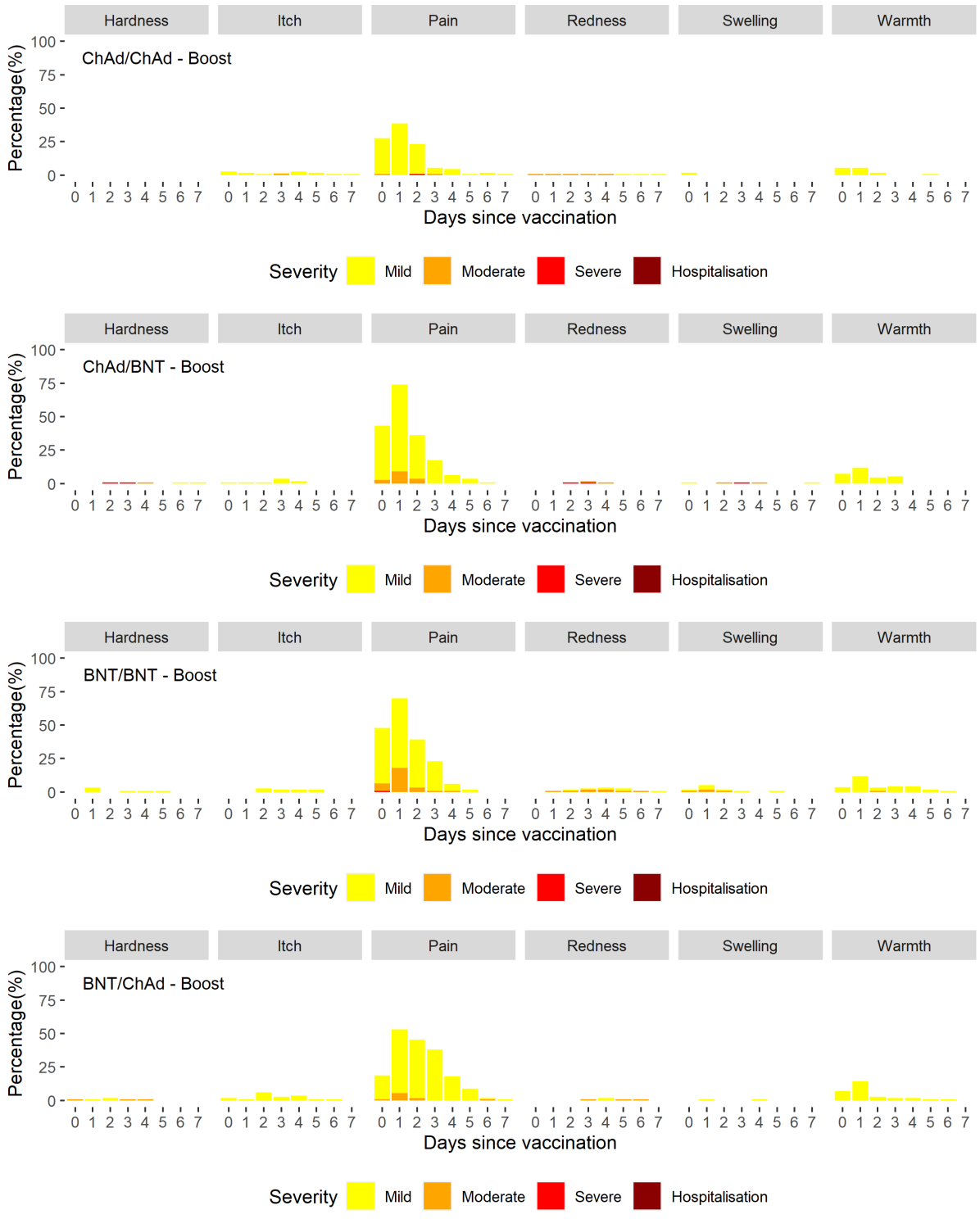
A



B


Chills
Fatigue
Fever
Feverish
Headache
Joint pain
Malaise
Muscle ache
Nausea
Vomiting
Diarrhoea
ChAd/ChAd - Prime
ChAd/BNT - Prime
BNT/BNT - Prime
BNT/ChAd - Prime
Percentage(%)
100
75
50
25
0
01234567
Days since vaccination
Severity
Mild
Moderate
Severe
Hospitalisation

19 ***C***


Hardness
Itch
Pain
Redness
Swelling
Warmth
ChAd/ChAd - Boost
ChAd/BNT - Boost
BNT/BNT - Boost
BNT/ChAd - Boost
Percentage(%)
100
75
50
25
0
0 1 2 3 4 5 6 7
Days since vaccination
Severity
Mild
Moderate
Severe
Hospitalisation

20

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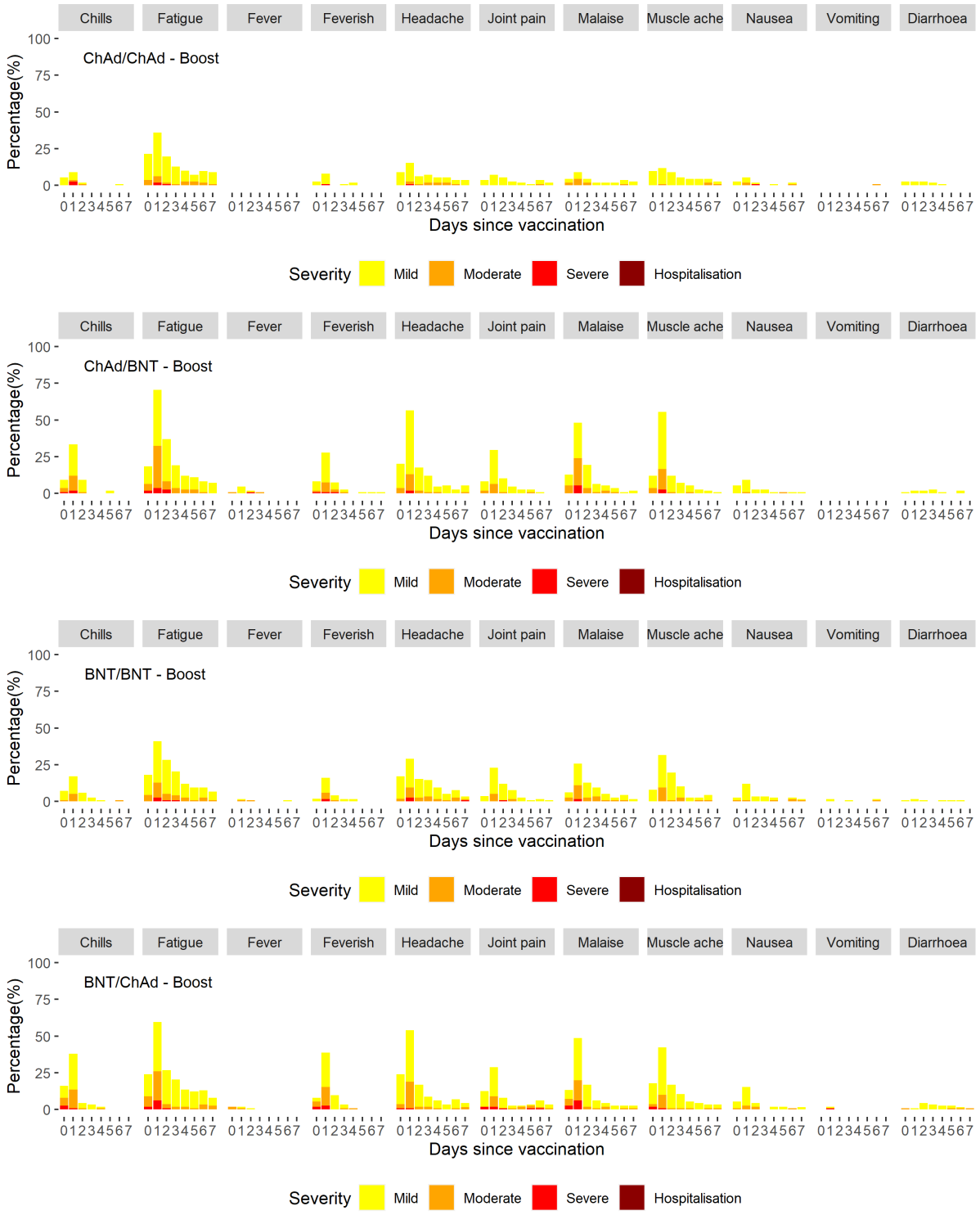
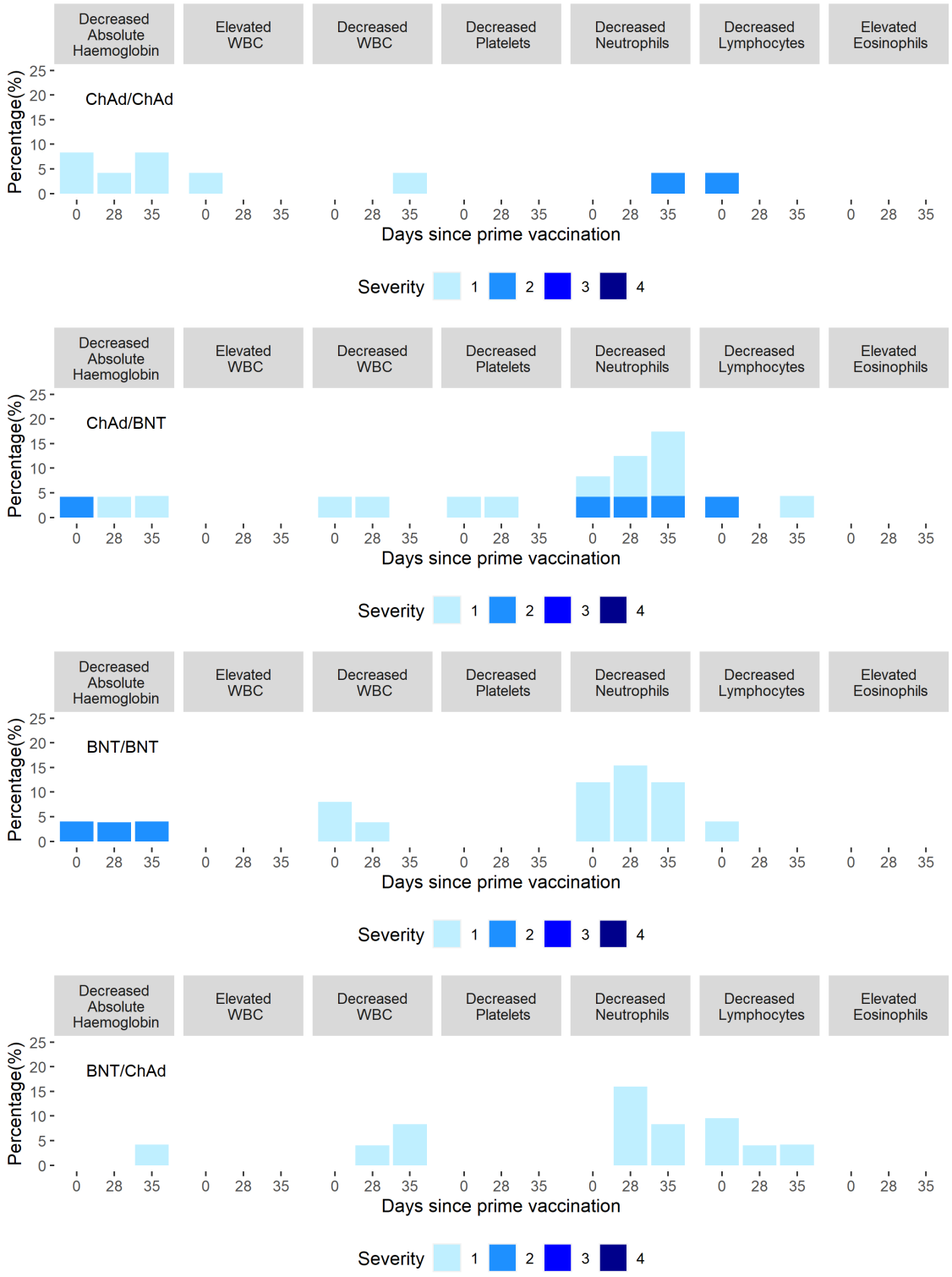
D



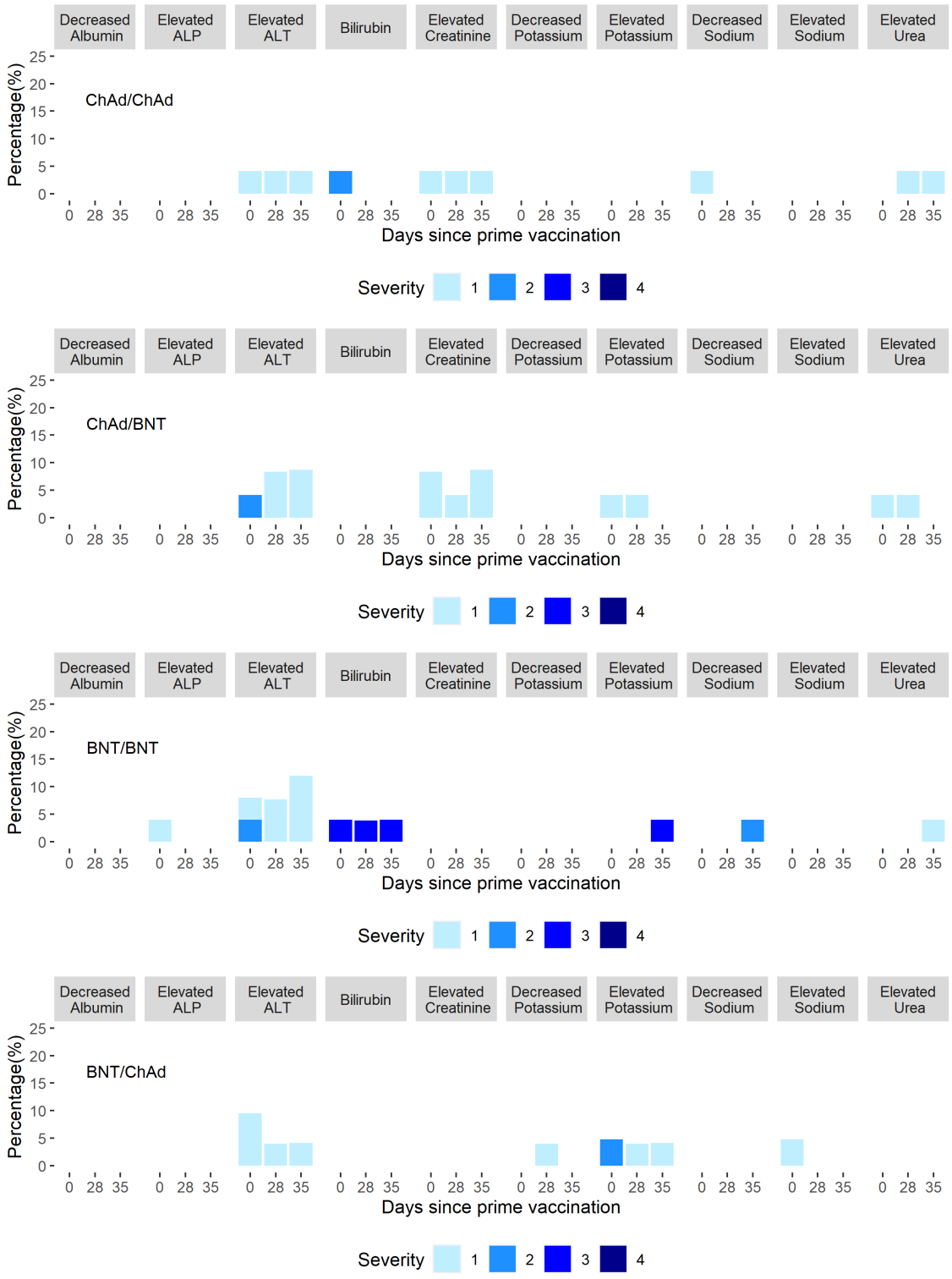
D0 is the day of prime/boost vaccination. Fever: Mild: 38·0°C to <38·5°C; moderate: 38·5°C to <39°C; severe: ≥39·0°C. Feverish: Self-reported feeling of feverishness. For systemic symptoms, grading was classified as: Mild – easily tolerated with no limitation on normal activity; Moderate – some limitation of daily activity; Severe – unable to perform normal daily activity

Supplementary Figure 4: Severity of haematology (A) and biochemistry (B) at day0 (prior to prime dose), day28 (prior to boost dose), and day 35 (7 days post boost dose) by study arm in the immunology cohort.

A



B



The details of grading are shown in supplementary table 1.

40 **Supplementary table 1: Modified FDA toxicity grading table for laboratory adverse events**

		Units	Lab range	Grade 1	Grade 2	Grade 3	Grade 4
Haematology							
Haemoglobin Absolute	Male	g/l	130-170	115-125	100-114	85-99	<85
Haemoglobin Absolute	Female	g/l	120-150	105-113	90-104	80-89	<80
Haemoglobin change from baseline			n/a	10-15	16-20	21-50	>50
White Blood Cells	Elevated	x 10^9/L	11.00	11.50-15.00	15.01-20.00	20.01-25.00	>25.00
White Blood Cells	Low	x 10^9/L	4.00	2.50-3.50	1.50-2.49	1.00-1.49	<1.00
Platelets	Low	x 10^9/L	150-400	125-140	100-124	25-99	<25
Neutrophils	Low	x 10^9/L	2.00-7.00	1.50-1.99	1.00-1.49	0.50-0.99	<0.50
Lymphocytes	Low	x 10^9/L	1.00-4.00	0.75-0.99	0.50-0.74	0.25-0.49	<0.25
Eosinophils	Elevated	x 10^9/L	0.02-0.50	0.65-1.50	1.51-5.00	>5.00	Hypereosinophilia
Biochemistry							
Sodium	Elevated	mmol/L	145	146-147	148-149	150-155	>155
Sodium	Low	mmol/L	135	132-134	130-131	125-129	<125
Potassium	Elevated	mmol/L	5.0	5.1-5.2	5.3-5.4	5.5-6.5	>6.5
Potassium	Low	mmol/L	3.5	3.2-3.3	3.1	2.5-3.0	<2.5
Urea	Elevated	mmol/L	2.5-7.4	8.2-9.3	9.4-11.0	>11.0	Requires dialysis
Creatinine	Elevated	μmol/L	49-104	1.1-1.5xULN 114-156	>1.5-3.0xULN 157-312	>3.0xULN >312	Requires dialysis
Bilirubin	Elevated Normal LFTs	μmol/L	0-21	1.1-1.5xULN 23-32	>1.5-2xULN 33-42	>2-3xULN 43-63	>3xULN >63
Bilirubin	Elevated Abnormal LFTs	μmol/L	0-21	1.1-1.25xULN 23-26	>1.25-1.5xULN 27-32	>1,5-1.75xULN 33-37	>1.75xULN >37
ALT	Elevated	IU/L	10-45	1.1-2.5xULN 49-112	>2.5-5xULN 113-225	>5-10xULN 226-450	>10xULN >450
ALP (Alkaline phosphatase)	Elevated	IU/L	30-130	1.1-2xULN 143-260	>2-3xULN 261-390	>3-10xULN 391-1300	>10xULN >1300
Albumin	Low	g/L	32-50	28-31	25-27	<25	-
CRP	Elevated	mg/L	0-10	11-30	31-100	101-200	>200

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43 **Supplementary Author List**

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