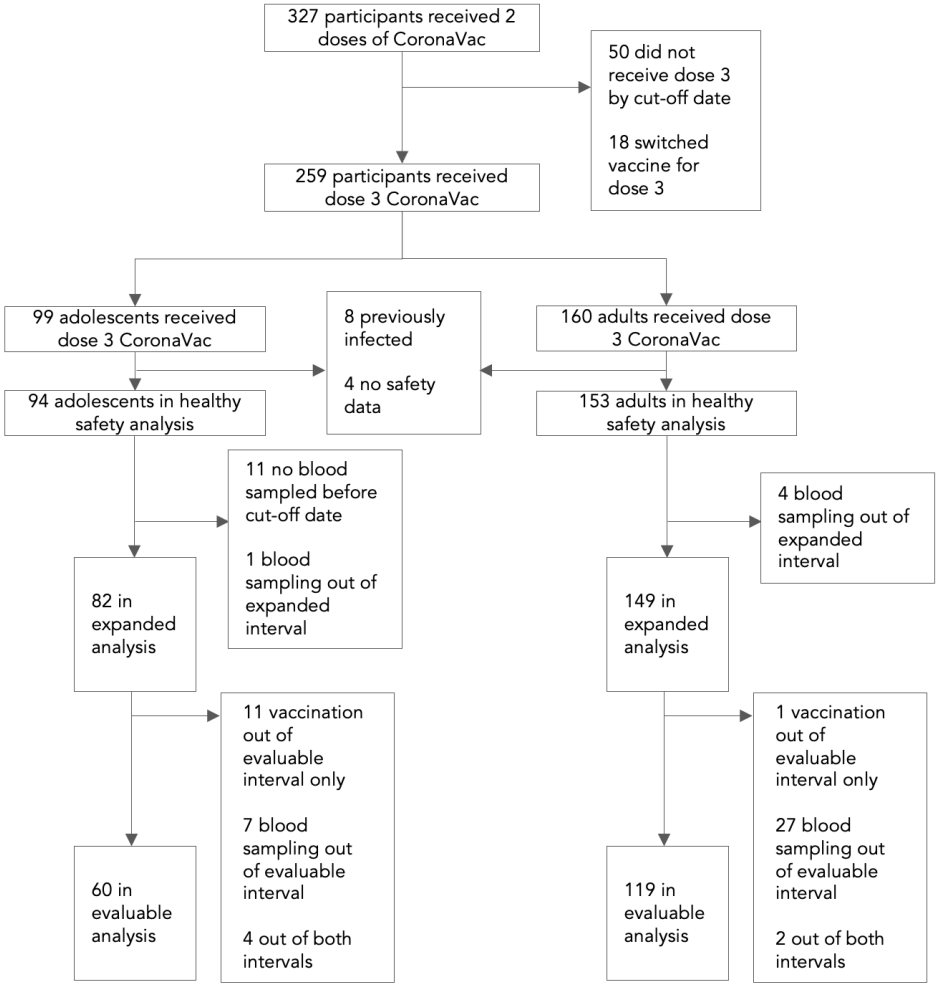
Tables and Figures

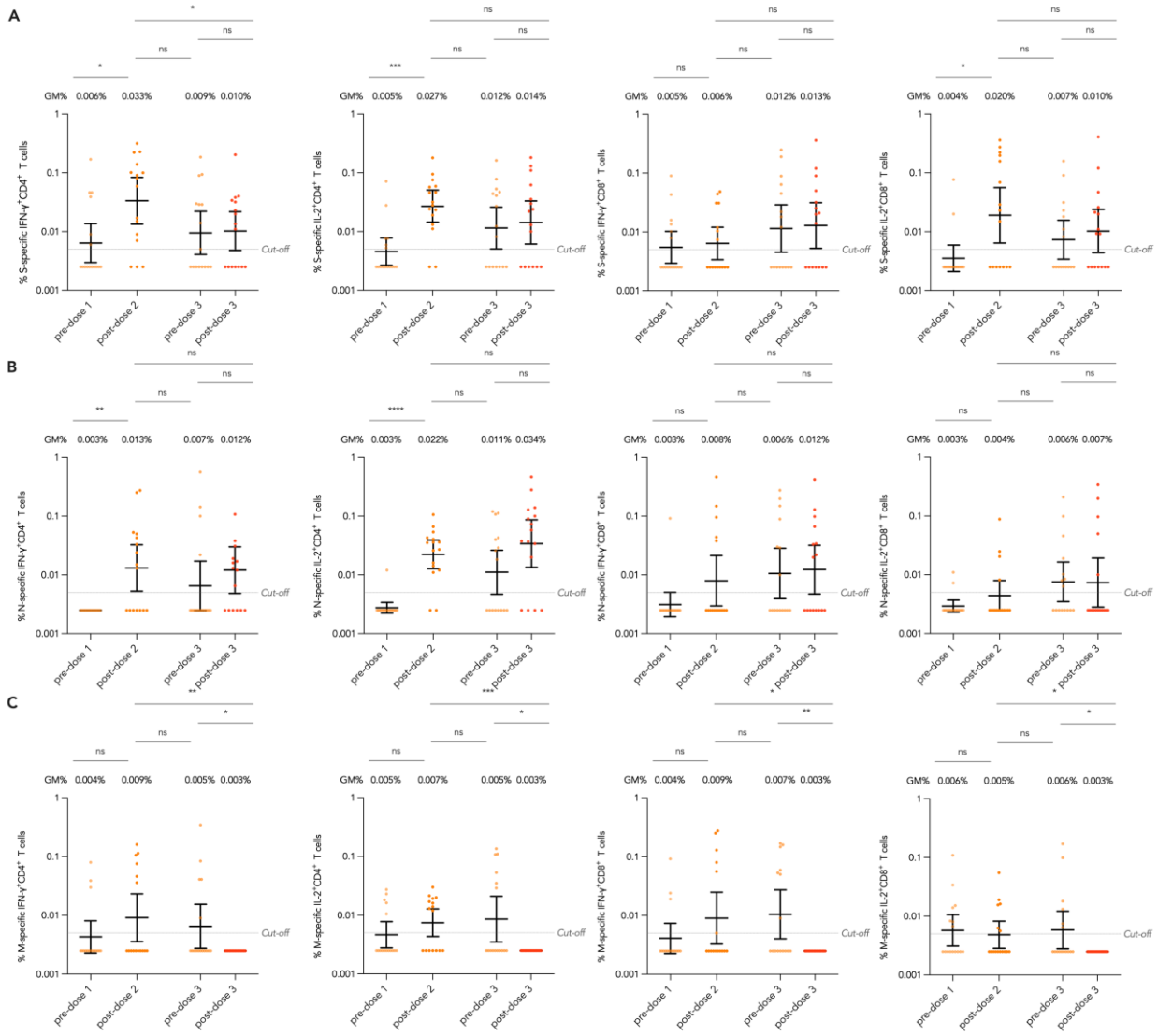
Supp. Tables 1-6

Supp. Figs. 1-5

Supp Fig 1 Study completion diagram



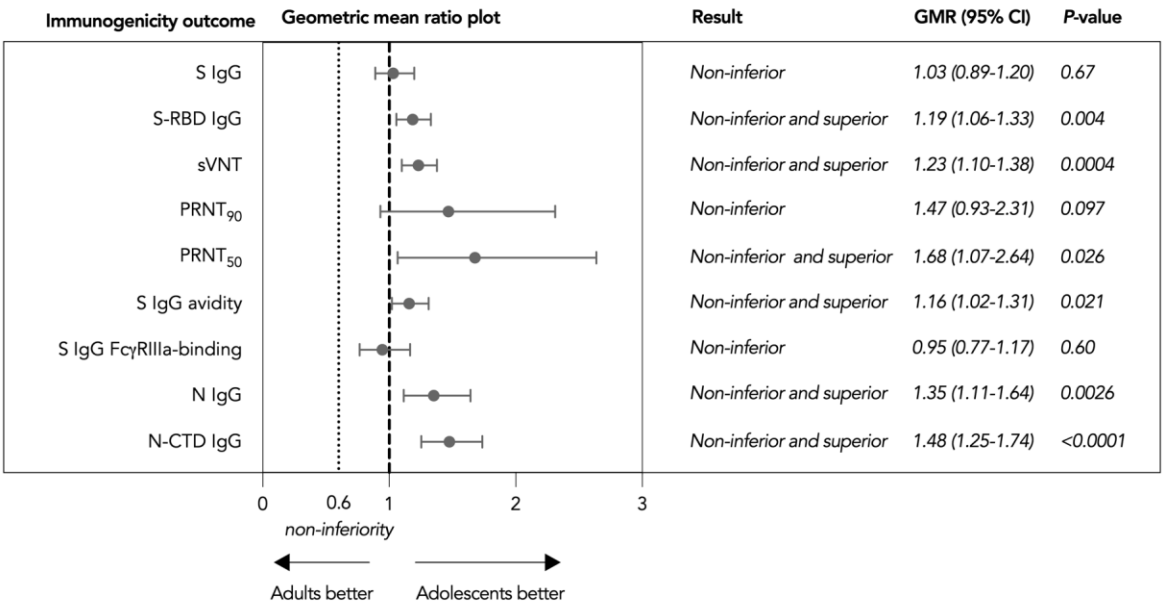
Supp Fig 2 Longitudinal interferon-γ (IFN-γ)$^+$ and interleukin-2 (IL-2)$^+$ CD4$^+$ and CD8$^+$ T cells against separate wild-type SARS-CoV-2 Spike (S), Nucleocapsid (N) and Membrane (M) peptide pools in evaluable adolescents receiving 3 doses of CoronaVac



Geometric means (GM) are shown with centre lines and stated above each column, with corresponding 95% confidence intervals shown by error bars. Samples from the same participant were paired across timepoints and compared with paired t test after natural

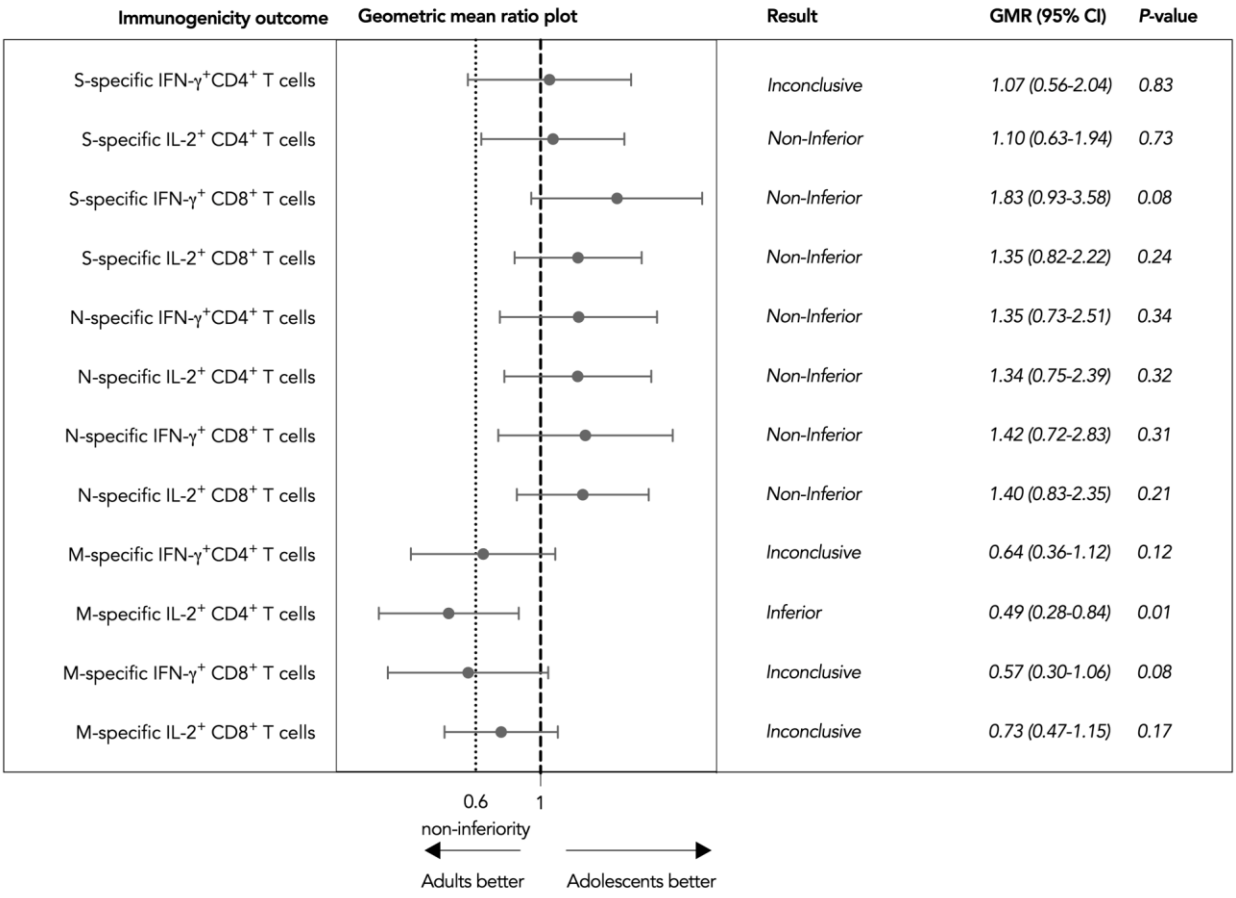
logarithmic transformation with p-values denoted (*, P<0.05; **, P<0.01; ***, P<0.001; ****, P<0.0001; ns, not significant). Cut-offs are drawn as grey lines.

Supp Fig 3 Non-inferiority hypothesis testing of humoral immunogenicity outcomes against wild-type SARS-CoV-2 after 3 doses of CoronaVac in expanded analysis population



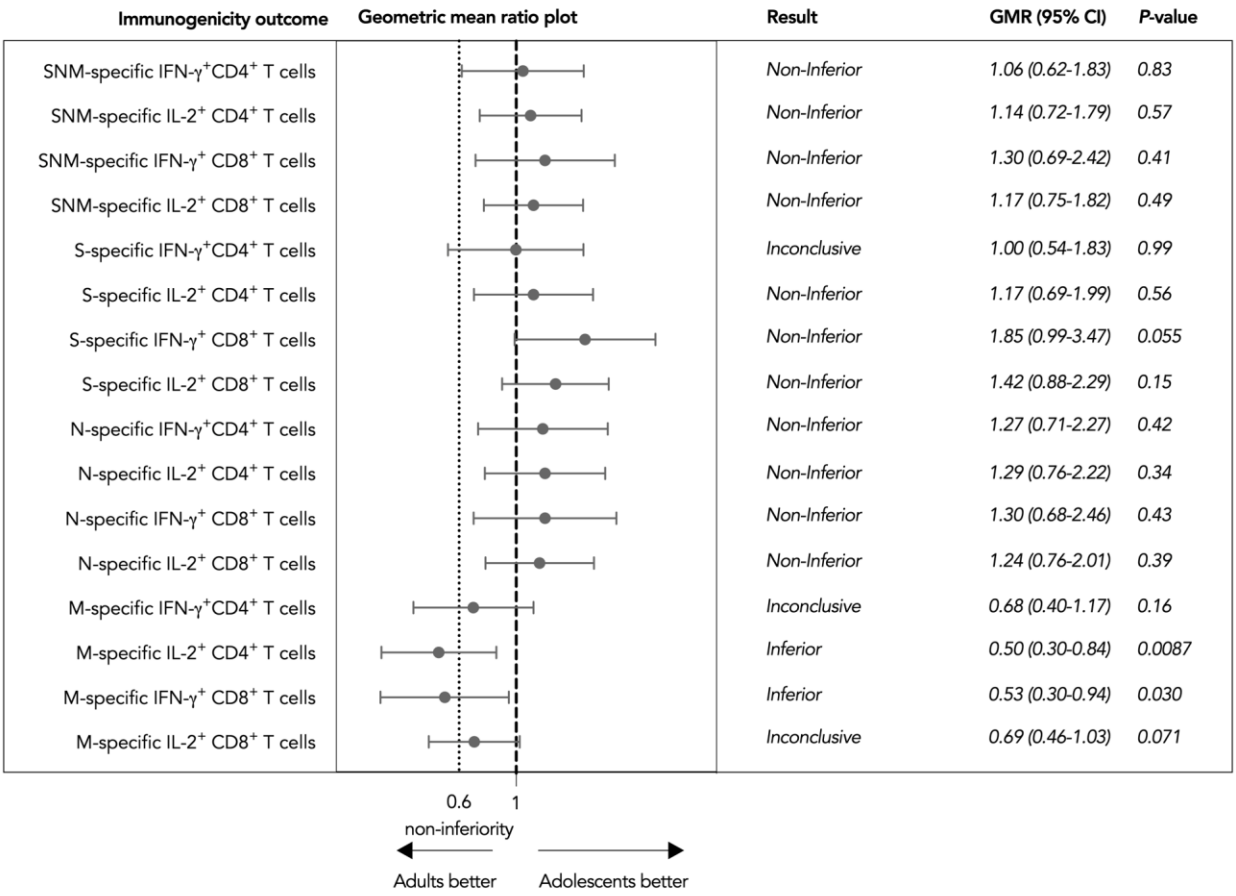
Non-inferiority tests of SARS-CoV-2 Spike (S) IgG, S-receptor binding domain (S-RBD) IgG, surrogate virus neutralization test (sVNT), plaque reduction neutralization test (PRNT), S IgG avidity, S IgG Fcγ receptor IIIa (FcγRIIIa)-binding, Nucleocapsid (N) IgG, and N-C-terminal domain (N-CTD) IgG were performed. Geometric mean ratios (GMR) and two-tailed 95% confidence intervals (CI) were plotted.

Supp Fig 4 Non-inferiority hypothesis testing of separate wild-type SARS-CoV-2 Spike (S), Nucleocapsid (N) and Membrane (M) peptide pools specific cellular immunogenicity outcomes after 3 doses of CoronaVac in evaluable analysis population



Non-inferiority testing of interferon-γ (IFN-γ)$^+$ and interleukin-2 (IL-2)$^+$ CD4$^+$ and CD8$^+$ T cells specific to separate S, N, and M peptide pools was performed. Geometric mean ratios (GMR) and two-tailed 95% confidence intervals (CI) were plotted.

Supp Fig 5 Non-inferiority hypothesis testing of cellular immunogenicity outcomes after 3 doses of CoronaVac in expanded analysis population



Non-inferiority testing of interferon-γ (IFN-γ)$^+$ and interleukin-2 (IL-2)$^+$ CD4$^+$ and CD8$^+$ T cells specific to total and separate Spike (S), Nucleocapsid (N), and Membrane (M) peptide pools was performed. Geometric mean ratios (GMR) and two-tailed 95% confidence intervals (CI) were plotted.

SUPPLEMENTARY TABLES

Supp Table 1. Participant disposition in the healthy safety population.	
Healthy adolescents	
Participants	94
Male sex	53 (56.4%)
Han Chinese	94 (100%)
Age (years)	14.2 (1.75)
Healthy adults	
Participants	153
Male sex	68 (44.4%)
Han Chinese	151 (98.7%)
Age (years)	48.1 (8.01)
Values are either count (%) or mean (standard deviations).	

Supp Table 2 Wild-type SARS-CoV-2 humoral immunogenicity outcomes after the third dose of CoronaVac in expanded analysis population

	Adolescents 3 doses	**Adults 3 doses**
S IgG on ELISA		
N	77	60
GM OD450 value (95% CI)	0.87 (0.78-0.97)	0.84 (0.76-0.94)
% positive (>/=LOD at 0.3)	97.4%, *P*>0.9999	98.3%
S-RBD IgG on ELISA		
N	82	149
GM OD450 value (95% CI)	1.69 (1.60-1.78)	1.42 (1.31-1.54)
% positive (>/=LOD at 0.5)	100%, *P*=0.16	96.6%
S-RBD ACE2-blocking antibody on sVNT		
N	82	149
GM % inhibition (95% CI)	84.0% (81.0-87.1%)	68.3% (62.9-74.1%)
% positive (>/=LOQ at 30%)	100%, *P*=0.0088	92.6%
Neutralizing antibody on PRNT		
N	60	25
GM $PRNT_{90}$ (95% CI)	17.8 (13.7-23.3)	12.1 (8.86-16.6)
% positive (>/=LOD at 10)	78.3%, *P=0.58*	72.0%
GM $PRNT_{50}$ (95% CI)	55.3 (43.2-70.7)	32.9 (22.1-49.2)
% positive (>/=LOD at 10)	100%, *P=0.29*	96.0%
S IgG avidity on ELISA		
N	75	59
GM avidity index (95% CI)	35.6% (32.5-39.1)	30.8% (28.4-33.4)
S IgG FcγRIIIa-binding on ELISA		
N	77	60
GM OD450 value (95% CI)	1.30 (1.14-1.49)	1.38 (1.16-1.64)
% positive (>/=LOD at 0.28)	97.4%, *P*=0.65	95.0%
N IgG on ELISA		
N	67	25
GM OD450 value (95% CI)	2.65 (2.42-2.90)	1.96 (1.58-2.43)
% positive (>/=LOD at 0.88)	97.0%, *P*=0.30	92.0%
N-CTD IgG on ELISA		
N	67	25
GM OD450 value (95% CI)	2.82 (2.61-3.05)	1.91 (1.61-2.28)
% positive (>/=LOD at 1.34)	97.0%, *P*=0.30	92.0%

S, spike protein; ELISA, enzyme-linked immunosorbent assay; GM, geometric mean; OD, optical density; LOD, limit of detection; LOQ, limit of quantification; CI, confidence interval; RBD, receptor-binding domain; ACE-2, angiotensin-converting enzyme-2; sVNT, surrogate virus neutralization test; PRNT, plaque reduction neutralization test; $PRNT_{90}$, 90% plaque reduction neutralization titre; $PRNT_{50}$, 50% plaque reduction neutralization titre; FcγRIIIa, Fc gamma receptor III-a; N, nucleocapsid protein; CTD, C-terminal domain. *P*-values compare the proportion of positive responses between adolescents and adults by Fisher's exact test.

Supp Table 3 Wild-type SARS-CoV-2 separate S, N and M peptide pools specific cellular immunogenicity outcomes after the third dose of CoronaVac in evaluable analysis population

	Adolescents 3 doses	**Adults 3 doses**
T cell responses		
S-specific T cell responses on flow cytometry		
N	59	118
GM % IFN-γ^+CD4$^+$ T cells (95% CI)	0.016% (0.010-0.027%)	0.015% (0.010-0.022%)
% positive (>/=cut-off at 0.005%)	57.6%, *P*=0.20	46.6%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.017% (0.011-0.027%)	0.015% (0.011-0.021%)
% positive (>/=cut-off at 0.005%)	61.0%, *P*=0.52	55.1%
GM % IFN-γ^+CD8$^+$ T cells (95% CI)	0.017% (0.010-0.031%)	0.009% (0.006-0.014%)
% positive (>/=cut-off at 0.005%)	49.2%, *P*=0.03	31.4%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.009% (0.006-0.015%)	0.007% (0.005-0.009%)
% positive (>/=cut-off at 0.005%)	47.5%, *P*=0.20	37.3%
N-specific T cell responses on flow cytometry		
N	58	118
GM % IFN-γ^+CD4$^+$ T cells (95% CI)	0.014% (0.008-0.024%)	0.010% (0.007-0.015%)
% positive (>/=cut-off at 0.005%)	53.5%, *P=0.11*	39.8%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.020% (0.012-0.033%)	0.015% (0.011-0.021%)
% positive (>/=cut-off at 0.005%)	60.3%, *P=0.42*	53.4%
GM % IFN-γ^+CD8$^+$ T cells (95% CI)	0.015% (0.008-0.028%)	0.010% (0.007-0.015%)
% positive (>/=cut-off at 0.005%)	41.4%, *P*=0.51	35.6%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.010% (0.006-0.016%)	0.007% (0.005-0.010%)
% positive (>/=cut-off at 0.005%)	41.4%, *P=0.62*	36.5%
M-specific T cell responses on flow cytometry		
N	59	118
GM % IFN-γ^+CD4$^+$ T cells (95% CI)	0.006% (0.004-0.009%)	0.009% (0.006-0.013%)
% positive (>/=cut-off at 0.005%)	23.7%, *P*=0.12	35.6%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.006% (0.004-0.009%)	0.012% (0.009-0.017%)
% positive (>/=cut-off at 0.005%)	25.4%, *P*=0.006	47.5%
GM % IFN-γ^+CD8$^+$ T cells (95% CI)	0.005% (0.003-0.008%)	0.009% (0.006-0.013%)
% positive (>/=cut-off at 0.005%)	13.6%, *P*=0.02	30.5%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.005% (0.003-0.006%)	0.006% (0.005-0.008%)
% positive (>/=cut-off at 0.005%)	18.6%, *P*=0.07	32.2%

S, Spike; N, Nucleocapsid; M, Membrane; GM, geometric mean; CI, confidence interval; IFN-γ, interferon-gamma; IL-2, interleukin-2. *P*-values compare the proportion of positive responses between adolescents and adults by Fisher's exact test.

Supp Table 4 Wild-type SARS-CoV-2 cellular immunogenicity outcomes after the third dose of CoronaVac in expanded analysis population		
	Adolescents 3 doses	**Adults 3 doses**
T cell responses		
Total S, N, M-specific T cell responses on flow cytometry		
N	69	122
GM % IFN-γ$^+$CD4$^+$ T cells (95% CI)	0.068% (0.045-0.104%)	0.064% (0.046-0.090%)
% positive (>/=cut-off at 0.01%)	73.9%, *P*=0.20	63.9%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.079% (0.055-0.112%)	0.069% (0.052-0.091%)
% positive (>/=cut-off at 0.01%)	81.2%, *P=0.29*	73.8%
GM % IFN-γ$^+$CD8$^+$ T cells (95% CI)	0.064% (0.038-0.107%)	0.050% (0.034-0.072%)
% positive (>/=cut-off at 0.01%)	59.4%, *P*=0.29	50.8%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.039% (0.026-0.057%)	0.033% (0.026-0.043%)
% positive (>/=cut-off at 0.01%)	60.9%, *P>0.9999*	60.7%
S-specific T cell responses on flow cytometry		
N	70	122
GM % IFN-γ$^+$CD4$^+$ T cells (95% CI)	0.015% (0.010-0.024%)	0.015% (0.011-0.022%)
% positive (>/=cut-off at 0.005%)	54.3%, *P*=0.45	47.5%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.018% (0.011-0.027%)	0.015% (0.011-0.021%)
% positive (>/=cut-off at 0.005%)	60.0%, *P*=0.65	55.7%
GM % IFN-γ$^+$CD8$^+$ T cells (95% CI)	0.017% (0.010-0.029%)	0.009% (0.006-0.013%)
% positive (>/=cut-off at 0.005%)	48.6%, *P*=0.02	31.2%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.010% (0.006-0.015%)	0.007% (0.005-0.009%)
% positive (>/=cut-off at 0.005%)	45.7%, *P*=0.22	36.1%
N-specific T cell responses on flow cytometry		
N	69	122
GM % IFN-γ$^+$CD4$^+$ T cells (95% CI)	0.013% (0.008-0.021%)	0.010% (0.007-0.015%)
% positive (>/=cut-off at 0.005%)	50.7%, *P*=0.17	40.2%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.019% (0.012-0.029%)	0.015% (0.011-0.020%)
% positive (>/=cut-off at 0.005%)	60.9%, *P=0.36*	53.3%
GM % IFN-γ$^+$CD8$^+$ T cells (95% CI)	0.013% (0.008-0.023%)	0.010% (0.007-0.015%)
% positive (>/=cut-off at 0.005%)	39.1%, *P*=0.64	35.3%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.009% (0.006-0.014%)	0.007% (0.005-0.010%)
% positive (>/=cut-off at 0.005%)	37.7%, *P=0.88*	36.1%
M-specific T cell responses on flow cytometry		
N	70	122
GM % IFN-γ$^+$CD4$^+$ T cells (95% CI)	0.006% (0.004-0.009%)	0.009% (0.007-0.013%)
% positive (>/=cut-off at 0.005%)	25.7%, *P*=0.15	36.9%
GM % IL-2$^+$CD4$^+$ T cells (95% CI)	0.006% (0.004-0.009%)	0.012% (0.009-0.017%)
% positive (>/=cut-off at 0.005%)	27.1%, *P*=0.006	48.4%
GM % IFN-γ$^+$CD8$^+$ T cells (95% CI)	0.005% (0.003-0.007%)	0.009% (0.006-0.012%)
% positive (>/=cut-off at 0.005%)	11.4%, *P*=0.004	29.5%
GM % IL-2$^+$CD8$^+$ T cells (95% CI)	0.004% (0.003-0.006%)	0.006% (0.005-0.008%)
% positive (>/=cut-off at 0.005%)	15.7%, *P*=0.02	31.2%
S, Spike; N, Nucleocapsid; M, Membrane; GM, geometric mean; CI, confidence interval; IFN-γ, interferon-gamma; IL-2, interleukin-2. *P*-values compare the proportion of positive responses between adolescents and adults by Fisher's exact test.		

Supp Table 5. Unsolicited adverse events within 28 days of vaccination in adolescent healthy safety population.	
Summary of adverse events and severe adverse events	
Any adverse event	1 (0.011)
Grade 1	1 (0.011)
Grade 2	0 (0.000)
Grade 3	0 (0.000)
Severe	0 (0.000)
N, total number of participants in adolescent healthy safety population. Data are number of events (events per participant).	

Supp Table 6. Peptide sequences of SARS-CoV-2 N and M BA.1 and wild-type reference mutation pools		
	BA.1 mutation pool	**Wild-type reference pool**
SARS-CoV-2 Nucleocapsid protein		
P13L	GPQNQRNAPRITFGG	GPQNQRNALRITFGG
31_33delERS	GSNQNGERSGARSKQ	GSNQNGGARSKQ
203_204delRGinsKR	STPGSSRGTSPARMA	STPGSSKRTSPARMA
SARS-CoV-2 Membrane protein		
D3G	MADSNGTITVEELKK	MAGSNGTITVEELKK
Q19E	LLEQWNLVIGFLFLT	LLEEWNLVIGFLFLT
A63T	WLLWPVTLACFVLAA	WLLWPVTLTCFVLAA