

Supplementary Material

Hesitancy, reactogenicity and immunogenicity of the mRNA and whole-virus inactivated COVID-19 vaccines in pediatric neuromuscular diseases

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1 Supplementary Data

Survey questions on COVID-19 vaccine hesitancy

No.	Questions	Answer
1	Patients consent	Agree / Not agree
2	Did your father receive COVID-19 vaccine?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
3	Did your mother receive COVID-19 vaccine?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
4	Did any other family member receive COVID-19 vaccine?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
5	Do you need to use wheelchair?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
6	Do you need to use Ryle's tube or PEG tube feeding?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
7	Do you need to use ventilator?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
8	Have you used spinal brace / performed spinal surgery?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
9	English full name	
10	Age (years)	
11	Gender	<input type="radio"/> Male (1) <input type="radio"/> Female (2)
12	Did you get the flu vaccine last year?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
13	Have you received the flu vaccine every year in the past three years?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
14	Have you been diagnosed with COVID-19?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
15	Have your family members or classmates been diagnosed with COVID-19 disease?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
16	Have you ever been classified as a close contact of COVID-19 that needs to undergo compulsory quarantine?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
17	Have you ever been required to compulsorily test the COVID-19 virus?	<input type="radio"/> Yes (1) <input type="radio"/> No (2)
18	What COVID-19 vaccine have you or do you plan to receive?	<input type="radio"/> BNT162b2 (1) <input type="radio"/> Coronavac (2)

		o Undecided (3)
19	Reasons to have vaccination?	<input type="checkbox"/> I think I am high risk group of COVID-19 (1) <input type="checkbox"/> I am worried that I will be infected (2) <input type="checkbox"/> I want to protect my family (3) <input type="checkbox"/> I want to attend religious ceremonies (4) <input type="checkbox"/> I want to travel (5) <input type="checkbox"/> I wish to return to my life before COVID-19 pandemic (6) <input type="checkbox"/> I am tired of the social distancing policies (7) <input type="checkbox"/> Because people around me received vaccination (8) <input type="checkbox"/> I want to resume full scale face-to-face teaching. (9) <input type="checkbox"/> I want to play sports at school with friends or in a competition without wearing mask (10) <input type="checkbox"/> I want to meet my family as I am currently living at special schools (11) <input type="checkbox"/> I want to play music safely (e.g. wind instruments, band, choir) (12) <input type="checkbox"/> I want to participate in large-scale events (e.g. open days, joint school events and Christmas balls) without wearing mask (13) <input type="checkbox"/> I want to study overseas (14) <input type="checkbox"/> I want to join study tours (15) <input type="checkbox"/> Socialize with large groups of friends, (e.g. dining out, karaoke, party room) (16) <input type="checkbox"/> Others (please specify): (17)
20	Reasons for not to have vaccination?	<input type="checkbox"/> Not allowed by my parents (1) <input type="checkbox"/> Medically not suitable (e.g. severe allergies, uncontrolled diabetes mellitus) (2) <input type="checkbox"/> I am concerned about its safety (3) <input type="checkbox"/> I am concerned about its efficacy (4) <input type="checkbox"/> I am concerned that receiving the vaccine will violate the rules of my religion (5) <input type="checkbox"/> I am concerned that I will have a higher chance to encounter adverse effects when compared to healthy individuals (6) <input type="checkbox"/> I am concerned that the vaccination would affect my current

treatment (7)

- COVID-19 is just a mild disease (8)
- I do not know where to receive the vaccines (9)
- I am difficult to access the vaccine centres (10)
- I do not know whether I should receive the vaccine (11)
- The community vaccine centres are inconvenient (12)
- I do not know which type of COVID-19 vaccine I should receive (13)
- Facemask and social distancing are sufficient (14)
- Depends on the progress of the pandemic (15)
- I am against vaccination (16)
- Others (please specify): (17)

2 Supplementary Tables and Figures

2.1 Supplementary Tables

Supplementary Table 1: Demographic and clinical characteristics of the patients with neuromuscular diseases in COVID-19 vaccine hesitancy survey arm of the study

	N/mean	%/SD
Demographics		
Age (years)	13.8	3.4
Female	18	43.9
Breakdown of NMDs		
Spinal muscular atrophy	18	43.9
5q type I	2	4.9
5q type II	10	24.4
5q type III	5	12.2
Non-5q spinal muscular atrophy	1	2.4
Dystrophinopathy	6	14.6
Duchenne muscular dystrophy	4	9.8
Becker muscular dystrophy	2	4.9
Congenital myopathy	5	12.2
Congenital muscular dystrophy	4	9.8
Peripheral neuropathies	2	4.9
Facioscapulohumeral muscular dystrophy	2	4.9
Myotonic disorder	2	4.9
Other NMDs [^]	2	4.9
Physical conditions		
Wheelchair-mobile	22	53.7
Nasogastric tube or PEG tube feeding use	4	9.8
Ventilator support	14	34.1
Using spinal brace or had spinal surgery	8	19.5

NMDs=neuromuscular diseases, PEG=percutaneous endoscopic gastrostomy, SD=standard deviation, N=numbers

[^]Congenital myasthenic syndrome and ocular myasthenia gravis

Supplementary Table 2: Intention of COVID-19 vaccination in patients with neuromuscular diseases in January and April 2022

Intention of COVID-19 vaccination	January 2022	April 2022	<i>p</i> -values
Have vaccinated/ planning to vaccinate	30 (73.2)	40 (97.6)	
Do not plan to vaccinate	11 (26.8)	1 (2.4)	
Total	41	41	0.003**
Will continue to receive future boosters, if any?			
Yes	26 (63.4)	30 (73.2)	
No	15 (36.6)	11 (26.8)	
Total	41	41	0.477

Data presented as number (%)

** $p < 0.01$

Supplementary Table 3: Preference on COVID-19 vaccines in patients with neuromuscular diseases

Types of vaccines	January 2022			April 2022		
	Planning to receive	Already vaccinated	Total	Planning to receive	Already vaccinated	Total
BNT162b2	5 (33.3)	14 (93.3)	19 (46.3)	3 (100.0)	17 (45.9)	20 (48.8)
CoronaVac	8 (53.3)	1 (6.7)	9 (22.0)	0 (0.0)	20 (54.1)	20 (48.8)
Undecided	2 (13.3)	0 (0.0)	2 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)
Do not plan to vaccinate	-	-	11 (26.8)	-	-	1 (2.4)
Total	15	15	41	3	37	41

Data presented as number (%)

Supplementary Table 4: Demographic and clinical characteristics of the patients with neuromuscular diseases in the COVID-19 vaccine reactogenicity and immunogenicity arm of the study

Patient	NMD type	Age (years)	Sex	Ambulatory status	Treatment	Dosage	Dose 1 & 2	Dose 3	COVID-19 infection
1	CIDP	14.6	Male	Independent walker	IVIG	2 g/kg/3months	BNT162b2	N/A	N
2	DMD	12.2	Male	Late ambulatory	Prednisolone	0.42 mg/kg/day	BNT162b2	BNT162b2	N
3	DMD	13.7	Male	Wheelchair mobile	Deflazacort	0.64 mg/kg/day	BNT162b2	N/A	N
4	CM	11.9	Female	Independent walker	N/A	N/A	BNT162b2	N/A	Y, before 1 st dose
5	SMA	10.5	Male	Wheelchair mobile	Risdiplam	0.13 mg/kg/day	BNT162b2	N/A	N
6	SMA	8.8	Male	Independent walker	Nusinersen	N/A	BNT162b2	BNT162b2	N
7	DMD	13.1	Male	Late ambulatory	Prednisolone	0.61 mg/kg/day	CoronaVac	CoronaVac	N
8	DMD	14.5	Male	Wheelchair mobile	Prednisolone	0.30 mg/kg/day	CoronaVac	N/A	N
9	DMD	4.7	Male	Independent walker	Deflazacort	0.64 mg/kg/day	CoronaVac	CoronaVac	N
10	SMA	8.4	Female	Wheelchair mobile	Nusinersen	0.56 mg/kg/day	CoronaVac	N/A	Y, after 1 st dose
11	SMA	5.8	Male	Wheelchair mobile	Nusinersen	0.56 mg/kg/day	CoronaVac	CoronaVac	N
12 [^]	CM	7.4	Female	Wheelchair mobile	N/A	N/A	CoronaVac	BNT162b2	N
13	DMD	6.6	Male	Late ambulatory	Deflazacort	0.74 mg/kg/day	CoronaVac	CoronaVac	N
14	SMA	2.9	Female	Wheelchair mobile	Nusinersen	0.83 mg/kg/4 months	CoronaVac	CoronaVac	N
15	DMD	11.3	Male	Wheelchair mobile	Deflazacort	0.67 mg/kg/day	CoronaVac	N/A	Y, before 1 st dose
16	MD	6.7	Female	Independent walker	Melatonin	5.45 mg/kg/day	CoronaVac	CoronaVac	N
17	DMD	21.0	Male	Wheelchair mobile	Prednisolone	0.49 mg/kg/day	CoronaVac	CoronaVac	N
18*	SMA	10.3	Male	Independent walker	Nusinersen	0.38 mg/kg/4months	CoronaVac	N/A	N
19*	DMD	6.0	Male	Independent walker	Prednisolone	0.72 mg/kg/day	CoronaVac	N/A	N
20*	SMA	12.8	Female	Wheelchair mobile	Nusinersen	0.48 mg/kg/4months	CoronaVac	N/A	N
21*	BMD	10.5	Male	Independent walker	N/A	N/A	CoronaVac	CoronaVac	N
22*	CM	14.0	Female	Late ambulatory	N/A	N/A	CoronaVac	CoronaVac	N

BMD=Becker muscular dystrophy, CIDP=chronic inflammatory demyelinating polyneuropathy, CM=congenital myopathy, DMD=Duchenne muscular dystrophy, IVIG=intravenous immunoglobulins, MD=myotonic disorder, N/A=not applicable, SMA=spinal muscular atrophy

[^]Blood samples for immunogenicity assay before the first and after the third dose of COVID-19 vaccination

*Blood samples for immunogenicity assay after the second dose of COVID-19 vaccination only

Supplementary Table 5: Comparison of age between patients with neuromuscular diseases (NMDs) and healthy children and adolescents (Healthy)

Dosage	B	C	BB	CC	BBB	CCC	CCB
Age							
NMD (N)	11.3 (5)	13.1 (7)	11.3 (5)	11.9 (13)	10.9 (2)	6.68 (9)	8.44 (1)
Healthy (N)	13.9 (107)	14.0 (173)	14.0 (104)	14.0 (173)	13.7 (28)	14.1 (60)	10.8 (6)
<i>p</i> -value	0.008**	0.061	0.011*	<0.001***	0.005**	0.003**	N/A

Data presented as median (number of patients in each group)

Healthy=healthy children and adolescents, NMDs=patients with neuromuscular diseases

B, 1 dose of BNT162b2; BB, 2 doses of BNT162b2; C, 1 dose of CoronaVac; CC, 2 doses of CoronaVac; BBB, 3 dose of BNT162b2; CCC, 3 doses of CoronaVac; CCB, 2 doses of CoronaVac and 1 dose of BNT162b2.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Supplementary Table 6: Comparison of reactogenicity for patients with neuromuscular diseases by age

Dosage	B	C	BB	CC	BBB	CCC	CCB
Pain at injection site							
2-11 years old	2 (67.7)	5 (62.5)	0 (0)	6 (75.0)	0 (0)	4 (66.7)	1 (100)
12-21 years old	3 (100)	0 (0)	3 (100)	0 (0)	1 (100)	1 (33.3)	0 (0)
<i>p</i> -value	1.000	0.182	0.100	0.061	1.000	0.524	1.000
Swelling, erythema and induration at injection site							
2-11 years old	0 (0)	2 (25.0)	0 (0)	1 (12.5)	0 (0)	1 (16.7)	0 (0)
12-21 years old	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<i>p</i> -value	N/A	1.000	N/A	1.000	N/A	1.000	N/A
Headache							
2-11 years old	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)
12-21 years old	0 (0)	1 (33.3)	2 (66.7)	1 (33.3)	1 (100)	2 (66.7)	0 (0)
<i>p</i> -value	N/A	0.273	1.000	0.273	1.000	0.083	N/A
Fatigue							
2-11 years old	0 (0)	2 (25.0)	1 (33.3)	4 (50.0)	0 (0)	2 (33.3)	1 (100)
12-21 years old	3 (100)	2 (66.7)	3 (100)	1 (33.3)	0 (0)	3 (100)	0 (0)
<i>p</i> -value	0.100	0.491	0.400	1.000	N/A	0.167	N/A
Myalgia							
2-11 years old	0 (0)	2 (25.0)	0 (0)	3 (37.5)	0 (0)	2 (33.3)	0 (0)
12-21 years old	2 (66.7)	1 (33.3)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)
<i>p</i> -value	0.400	1.000	1.000	0.491	N/A	0.500	N/A
Fever							
2-11 years old	0 (0)	2 (25.0)	1 (33.3)	1 (12.5)	0 (0)	0 (0)	0 (0)
12-21 years old	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
<i>p</i> -value	N/A	1.000	1.000	1.000	1.000	N/A	N/A
Abdominal pain							
2-11 years old	0 (0)	1 (12.5)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)
12-21 years old	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<i>p</i> -value	N/A	1.000	N/A	1.000	N/A	N/A	N/A
Antipyretic use							
2-11 years old	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
12-21 years old	1 (33.3)	0 (0)	2 (66.7)	0 (0)	1 (100)	0 (0)	0 (0)
<i>p</i> -value	1.000	N/A	0.670	N/A	1.000	N/A	N/A

Data presented as number (%)

No patient reported any of the following symptoms within 7 days after vaccination: pruritis at injection site, reduced appetite or sore throat.

One patient reported any of the following symptoms within 7 days after vaccination: nausea, diarrhea, vomiting, arthralgia, cough, chills, rhinorrhea, nasal congestion

B, 1 dose of BNT162b2; BB, 2 doses of BNT162b2; C, 1 dose of CoronaVac; CC, 2 doses of CoronaVac; BBB, 3 dose of BNT162b2; CCC, 3 doses of CoronaVac; CCB, 2 doses of CoronaVac and 1 dose of BNT162b2.

Supplementary Table 7: Comparison of immunogenicity for patients with neuromuscular diseases by corticosteroids use

Dosage	B	C	BB	CC	BBB	CCC	CCB
ELISA OD450							
CS user median (N)	0.87 (2)	0.25 (5)	1.82 (2)	1.82 (5)	3.04 (1)	2.26 (4)	N/A
Non-CS user median (N)	1.35 (3)	1.30 (2)	2.58 (3)	2.37 (8)	3.19 (1)	3.04 (5)	3.42 (1)
<i>p</i> -value	0.800	0.238	0.20	0.020*	N/A	0.111	N/A
sVNT % inhibition							
CS user median (N)	55.3 (2)	15.0 (5)	93.9 (2)	84.5 (5)	97.2 (1)	83.1 (4)	N/A
Non-CS user median (N)	50.5 (3)	37.6 (2)	96.3 (3)	89.3 (8)	97.3 (1)	95.7 (5)	97.2 (1)
<i>p</i> -value	0.800	0.857	0.80	0.354	N/A	0.191	N/A

Data presented as median (number of patients in group)

CS=corticosteroids, ELISA=enzyme linked immunosorbent assay, N/A=Not applicable,

OD=optical density, sVNT=surrogate virus neutralization test

B, 1 dose of BNT162b2; BB, 2 doses of BNT162b2; C, 1 dose of CoronaVac; CC, 2 doses of CoronaVac; BBB, 3 dose of BNT162b2; CCC, 3 doses of CoronaVac; CCB, 2 doses of CoronaVac and 1 dose of BNT162b2.

**p*<0.05

Supplementary Table 8: Comparison of immunogenicity for patients with neuromuscular diseases by disease subtypes

Dosage		B	C	BB	CC	BBB	CCC	CCB
ELISA OD450								
	DMD	0.87 (2)	0.25 (5)	1.82 (2)	1.82 (6)	3.04 (1)	2.26 (4)	N/A
	SMA	1.44 (2)	1.52 (1)	2.74 (2)	2.54 (4)	3.25 (1)	3.39 (2)	N/A
	CM	N/A	N/A	N/A	2.03 (1)	N/A	3.04 (1)	3.42 (1)
	BMD	N/A	N/A	N/A	1.97 (1)	N/A	2.52 (1)	N/A
	CIDP	0.56 (1)	N/A	2.19 (1)	N/A	N/A	N/A	N/A
	MD	N/A	1.08 (1)	N/A	2.43 (1)	N/A	4.31 (1)	N/A
	<i>p</i> -value	0.200	0.238	0.200	0.015*	N/A	0.20	N/A
sVNT % inhibition								
	DMD	55.3 (2)	15.0 (5)	93.8 (2)	74.4 (6)	97.2 (1)	83.1 (4)	N/A
	SMA	45.9 (2)	43.0 (1)	95.3 (2)	91.1 (4)	97.3 (1)	95.4 (2)	N/A
	CM	N/A	N/A	N/A	64.3 (1)	N/A	95.7 (1)	97.2 (1)
	BMD	N/A	N/A	N/A	80.9 (1)	N/A	86.0 (1)	N/A
	CIDP	66.7 (1)	N/A	97.2 (1)	N/A	N/A	N/A	N/A
	MD	N/A	32.1 (1)	N/A	97.0 (1)	N/A	97.3 (1)	N/A
	<i>p</i> -value	0.200	1.000	0.600	0.033*	N/A	0.470	N/A

Data presented as median (number of patients in each group)

No patient reported any of the following symptoms within 7 days after vaccination: pruritis at injection site, reduced appetite or sore throat.

BMD=Becker muscular dystrophy, CIDP=chronic inflammatory demyelinating polyneuropathy, CM=congenital myopathy, DMD=Duchenne muscular dystrophy, ELISA=enzyme linked immunosorbent assay, MD=myotonic disorder, N/A=not applicable, OD=optical density, SMA=spinal muscular atrophy, sVNT=surrogate virus neutralization test

B, 1 dose of BNT162b2; BB, 2 doses of BNT162b2; C, 1 dose of CoronaVac; CC, 2 doses of CoronaVac; BBB, 3 dose of BNT162b2; CCC, 3 doses of CoronaVac; CCB, 2 doses of CoronaVac and 1 dose of BNT162b2.

* $p < 0.05$

Supplementary Table 9: Immunogenicity of patients with neuromuscular diseases who had COVID-19 infection

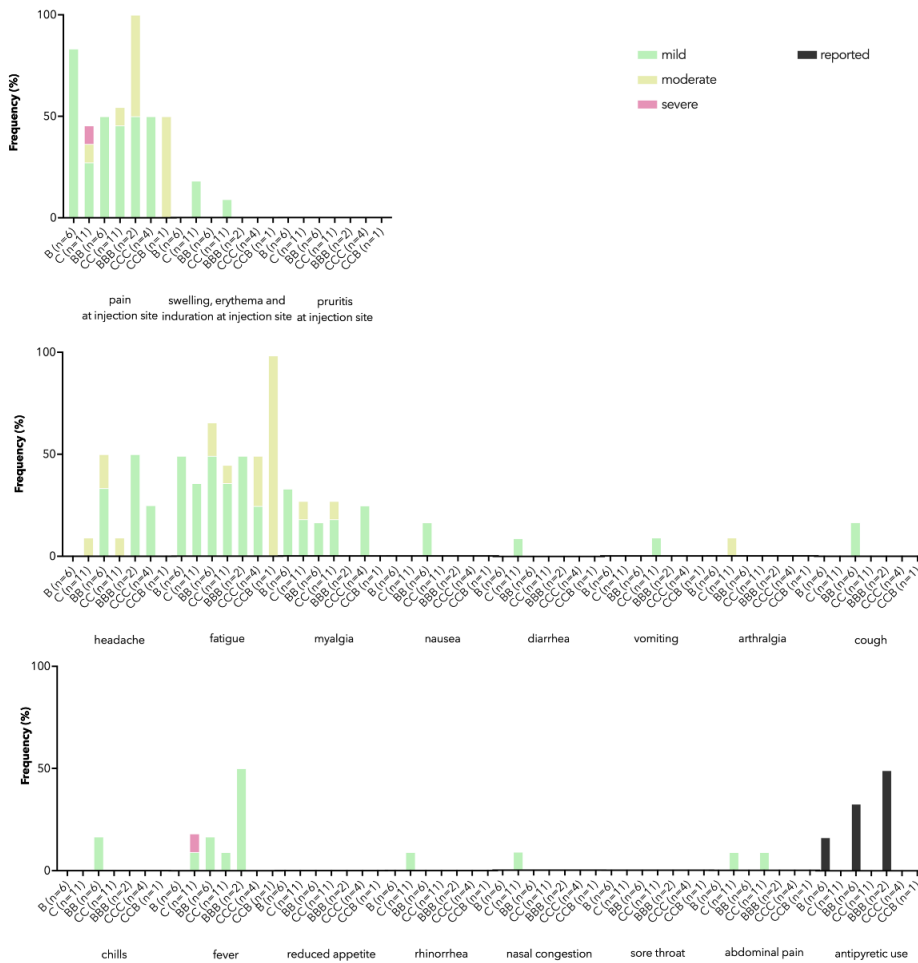
Patient No.	Vaccine	Age	Sex	COVID-19 history	Pre-dose 1 ELISA OD450	Pre-dose 1 sVNT % inhibition	Dose 1 ELISA OD450	Dose 1 sVNT % inhibition	Dose 2 ELISA OD450	Dose 2 sVNT % inhibition
4	BB	11.9	F	6 weeks before dose 1	0.25	15	2.56	86.6	3.14	97.8
10	CC	8.4	F	3 weeks after dose 1	N/A	N/A	1.14	36.1	2.98	92.4
15	CC	11.3	M	1 month before dose 1	0.51	15	0.53	15	1.34	15

These patients were excluded from the main immunogenicity analyses.

ELISA=enzyme linked immunosorbent assay, OD=optical density, sVNT=surrogate virus neutralization test

BB, 2 doses of BNT162b2; CC, 2 doses of CoronaVac

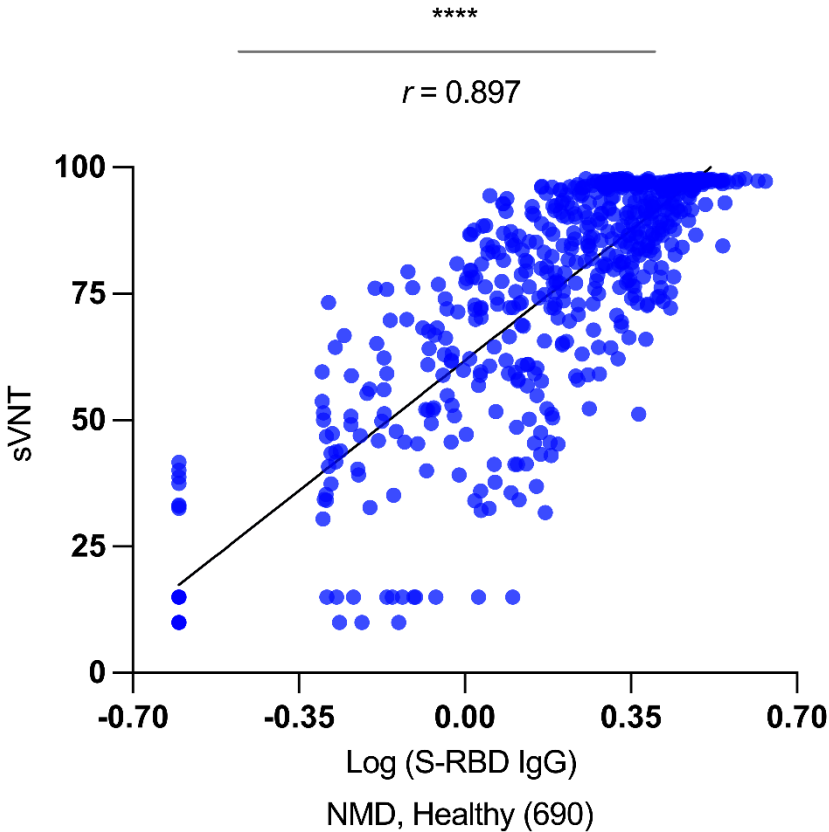
2.2 Supplementary Figures



Supplementary Figure 1: Reactogenicity for patients with neuromuscular diseases

Pain at the injection site (BB: 3 of 6, 50.0%, 6 of 11, CC: 54.5%), fatigue (BB: 4 of 6, 66.7%, 5 of 11, CC: 45.5%) and myalgia (BB: 1 of 6, 16.7%, 3 of 11, CC: 27.3%) were the commonest ARs in NMD patients. Most ARs were mild (75.5%, n=71/94). Adverse reactions were reported by the patients for 7 days after vaccination. No patient reported any of the following symptoms within 7 days after vaccination: pruritis at injection site, reduced appetite or sore throat. There were no vaccine-related severe adverse events, such as hospitalizations, life-threatening complications, disabilities or deaths. B, 1 dose of BNT162b2; BB, 2 doses of BNT162b2; C, 1 dose of CoronaVac; CC, 2 doses of CoronaVac; BBB, 3 dose of BNT162b2; CCC, 3 doses of CoronaVac; CCB, 2 doses of CoronaVac and 1 dose of BNT162b2.

Supplementary Figure 2: Correlation between the enzyme linked immunosorbent assay (ELISA) after \log_{10} transformation and the surrogate virus neutralization test (sVNT) after BNT162b2 and CoronaVac in patients with neuromuscular diseases (NMDs) (n=42) and healthy children and adolescents (Healthy) (n=648); total n=690.



The Pearson correlation coefficient was 0.897 ($p < 0.0001$). ELISA OD450 and sVNT% inhibition were determined before the first dose, second dose, 7-43 days after the second dose and 14-49 days after the third dose of BNT162b2 or CoronaVac. Three patients with neuromuscular diseases who had COVID-19 infection were excluded from the correlation analysis. ELISA=enzyme linked immunosorbent assay, Healthy=healthy children and adolescents, NMDs=patients with neuromuscular diseases, S-RBD=SARS-CoV-2 S receptor-binding domain, sVNT=surrogate virus neutralization test **** $p < 0.0001$