

Table S1. Characteristics of children with acute COVID-19 across their clinical spectrum.

	Acute				P
	Asymptomatic n= 84	Mild n= 358	Moderate n= 100	Severe n= 8	
Age, years, median (range)	6.0 (0.6-13.0)	2.0 (0.6-9.2)	5.0 (1.4-10.0)	1.0 (0.3-3.6)	
<1 y, n (%)	29 (35)	135 (38)	18 (18)	4 (50)	* Mild vs Mod
1-5 y, n (%)	13 (15)	91 (25)	39 (39)	3 (38)	*Asy, Mild vs Mod
6-10 y, n (%)	14 (17)	45 (13)	17 (17)	0	
>10 y, n (%)	28 (33)	87 (24)	26 (26)	1 (12)	
Sex, n (%)					
Female	43 (51)	171 (48)	47 (47)	6 (75)	
Male	41 (49)	187 (52)	53 (53)	2 (25)	
Days after symptom onset (range) ^a	N/A	1 (1-3)	2 (1-3)	1 (1-2)	* Asy vs Mild, Mod
SARS-CoV-2 IgG positive, n (%) ^b	31 (37)	82 (23)	26 (26)	0	**Asy vs Mild, Sev
SARS-CoV-2 IgM positive, n (%) ^b	38 (45)	115 (32)	38 (38)	0	*Asy vs Mild, Sev; *Mod vs Sev
Comorbidities, n (%)					
None	70 (83)	327 (91)	44 (44)	1 (12.5)	*Asy, Mild vs Mod, Sev
Skin disease	0	1 (0.3)	1 (1)	1 (12.5)	* Asy, Mild, Mod vs Sev
Heart disease	0	1 (0.3)	6 (6)	2 (25)	* Asy, Mild vs Mod, Sev; * Mod vs Sev
Renal disease	3 (3.6)	1 (0.3)	4 (4)	1 (12.5)	*Asy, Mod, Sev vs Mild
Lung disease	3 (3.6)	13 (3.6)	24 (24)	3 (38)	**Asy, Mild vs Mod, Sev
Prematurity	1 (1.2)	3 (0.8)	6 (6)	1 (12.5)	* Mild vs Mod, Sev
Autoimmunity	4 (4.8)	0	2 (2)	2 (25)	* Asy, Mod vs Mild, Sev; * Mild vs Sev
Cancer	2 (2.3)	1 (0.3)	9 (9)	2 (25)	* Asy, Mild vs Mod, Sev
Obesity	0	12 (3.4)	11 (11)	0	* Asy, Mild vs Mod
Undernutrition	2 (2.3)	1 (0.3)	6 (6)	2 (25)	* Asy, Mild vs Mod, Sev; * Mod vs Sev
Diabetes	3 (3.6)	3 (0.8)	1 (1)	0	
Genetic disorder	0	1 (0.3)	2 (2)	2 (25)	
Coinfections, n (%)					* Mild vs Mod
None	82 (97.6)	348 (97.2)	91 (91)	6 (75)	
Bacterial	2 (2.4)	10 (2.8)	9 (9)	1 (12.5)	
Viral	0	0	0	1 (12.5)	
Pneumonia, n (%)	0	0	26 (26)	4 (50)	** Asy, Mild vs Mod, Sev
PICU admission, n (%)	0	0	4 (4)	8 (100)	* Asy, Mild vs Mod, Sev; * Mod vs Sev
Respiratory status, n (%)					
Mechanical ventilation	0	0	1 (1)	3 (38)	* Asy, Mild, Mod vs Sev
Oxygen requirement	0	0	8 (8)	5 (62)	* Asy, Mild vs Mod, Sev; * Mod vs Sev
Room air	84 (100)	358 (100)	91 (91)	0	
Outcome, n (%)					
Discharged	84 (100)	358 (100)	69 (69)	0	

Remained hospitalized	0	0	31 (31)	6 (75)	** Asy, Mild vs Mod, Sev; * Mod vs Sev
Deceased	0	0	0	2 (25)	* Asy, Mild, Mod vs Sev

Data are expressed as median values (IQR) unless otherwise indicated.
Abbreviations: PICU, pediatric intensive care unit. ^a at hospital admission. ^b at time
of blood collection. Only significant p values are shown. * p<0.05, ** p<0.01.

Table S2. Characteristics of children under convalescence phase of infection.

	Convalescent				P
	Asymptomatic n= 10	Mild n= 88	Moderate n= 31	Severe n= 9	
Age, years, median (range)	13 (0.8-16.2)	5.7 (1-11)	4 (1.3-14)	1.4 (0.3-3.3)	*Asy vs Sev
<1 y, n (%)	2 (20)	16 (18)	6 (19)	4 (45)	
1-5 y, n (%)	2 (20)	23 (26)	11 (36)	5 (55)	
6-10 y, n (%)	0	18 (21)	4 (13)	0	
>10 y, n (%)	6 (60)	31 (35)	10 (32)	0	*Asy vs Sev
Sex, n (%)					*Asy vs Mild, Mod, Sev
Female	1 (10)	41 (47)	19 (61)	6 (67)	
Male	9 (90)	47 (53)	12 (39)	3 (33)	
Days after symptom onset (range) ^a	N/A	31 (21-36)	33 (25-39)	28 (24-33)	
SARS-CoV-2 IgG positive, n (%) ^a	7 (70)	59 (66)	19 (61)	2 (22)	* Mild vs Sev
SARS-CoV-2 IgM positive, n (%) ^a	6 (60)	47 (54)	14 (45)	3 (33)	
Comorbidities, n (%)					
None	6 (60)	77 (88)	9 (29)	2 (22)	** Mild vs Mod, Sev
Skin disease	0	0	0	0	
Heart disease	0	0	2 (6.5)	2 (22)	* Mild vs Sev
Renal disease	1 (10)	0	2 (6.5)	1 (11)	
Lung disease	1 (10)	6 (7)	9 (29)	3 (33)	* Mild vs Mod, Sev
Prematurity	0	2 (2.3)	4 (13)	0	
Autoimmunity	1 (10)	0	0	1 (11)	* Asy, Sev vs Mild
Cancer	1 (10)	0	7 (23)	1 (11)	** Mild vs Asy, Mod, Sev
Obesity	0	3 (3.4)	4 (13)	0	
Undernutrition	2 (20)	0	4 (13)	1 (11)	** Mild vs Asy, Mod, Sev
Diabetes	0	1 (1.1)	0	1 (11)	
Genetic disorder	1 (10)	0	0	1 (11)	* Asy, Sev vs Mild
Coinfections, n (%)					
None	9 (90)	85 (96.6)	26 (84)	7 (78)	
Bacterial	1 (10)	3 (3.4)	5 (16)	1 (11)	
Viral	0	0	0	1 (11)	
Pneumonia, n (%)	0	0	11 (35)	4 (44)	** Asy, Mild vs Mod, Sev
PICU admission, n (%)	0	0	3 (10)	9 (100)	** Asy, Mild vs Mod, Sev; * Mod vs Sev
Respiratory status, n (%)					
Mechanical ventilation	0	0	1 (3.2)	4 (45)	*Asy, Mild, Mod vs Sev
Oxygen requirement	0	2 (2.3)	9 (29)	5 (55)	*Asy, Mild vs Sev; *Mild vs Mod
Room air	10 (100)	86 (97.7)	21 (68)	0	*Asy, Mild, Mod vs Sev

Data are expressed as median values (IQR) unless otherwise indicated. Abbreviations:
PICU, pediatric intensive care unit. ^a at time of testing. Only significant p values are shown.
* p<0.05, ** p<0.01.

Table S3. Characteristics of severe children with COVID-19.

	Patient	Age (y)	Sex	SARS-CoV-2 Ab		Main Comorbidities	Coinfection	Pneumonia	PICU	^a Outcome
				IgG+	IgM+					
Acute	#1	15.0	F	NR	NR	Common variable immunodeficiency-Psoriasis	No	Yes	Yes	Recovered
	#2	0.3	M	NR	NR	Acute lymphoblastic leukemia	Yes. Bacteria	Yes	Yes	Recovered
	#3	0.3	F	NR	NR	Prematurity-Microcephaly-Undernutrition-Genetic	No	No	Yes	Recovered
	#4	2.5	F	NR	NR	Undernutrition-Dermatomyositis-Pulmonary fibrosis	No	Yes	Yes	Deceased
	#5	4.0	F	NR	NR	Respiratory disease	No	N/D	Yes	Recovered
	#6	0.1	F	NR	NR	Congenital heart disease-Renal failure	No	Yes	Yes	Deceased
	#7	0.5	F	NR	NR	Down syndrome- Heart disease-Lung disease	No	No	Yes	Recovered
	#8	1.4	M	NR	NR	No	Yes. Virus	No	Yes	Recovered
Convalescent	#2 ^b	0.3	M	R	R	Acute lymphoblastic leukemia	Yes. Bacteria	Yes	Yes	Recovered
	#4 ^b	2.5	F	NR	R	Undernutrition-Dermatomyositis-Pulmonary fibrosis	No	Yes	Yes	Deceased
	#5 ^b	0.3	F	NR	NR	Respiratory disease	No	N/D	Yes	Recovered
	#6 ^b	0.1	F	NR	NR	Cardiopathy congenital-Renal failure	No	Yes	Yes	Deceased
	#7 ^b	0.5	F	NR	NR	Down syndrome- Heart disease-Lung disease	No	No	Yes	Recovered
	#8 ^b	1.4	M	NR	NR	No	Yes. Virus	No	Yes	Recovered
	#9	4.0	M	R	R	Diabetes	No	No	Yes	Recovered
	#10	1.5	F	NR	NR	Non-progressive chronic encephalopathy	No	No	Yes	Recovered
	#11	4.0	F	NR	NR	No	No	Yes	Yes	Recovered

Abbreviations: PICU, pediatric intensive care unit; F, female; M, male; R, reactive; NR, no reactive. ^aOutcome refers to the disease course. ^bPaired samples.

Figure S1.

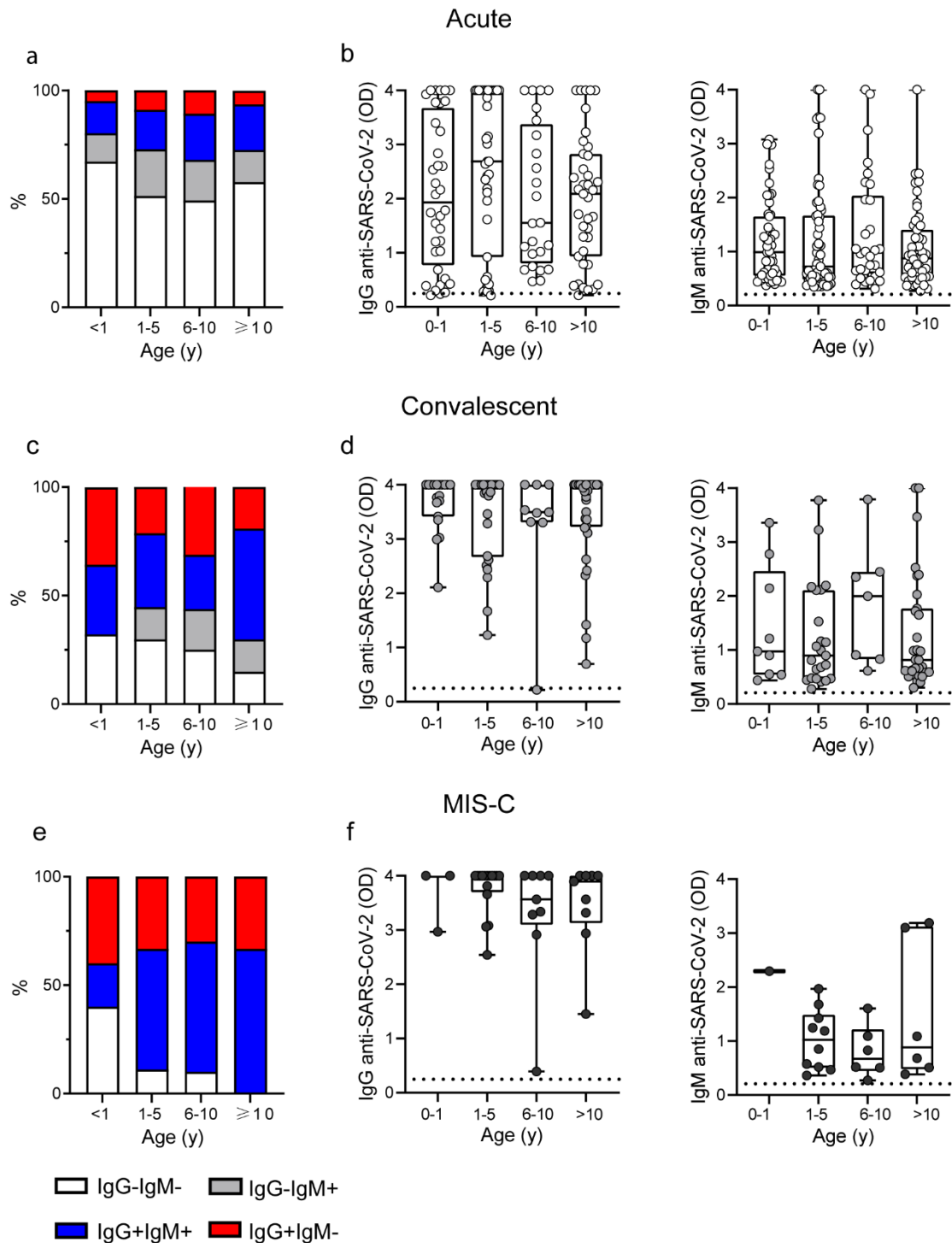


Figure S1. Antibody response against SARS-CoV-2 in children with COVID-19 and MIS-C stratified according to age. (a) Frequency of children in the acute phase of infection that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2: <1 year, n=186; 1 to 5 years, n=146; 6 to 10 years, n=76; and >10 years, n=142. **(b)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein in SARS-CoV-2-seropositive

children under the acute phase of the infection are shown: <1 year, n=37 and n=52; 1 to 5 years, n=39 and n=57; 6 to 10 years, n=24 and n=30; and >10 years, n=39 and n=52, for IgG and IgM respectively. **(c)** Frequency of children in the convalescent phase of the infection that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2: <1 year, n=28; 1 to 5 years, n=47; 6 to 10 years, n=16; and >10 years, n=47. **(d)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein in SARS-CoV-2-seropositive children under the convalescent phase of the infection are shown: <1 year, n=19 and n=9; 1 to 5 years, n=26 and n=23; 6 to 10 years, n=9 and n=7; and >10 years, n=33 and n=31, for IgG and IgM respectively. **(e)** Frequency of MIS-C that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2: <1 year, n=5; 1 to 5 years, n=18; 6 to 10 years, n=10; and >10 years, n=9. **(f)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein were measured in MIS-C: <1 year, n=3 and n=1; 1 to 5 years, n=16 and n=10; 6 to 10 years, n=9 and n=6; and >10 years, n=9 and n=6, for IgG and IgM respectively. Dotted line indicates the cut-off value in b, d, f. Median and min to max of n donors are shown in b, d, f. P values were determined by Pearson's Chi square test and Kruskal-Wallis test. Acute (white circle), Convalescent (grey circle), MIS-C (black circle).

Figure S2.

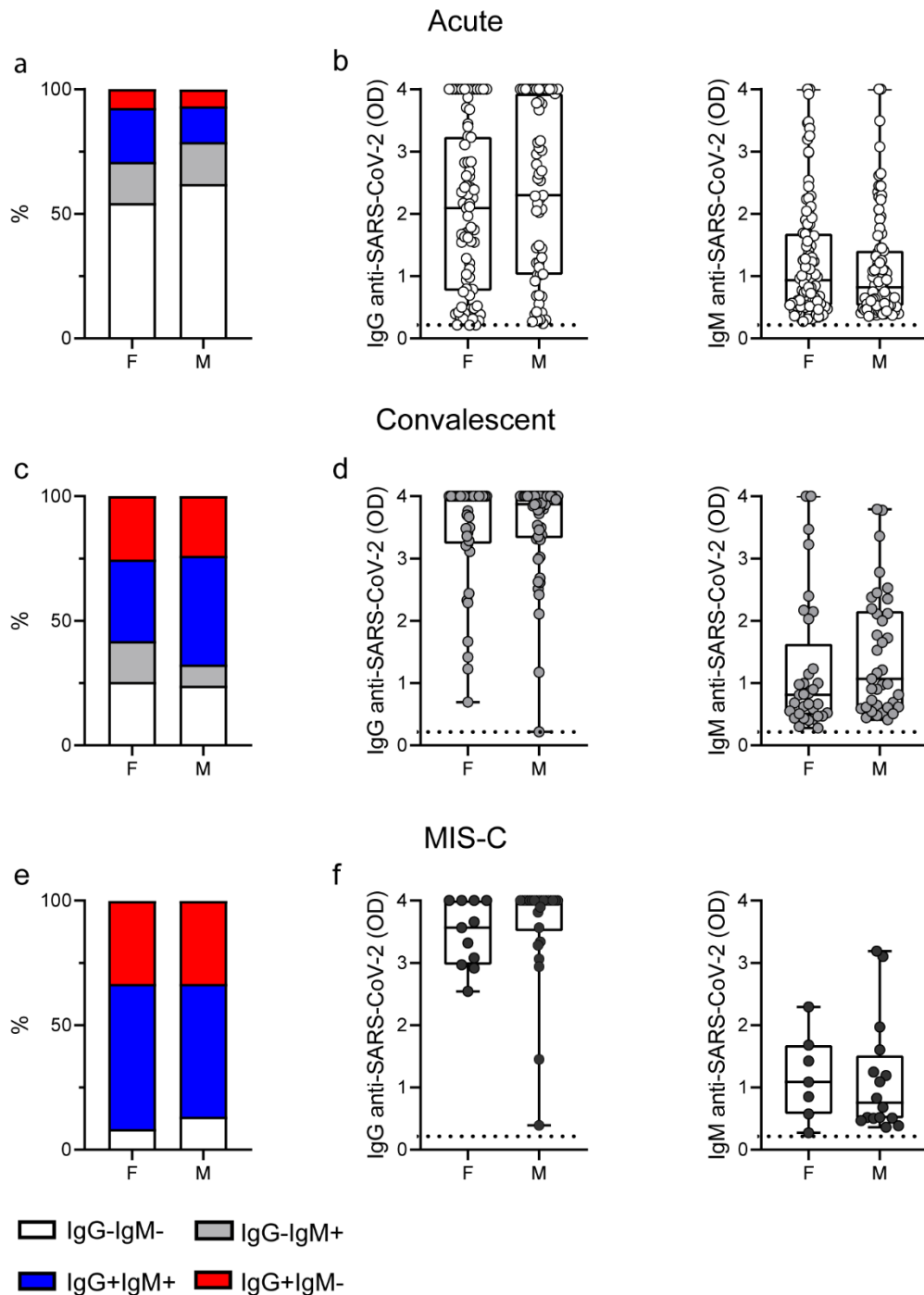


Figure S2. Antibody response against SARS-CoV-2 in children with COVID-19 and MIS-C according to sex. (a) Frequency of girls (n=267) and boys (n=283) in the acute phase of infection that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2. **(b)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein in SARS-CoV-2-seropositive children under the acute phase of the infection are shown: girls, n=79 and n=103; boys, n=60 and n=88, for IgG and IgM, respectively. **(c)** Frequency of girls (n= 67) and boys (n=71) during the convalescent phase of the infection that produced IgG

and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2. **(d)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein in SARS-CoV-2-seropositive children under the convalescent phase of the infection are shown: girls, n=39 and n=33; boys, n=48 and n=37, for IgG and IgM, respectively. **(e)** Frequency of girls (n=12) and boys (n=30) with MIS-C that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2. **(f)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein were measured in MIS-C: girls, n=11 and n=7; boys, n=26 and n=16, for IgG and IgM, respectively. Dotted line indicates the cut-off value in b, d, f. Median and min to max of n donors are shown in b, d, f. P values were determined by Pearson's Chi square test and Mann-Whitney U test. Acute (white circle), Convalescent (grey circle), MIS-C (black circle).

Figure S3.

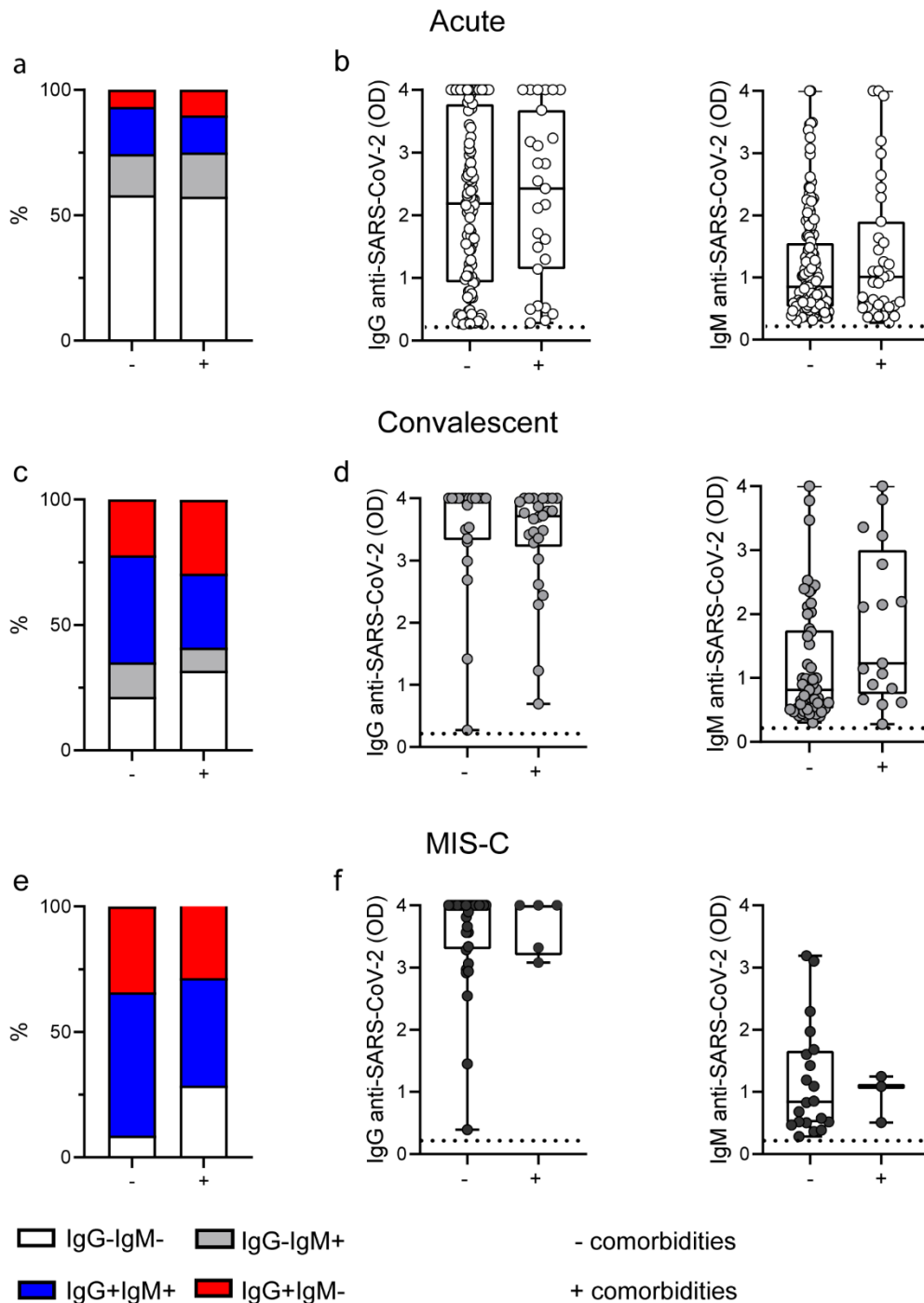


Figure S3. Antibody response against SARS-CoV-2 in children with COVID-19 and MIS-C according to the presence of comorbidities. (a) Frequency of children having comorbidities (n=108) and or not (n=442) in the acute phase of infection that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2. **(b)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein in SARS-CoV-2-seropositive children under the acute phase of the infection are shown: with comorbidities, n=27 and n=35; without comorbidities, n=112 and n=156, for IgG and IgM, respectively. **(c)** Frequency of children

having comorbidities (n=44) and or not (n=94) during the convalescent phase of the infection that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2. **(d)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein in SARS-CoV-2-seropositive children under the convalescent phase of the infection are shown: with comorbidities, n=26 and n=17; without comorbidities, n=61 and n=53, for IgG and IgM, respectively. **(e)** Frequency of children having comorbidities (n=7) and or not (n=35) with MIS-C that produced IgG and/or IgM antibodies to the Spike/RBD protein of SARS-CoV-2. **(f)** Plasma levels of IgG and IgM antibodies directed to the Spike/RBD protein were measured in MIS-C: with comorbidities, n=5 and n=3; without comorbidities, n=32 and n=20, for IgG and IgM, respectively. Dotted line indicates the cut-off value in b, d, f. Median and min to max of n donors are shown in b, d, f. P values were determined by Pearson's Chi square test and Mann-Whitney U test. Acute (white circle), Convalescent (grey circle), MIS-C (black circle).

Figure S4.

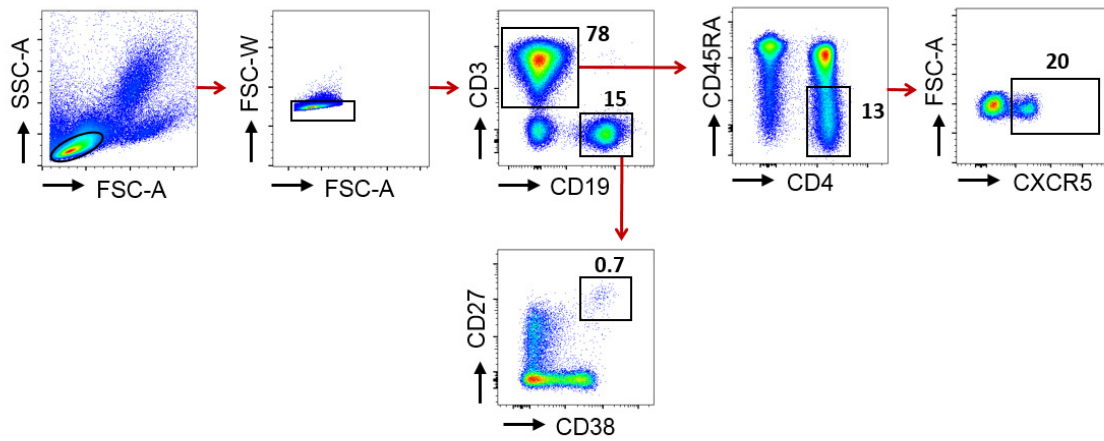


Figure S4. Gating strategy. Representative FACS profile showing the gating strategy for the analysis of cTfh cells and plasmablasts. Peripheral blood mononuclear cells (1×10^6) were stained with the antibody cocktail mix (anti-CD3, anti-CD4, anti-CD45RA, anti CXCR5, anti-CD19, anti-CD27 y anti-CD38) for 20 min at room temperature. After washing, data were acquired using a FACSCanto II (Becton Dickinson). cTfh were defined as CD3+CD4+CD45RA-CXCR5+ cells and plasmablasts were defined as CD19+CD27^{hi}CD38^{hi}. A representative experiment is shown.