Supplementary material

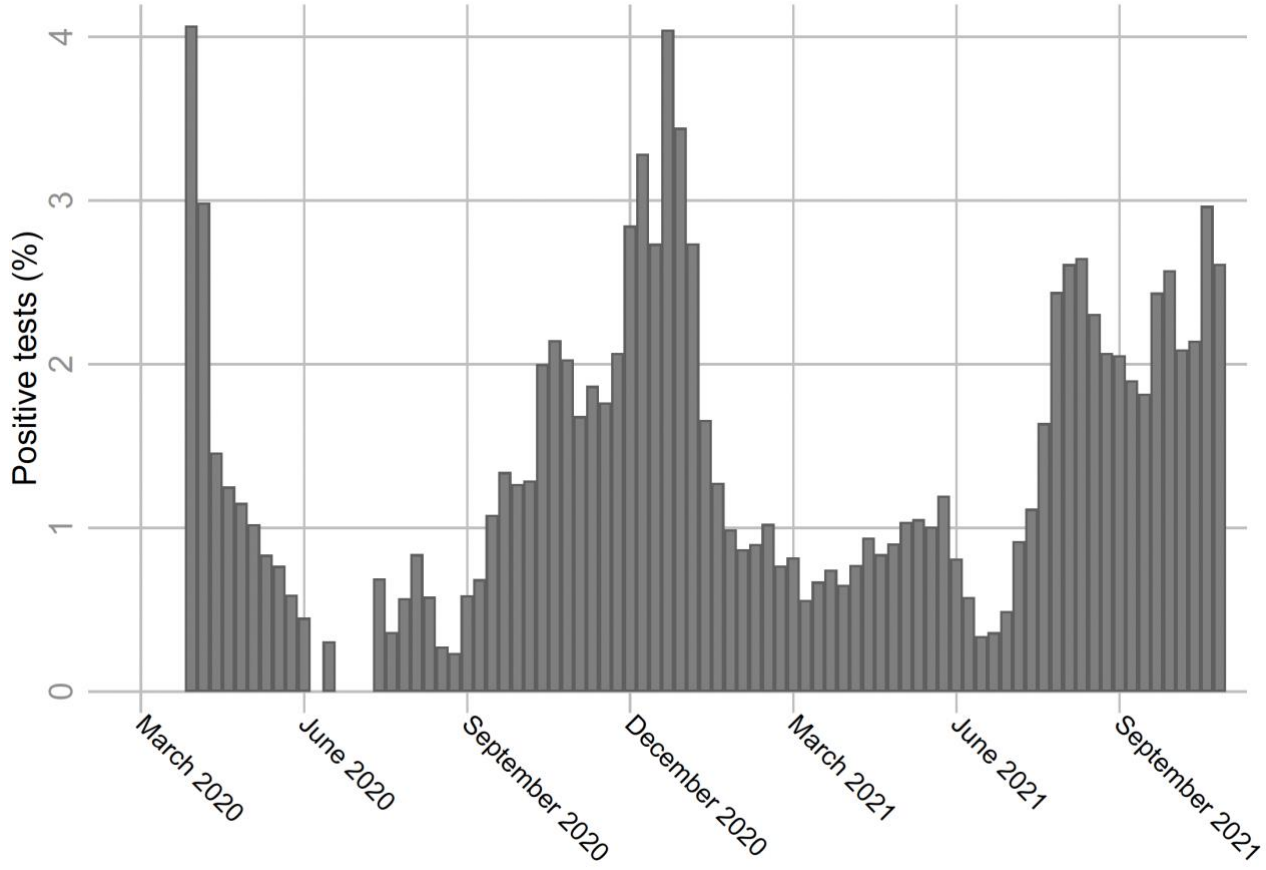
Supplement to: Kildegaard H, Lund LC, Højlund M, Stensballe LG, Pottegård A. Comprehensive assessment of paediatric SARS-CoV-2 infection: a Danish population-based cohort study.

Appendix

Figures

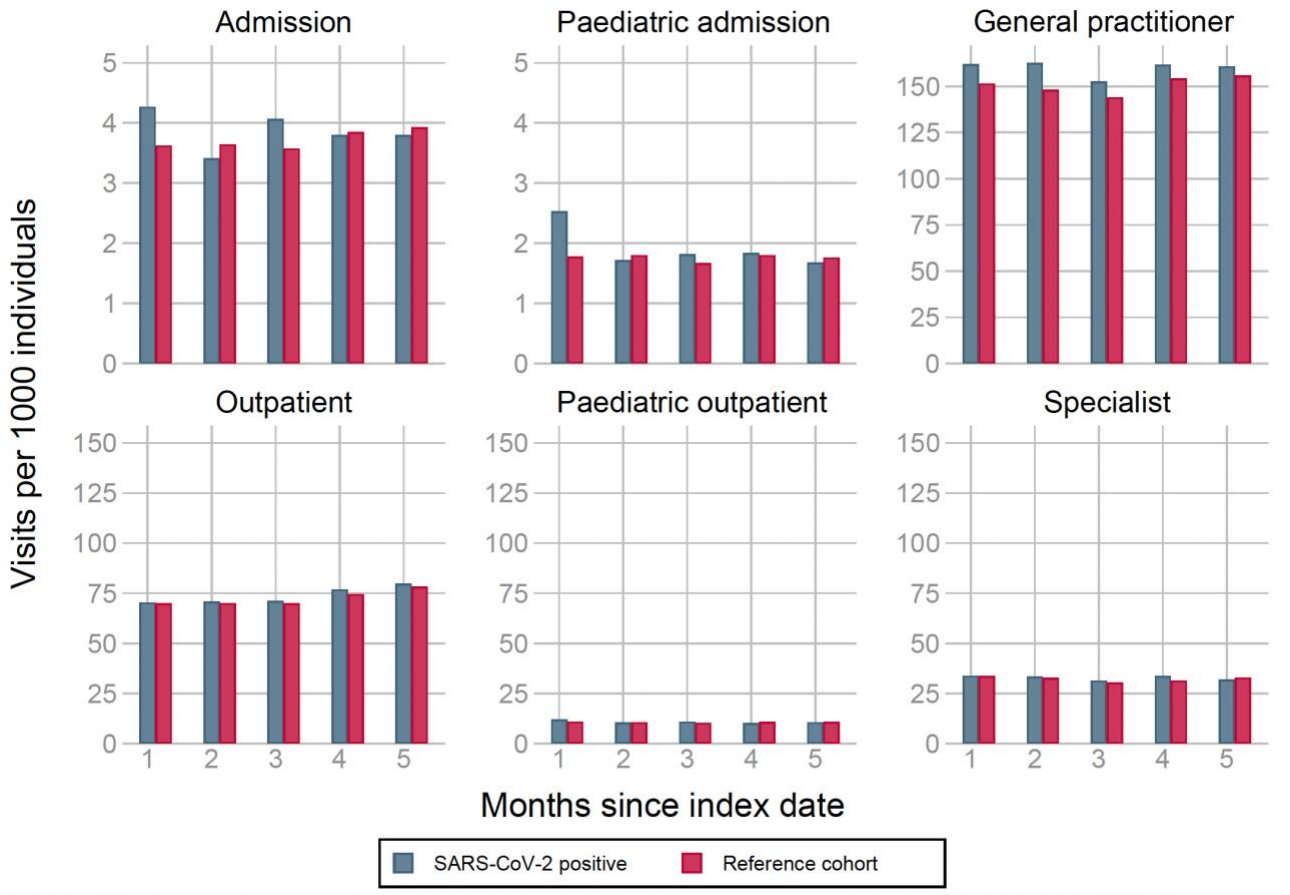
Tables

Figure S1: Weekly share of total SARS-CoV-2 tests that were positive during the epidemic



The weekly number of PCR-test confirmed paediatric SARS-CoV-2 cases as a share of the total number of PCR-tests performed in individuals <18 years. Weeks with less than five paediatric cases are not reported due to Danish privacy regulation.

Figure S2. Bar chart of health care utilisation



The figure illustrates the monthly rates for six types of healthcare visits during follow up among SARS-CoV-2 positive children and the reference cohort. Each bar illustrates the monthly rate, e.g. month 1 is day 30-59, month 2 day 60-89 and so forth.
Admission = Physical hospital contact with a duration of 12 hours or more.
Outpatient = Physical hospital contact with a duration of less than 6 hours.
Specialist = Visit at a primary care dermatologist, ENT-specialist or ophthalmologist.

Table S1. ICD-10 and ATC codes used to define outcomes

	Coding system	Codes
Diagnosis-based outcomes		
Myocarditis	ICD-10	I40, I41, I514
MIS-C†	ICD-10	B972B, M303
Venous thromboembolism	ICD-10	I26, I801, I802, I803, I808. I809, I822, I823, I829
Pneumonia	ICD-10	A481, B012, J12-J18, J100
Guillian-Barré syndrome	ICD-10	G610
Encephalitis	ICD-10	A858, A869, G04-05
Other neuroimmune disorders	ICD-10	G35, G360, G368, G369, G373, G378, G379, H46
Hospital referral for suspicion of sequelae after COVID-19 infection	ICD-10	B948A, Z038Q
Medication outcomes		
Short-acting beta2-agonists	ATC	R03AC02-4, R03AL01-02, R03CC02
Inhaled corticosteroids	ATC	R03BA, R03AK, R03AL08, R03AL09
Paracetamol	ATC	N02BE01
NSAIDs	ATC	M01 excl. M01AX
Antibiotics for respiratory tract infections	ATC	J01CA04, J01CE02, J01CR02, J01FA
Other antibiotics	ATC	J01 excl. J01CE02, J01CA04, J01CR02, J01FA

Information on diagnoses representing possible complications from SARS-CoV-2 infection was obtained from inpatient and outpatient hospital diagnoses recorded in the Danish National Patient Registry.[1] Use of prescription drugs was identified from the Danish National Prescription Registry.[2] †MIS-C is a combined endpoint of MIS-C and Kawasaki disease. The ICD-10 diagnosis code for MIS-C was not implemented in Denmark until April 1, 2021. Therefore, cases of Kawasaki disease occurring within two months of SARS-CoV-2 infection were considered as MIS-C.

Abbreviations:
ICD-10 = International Classification of Diseases and Health Related Problems, 10th revision
ATC = Anatomical Therapeutical Chemical Classification
MIS-C = Multisystem inflammatory syndrome in children
COVID-19 = Coronavirus disease 2019.
NSAIDs = Non-steroidal anti-inflammatory drugs.

Table S2. ICD-10 and ATC codes used to define baseline covariates

	Coding system	Codes
Perinatal history		
Prematurity	ICD-10	P073
Immaturity	ICD-10	P072
Small for gestational age	ICD-10	P050
Low birth weight	ICD-10	P070, P071
Comorbidities		
Asthma	ICD-10	J45-46
Other chronic respiratory diseases	ICD-10	E84, J41-44, J47, J84, P27
Chronic cardiac disease	ICD-10	I05-08, I20-28, I34-37, I42-49, I50-51
Renal disease	ICD-10	N03, N05, N07, N18, N19, N25-27
Diabetes	ICD-10	E10-14
Autoimmune disease, not including diabetes	ICD-10	D510, D590, D591, D690, D693, D86 E035, E039, E050, E055, E059, E063, E065, E271, E272, E310 G04, G131, G35, G36, G61, G700 H20 I00-I02 K50, K51, K732, K743, K900 L10, L12, L130, L40, L63, L80 M05-06, M08, M30, M311, M313, M315-7, M32-34, M350-M353, M358-M359, M45, M60
Epilepsy or convulsions	ICD-10	G40, R56
Congenital malformations and chromosomal abnormalities	ICD-10	Q00-07, Q20-28, Q30-34, Q60-64, Q90-99
Malignancy or immunodeficiency	ICD-10	C00-96, D70-72, D730, D81-84
Psychiatric disorder	ICD-10	Any chapter F diagnosis
Current drug use		
Short-acting beta2-agonists	ATC	R03AC02-4, R03AL01-02, R03CC02
Inhaled corticosteroids	ATC	R03BA, R03AK, R03AL08, R03AL09
Leukotrine D4-receptor antagonists	ATC	R03DC
Nasal corticosteroids	ATC	R01AD
Systemic antihistamines	ATC	R06A
Systemic corticosteroids	ATC	H02AB
Systemic antibiotics, no. of prescription fills (0,1,+2)	ATC	J01
Paracetamol	ATC	N02BE01
NSAIDs	ATC	M01 excl. M01AX

Information on medical history was obtained from inpatient and outpatient hospital diagnoses recorded in the Danish National Patient Registry.[1] Use of prescription drugs was identified from the Danish National Prescription Registry.[2]
Abbreviations:
ICD-10 = International Classification of Diseases and Health Related Problems, 10th revision
ATC = Anatomical Therapeutical Chemical Classification
NSAIDs = Non-steroidal anti-inflammatory drugs.

Table S3: Estimated percentage of individuals tested for SARS-CoV-2 of the total Danish child population evaluated on 1 October 2021, stratified on age.

Age	Tested (N)	Residents (N)	Tested (%)
0	7328	62551	12
1	31836	61708	52
2	44475	61819	72
3	45265	62628	72
4	47272	62063	76
5	49156	62658	78
6	48585	59239	82
7	50302	58674	86
8	52176	59497	88
9	53997	60761	89
10	57486	63632	90
11	61165	66795	92
12	62020	67160	92
13	64221	69256	93
14	63590	67691	94
15	65084	68881	94
16	65436	68548	95
17	65501	68288	96

Number of Danish residents under 18 years of age RT-PCR-tested for SARS-CoV-2 at some point until 1 October 2021 as a percentage of the total number of Danish residents < 18 years of age, evaluated on 1 October 2021. The total number of Danish residents under 18 years of age was obtained from Statistics Denmark. [3] Age was evaluated on 1 October 2021 and not on the date of testing to correspond to population numbers obtained from Statistics Denmark. Therefore, the total number of individuals tested for SARS-CoV-2 is less than the number listed in the main paper as adolescents who turned 18 years during the study period are not included in this estimation.

Table S4: Absolute risks of main study outcomes stratified by SARS-CoV-2 variant

	Any variant		B.1.177		Alpha variant		Delta variant	
Outcome	**Events**	**Risk (%)**	**Events**	**Risk (%)**	**Events**	**Risk (%)**	**Events**	**Risk (%)**
Hospital admission	361/74350	0.49 (0.44, 0.54)	153/30798	0.50 (0.42, 0.58)	98/20102	0.49 (0.40, 0.59)	80/16649	0.48 (0.38, 0.60)
MIS-C†	32/70666	0.05 (0.03, 0.06)	11/30888	0.04 (0.02, 0.06)	9/20164	0.04 (0.02, 0.08)	5/12778	0.04 (0.01, 0.09)
Long-COVID	58/48948	0.12 (0.09, 0.15)	44/30894	0.14 (0.10, 0.19)	7/13009	0.05 (0.02, 0.11)	-	-
Initiation of prescription drugs								
Short-acting beta-2 agonists	608/46728	1.30 (1.20, 1.41)	328/29498	1.11 (1.00, 1.24)	202/12434	1.62 (1.41, 1.86)	-	-
Inhaled corticosteroids	292/47163	0.62 (0.55, 0.69)	169/29741	0.57 (0.49, 0.66)	79/12573	0.63 (0.50, 0.78)	-	-
Paracetamol	338/47620	0.71 (0.64, 0.79)	248/30099	0.82 (0.72, 0.93)	61/12648	0.48 (0.37, 0.62)	-	-
NSAIDs	433/47821	0.91 (0.82, 0.99)	280/30146	0.93 (0.82, 1.04)	104/12731	0.82 (0.67, 0.99)	-	-
Antibiotics for respiratory Tract infections	1306/44072	2.96 (2.81, 3.13)	679/27604	2.46 (2.28, 2.65)	493/12011	4.10 (3.76, 4.47)	-	-
Other antibiotics	790/46701	1.69 (1.58, 1.81)	510/29381	1.74 (1.59, 1.89)	200/12479	1.60 (1.39, 1.84)	-	-

Absolute risks of hospital-based, diagnosis-based outcomes, and initiation of new medication during follow-up in SARS-CoV-2 positive children and a reference cohort sampled among children tested for SARS-CoV-2, stratified by dominating SARS-CoV-2 variant. Periods of dominating SARS-CoV-2 strain was defined based on Danish large-scale genome sequencing of SARS-CoV-2 provided by the Global Initiative in Sharing All Influenza Data to https://covariants.org/per-country.[4] Because of limited number of events, stratification on SARS-CoV-2 variant was not possible for all study outcomes. Evaluation of Long-COVID and initiation of prescription drugs required six months of follow-up and was therefore not possible for the period dominated by the delta variant.
MIS-C=Multisystem inflammatory syndrome in children. NSAIDs= non-steroidal anti-inflammatory drugs.

Table S5. Baseline characteristics of SARS-CoV-2 positive cases and children and adolescents in the reference cohort before and after propensity score weighting.

	SARS-CoV-2 positive (n=74,611)	Reference (n=920,893)	SMD	Reference (weighted) (n=74,559)	SMD
Demographics					
Median age (IQR)	11 (7-15)	10 (5-14)	0.22	11 (7-15)	0
Age category (years)					
0-1	3,369 (4.5)	59,481 (6.5)	0.09	2,759 (3.7)	0.04
2-5	9,665 (13)	181,411 (20)	0.18	10,984 (15)	0.05
6-11	26,641 (36)	315,599 (34)	0.03	25,229 (34)	0.04
12-15	21,689 (29)	243,994 (26)	0.06	22,735 (30)	0.03
16-17	13,247 (18)	120,408 (13)	0.13	12,853 (17)	0.01
Female sex	36,488 (49)	449,017 (49)	0	36,474 (49)	0
Immigration status					
1st generation	4,846 (6.5)	29,941 (3.3)	0.15	4,847 (6.5)	0
2nd generation	15,571 (21)	81,428 (8.8)	0.34	15,497 (21)	0
Temporality					
27 Feb 2020 to 31 Jul 2020	921 (1.2)	11,646 (1.3)	0	938 (1.3)	0
01 Aug 2021 to 31 Jan 2021	35,027 (47)	437,076 (47)	0.01	35,364 (47)	0.01
01 Feb 2021 to 30 Jun 2021	20,701 (28)	257,486 (28)	0	20,827 (28)	0
01 Jul 2021 to 31 Oct 2021	17,962 (24)	214,685 (23)	0.02	17,430 (23)	0.02
Perinatal history					
Prematurity (28-37 weeks)	3,182 (4.3)	44,277 (4.8)	0.03	3,320 (4.5)	0.01
Immaturity (<28 weeks)	NR	2,152 (0.2)	NR	172 (0.2)	NR
Small for gestational age	868 (1.2)	13,000 (1.4)	0.02	865 (1.2)	0
Low birth weight (<2500g)	2,160 (2.9)	28,502 (3.1)	0.01	2,159 (2.9)	0
Medical history					
Asthma	4,040 (5.4)	50,568 (5.5)	0	4,031 (5.4)	0
Other chronic respiratory diseases	470 (0.6)	6,488 (0.7)	0.01	471 (0.6)	0
Chronic cardiac disease	362 (0.5)	4,046 (0.4)	0.01	360 (0.5)	0
Diabetes mellitus	NR	2,664 (0.3)	NR	192 (0.3)	NR
Autoimmune disorders	854 (1.1)	9,991 (1.1)	0.01	854 (1.1)	0
Epilepsy or convulsions	3,159 (4.2)	40,062 (4.4)	0.01	3,152 (4.2)	0
Congenital malformations and chromosomal abnormalities	1,971 (2.6)	25,127 (2.7)	0.01	1,966 (2.6)	0
Malignancy or immunodeficiency	343 (0.5)	4,179 (0.5)	0	340 (0.5)	0
Psychiatric disorders	4,564 (6.1)	63,844 (6.9)	0.03	4,569 (6.1)	0
Number of comorbidities					
0	58,134 (78)	706,834 (77)	0.03	58,091 (78)	0
1	12,254 (16)	156,760 (17)	0.02	12,192 (16)	0
2+	4,223 (5.7)	57,299 (6.2)	0.02	4,276 (5.7)	0
Hospital admissions within the last year					
0	74,350 (100)	917,118 (100)	0.01	74,295 (100)	0
1	NR	3,543 (0.4)	NR	248 (0.3)	NR
2+	NR	232 (0.0)	NR	16 (0.0)	NR
Current drug use					
Short-acting beta-2 agonists	3,023 (4.1)	44,040 (4.8)	0.04	3,020 (4.1)	0
Inhaled corticosteroids	2,501 (3.4)	33,142 (3.6)	0.01	2,501 (3.4)	0
Leukotriene D4-receptor antagonists	433 (0.6)	6,000 (0.7)	0.01	433 (0.6)	0
Nasal corticosteroids	3,409 (4.6)	38,766 (4.2)	0.02	3,410 (4.6)	0
Systemic antihistamines	3,508 (4.7)	42,929 (4.7)	0	3,510 (4.7)	0

Systemic corticosteroids	NR	1,661 (0.2)	NR	163 (0.2)	NR
Systemic antibiotics					
0	65,820 (88)	813,554 (88)	0	65,776 (88)	0
1	6,130 (8.2)	74,262 (8.1)	0.01	6,124 (8.2)	0
2+	2,661 (3.6)	33,077 (3.6)	0	2,659 (3.6)	0
Paracetamol	1,705 (2.3)	22,634 (2.5)	0.01	1,704 (2.3)	0
NSAIDs	1,610 (2.2)	18,990 (2.1)	0.01	1,605 (2.2)	0
Number of unique drugs					
0	41,617 (56)	506,281 (55)	0.02	41,753 (56)	0
1	16,411 (22)	208,584 (23)	0.02	16,385 (22)	0
2+	16,583 (22)	206,028 (22)	0	16,422 (22)	0

Data are n(%) unless stated otherwise. SMD=standardized mean difference. IQR=Interquartile range. NR=not reported because of Danish data protection laws. NSAIDs=non-steroidal anti-inflammatory drugs. †Defined as having redeemed a prescription for the drug of interest during one year prior to the start of follow-up.

Table S6 Risk of health care utilisation
The table provides the number of individuals with six types of healthcare visits during one to six months of follow up among SARS-CoV-2 positive children and the reference cohort.

	SARS-CoV-2 positive (N=48,962)		Reference (N=608,013)	
Visit type	**Events**	**Risk, %**	**Events**	**Risk, %**
Admission	775	1.6	9369	1.5
Paediatric admission	400	0.8	4584	0.8
General practitioner	20616	42.1	247620	40.7
Outpatient	9062	18.5	111810	18.4
Paediatric outpatient	1910	3.9	23954	3.9
Specialist	5271	10.8	65348	10.7

Admission = Physical hospital contact with a duration of 12 hours or more.
Outpatient = Physical hospital contact with a duration of less than 6 hours.
Specialist = Visit at a primary care dermatologist, ENT-specialist or ophthalmologist.
Information on inpatient and outpatient hospital visits was obtained from the Danish National Patient Registry.[1] Data on visits at general practitioners and private practicing specialists was obtained from the Danish National Health Service Register.[5]

Table S7. Baseline characteristics of SARS-CoV-2 positive and test-negative children and adolescents before and after propensity score weighting.

	SARS-CoV-2 positive (n=74,611)	SARS-CoV-2 negative (n=745,540)	SMD	SARS-CoV-2 negative (weighted) (n=74,563)	SMD
Demographics					
Median age (IQR)	11 (7-15)	11 (7-15)	0.04	11 (7-15)	0.01
Age category (years)					
0-1	3,369 (4.5)	24,051 (3.2)	0.07	2,644 (3.5)	0.05
2-5	9,665 (13)	100,168 (13)	0.01	11,171 (15)	0.06
6-11	26,641 (36)	252,231 (34)	0.04	25,560 (34)	0.03
12-15	21,689 (29)	239,924 (32)	0.07	22,155 (30)	0.01
16-17	13,247 (18)	129,166 (17)	0.01	13,034 (17)	0.01
Female sex	36,488 (49)	376,509 (51)	0.03	36,447 (49)	0
Immigration status					
1st generation	4,846 (6.5)	17,020 (2.3)	0.21	4,847 (6.5)	0
2nd generation	15,571 (21)	51,364 (6.9)	0.41	15,567 (21)	0
Temporality					
27 Feb 2020 to 31 Jul 2020	921 (1.2)	9,315 (1.2)	0	926 (1.2)	0
01 Aug 2021 to 31 Jan 2021	35,027 (47)	349,707 (47)	0	35,656 (48)	0.02
01 Feb 2021 to 30 Jun 2021	20,701 (28)	206,934 (28)	0	19,735 (26)	0.03
01 Jul 2021 to 31 Oct 2021	17,962 (24)	179,584 (24)	0	18,246 (24)	0.01
Perinatal history					
Prematurity (28-37 weeks)	3,182 (4.3)	34,884 (4.7)	0.02	3,272 (4.4)	0.01
Immaturity (<28 weeks)	NR	1,699 (0.2)	NR	172 (0.2)	NR
Small for gestational age	868 (1.2)	9,248 (1.2)	0.01	865 (1.2)	0
Low birth weight (<2500g)	2,160 (2.9)	22,458 (3.0)	0.01	2,162 (2.9)	0
Medical history					
Asthma	4,040 (5.4)	46,211 (6.2)	0.03	4,028 (5.4)	0
Other chronic respiratory diseases	470 (0.6)	5,167 (0.7)	0.01	470 (0.6)	0
Chronic cardiac disease	362 (0.5)	3,790 (0.5)	0	359 (0.5)	0
Diabetes mellitus	NR	2,490 (0.3)	NR	192 (0.3)	NR
Autoimmune disorders	854 (1.1)	9,889 (1.3)	0.02	853 (1.1)	0
Epilepsy or convulsions	3,159 (4.2)	33,897 (4.5)	0.02	3,159 (4.2)	0
Congenital malformations and chromosomal abnormalities	1,971 (2.6)	20,205 (2.7)	0	1,967 (2.6)	0
Malignancy or immunodeficiency	343 (0.5)	4,112 (0.6)	0.01	340 (0.5)	0
Psychiatric disorders	4,564 (6.1)	55,279 (7.4)	0.05	4,575 (6.1)	0
Number of comorbidities					
0	58,134 (78)	564,033 (76)	0.05	58,076 (78)	0
1	12,254 (16)	133,309 (18)	0.04	12,240 (16)	0
2+	4,223 (5.7)	48,198 (6.5)	0.03	4,247 (5.7)	0
Hospital admissions within the last year					
0	74,350 (100)	741,852 (100)	0.02	74,179 (99)	0.03
1	NR	3,316 (0.4)	NR	346 (0.5)	NR
2+	NR	372 (0.0)	NR	38 (0.1)	NR
Current drug use					
Short-acting beta-2 agonists	3,023 (4.1)	35,912 (4.8)	0.04	3,033 (4.1)	0
Inhaled corticosteroids	2,501 (3.4)	29,379 (3.9)	0.03	2,506 (3.4)	0
Leukotriene D4-receptor antagonists	433 (0.6)	5,790 (0.8)	0.02	435 (0.6)	0
Nasal corticosteroids	3,409 (4.6)	40,617 (5.4)	0.04	3,403 (4.6)	0

Systemic antihistamines	3,508 (4.7)	40,253 (5.4)	0.03	3,514 (4.7)	0
Systemic corticosteroids	NR	1,867 (0.3)	NR	164 (0.2)	NR
Systemic antibiotics					
0	65,820 (88)	652,595 (88)	0.02	65,751 (88)	0
1	6,130 (8.2)	62,433 (8.4)	0.01	6,150 (8.2)	0
2+	2,661 (3.6)	30,512 (4.1)	0.03	2,663 (3.6)	0
Paracetamol	1,705 (2.3)	18,371 (2.5)	0.01	1,703 (2.3)	0
NSAIDs	1,610 (2.2)	19,145 (2.6)	0.03	1,602 (2.1)	0
Number of unique drugs					
0	41,617 (56)	391,948 (53)	0.06	40,882 (55)	0.02
1	16,411 (22)	168,331 (23)	0.01	16,739 (22)	0.01
2+	16,583 (22)	185,261 (25)	0.06	16,942 (23)	0.01

Data are n(%) unless stated otherwise. Data on race and socioeconomic status are not available from our data sources. SMD=standardized mean difference. IQR=Interquartile range. NR=not reported because of Danish data protection laws. NSAIDs=non-steroidal anti-inflammatory drugs. †Defined as having redeemed a prescription for the drug of interest during one year prior to the start of follow-up.

Table S8. Absolute risks, adjusted risk differences and risk ratios for hospital-based, diagnosis-based outcomes, and initiation of new medication during follow-up in SARS-CoV-2 positive children and a comparator cohort of SARS-CoV-2 test-negative children and adolescents.

	SARS-CoV-2 positive		SARS-CoV-2 negative			
Outcome	**Events**	**Risk (%)**	**Events**	**Risk (%)**	**RD (95% CI)**	**RR 95% CI**
Follow-up: 30 days						
Hospital admission	361/74350	0.49 (0.44, 0.54)	6294/741852	0.85 (0.83, 0.87)	-0.38 (-0.44, -0.33)	0.56 (0.50, 0.62)
Intensive care unit admission	10/73187	0.01 (0.01, 0.03)	268/729013	0.04 (0.03, 0.04)	-0.03 (-0.04, -0.01)	0.35 (0.18, 0.66)
Mechanical ventilation	n<5	NR	93/737835	0.01 (0.01, 0.02)	-	-
Renal replacement therapy	n<5	NR	n<5	NR	-	-
Follow-up: 60 days						
MIS-C†	32/70666	0.05 (0.03, 0.06)	22/706031	0.00 (0.00, 0.00)	0.04 (0.03, 0.06)	11.55 (5.73, 23.28)
Myocarditis	0/70693	0.00 (0.00, 0.01)	11/706372	0.00 (0.00, 0.00)	-	-
Venous thromboembolism	n<5	NR	5/706324	0.00 (0.00, 0.00)	-	-
Pneumonia	13/66682	0.02 (0.01, 0.03)	304/667536	0.05 (0.04, 0.05)	-0.03 (-0.04, -0.02)	0.39 (0.22, 0.68)
Guillian-Barré syndrome	n<5	NR	n<5	NR	-	-
Encephalitis	0/70669	0.00 (0.00, 0.01)	8/706104	0.00 (0.00, 0.00)	-	-
Other neuroimmune disorders	0/70681	0.00 (0.00, 0.01)	n<5	NR	-	-
Follow-up: 1-6 months						
Long-COVID	58/48948	0.12 (0.09, 0.15)	35/489318	0.01 (0.00, 0.01)	0.11 (0.08, 0.14)	18.15 (11.46, 28.74)
Short-acting beta-2 agonists	608/46728	1.30 (1.20, 1.41)	5892/462410	1.27 (1.24, 1.31)	0.03 (-0.08, 0.14)	1.02 (0.94, 1.11)
Inhaled corticosteroids	292/47163	0.62 (0.55, 0.69)	3197/468427	0.68 (0.66, 0.71)	-0.06 (-0.14, 0.02)	0.91 (0.81, 1.03)
Paracetamol	338/47620	0.71 (0.64, 0.79)	3965/474248	0.84 (0.81, 0.86)	-0.07 (-0.16, 0.01)	0.90 (0.81, 1.01)
NSAIDs	433/47821	0.91 (0.82, 0.99)	5288/474683	1.11 (1.08, 1.14)	-0.11 (-0.20, -0.02)	0.90 (0.81, 0.99)
Antibiotics for respiratory tract infections	1306/44072	2.96 (2.81, 3.13)	12507/435225	2.87 (2.82, 2.92)	0.11 (-0.06, 0.28)	1.04 (0.98, 1.10)
Other antibiotics	790/46701	1.69 (1.58, 1.81)	8341/463979	1.80 (1.76, 1.84)	0.04 (-0.08, 0.17)	1.03 (0.95, 1.10)

Because of Danish legislation, counts less than five cannot be reported. Risk differences (RD) and risk ratios (RR) are propensity-score weighted estimates adjusted for age, sex, calendar time, immigration status, gestational age, comorbidities and current drug use as specified in appendix.

NR= not reported. MIS-C=Multisystem inflammatory syndrome in children. NSAIDs= non-steroidal anti-inflammatory drugs.

†MIS-C is reported as a combined endpoint of MIS-C and Kawasaki disease. The ICD-10 diagnosis code for MIS-C was not implemented in Denmark until late in the epidemic. Therefore, cases of Kawasaki disease occurring within two months of SARS-CoV-2 infection were considered as MIS-C.

Table S9. Rates of health care services 6 months to 1 month before and 1 to 6 months after the index date in SARS-CoV-2 positive and test-negative children and adolescents.

	SARS-CoV-2 positive		SARS-CoV-2 negative		
	Rate/1000 individuals (total visits)				
Visit type	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**	**PERR (95% CI)**
Admission	22 (1094)	19 (947)	24 (11876)	22 (10610)	0.97 (0.88-1.06)
Paediatric admission	10 (506)	10 (469)	11 (5497)	10 (4674)	1.09 (0.95-1.23)
General practitioner	913 (44722)	800 (39163)	1,005 (491742)	826 (404059)	1.07 (1.05-1.08)
Outpatient	366 (17929)	369 (18064)	421 (205813)	429 (209946)	1.01 (0.97-1.05)
Paediatric outpatient	57 (2783)	54 (2654)	61 (29758)	61 (29696)	0.96 (0.90-1.01)
Specialist	159 (7783)	164 (8038)	163 (79979)	167 (81871)	0.99 (0.96-1.02)

Rates are reported as the number of events per 1000 individuals under 18 years during the baseline period from day -179 to -30 before testing and the post-acute follow-up from day +30 to +179 after testing. PERR=prior event rate ratio adjusted rate ratio. Admissions are defined as any physical hospital contact with a duration of 12 hours or more.

Table S10. Demographic characteristics of Danish vaccine recipients aged 12 to 17 years

	Vaccinated adolescents (N=279,655)
Vaccine	
BNT162b2	278,649 (99.6%)
mRNA-1273	973 (0.3%)
Other*	33 (0.0%)
Completed immunisation	268,508 (96.0%)
Year of birth	
2004	56,811 (20.3%)
2005	54,866 (19.6%)
2006	50,255 (18.0%)
2007	46,224 (16.5%)
2008	42,945 (15.4%)
2009	28,554 (10.2%)
Male sex	142,632 (51.0%)
Region	
Hovedstaden	80,233 (28.7%)
Midtjylland	67,773 (24.2%)
Nordjylland	29,254 (10.5%)
Sjælland	41,336 (14.8%)
Syddanmark	61,059 (21.8%)
Immigration status	
First generation	8,827 (3.2%)
Second generation	12,211 (4.4%)

Characteristics of all Danish vaccine recipients vaccinated against SARS-CoV-2 before or on 31 October 2021. Data on vaccination status was obtained from The Danish Vaccination Register.[6]
* AZD1222 or Ad26.CoV2-S

Table S11. Demographic characteristics on BNT162b2 vaccine recipients included in analyses

	BNT162b2 (first dose)	Unvaccinated	BNT162b2 (second dose)	Unvaccinated
	N=229,799	N=2,296,231	N=175,176	N=1,748,086
Year of birth				
2004	47,377 (20.6%)	473,207 (20.6%)	44,590 (25.5%)	444,038 (25.4%)
2005	45,985 (20.0%)	459,393 (20.0%)	41,740 (23.8%)	416,571 (23.8%)
2006	41,580 (18.1%)	415,537 (18.1%)	30,146 (17.2%)	301,067 (17.2%)
2007	38,334 (16.7%)	383,109 (16.7%)	25,725 (14.7%)	256,894 (14.7%)
2008	35,295 (15.4%)	352,802 (15.4%)	22,458 (12.8%)	224,414 (12.8%)
2009	21,228 (9.2%)	212,183 (9.2%)	10,517 (6.0%)	105,102 (6.0%)
Male sex	117,491 (51.1%)	1,174,089 (51.1%)	89,331 (51.0%)	891,943 (51.0%)
Region				
Hovedstaden	64,928 (28.3%)	649,121 (28.3%)	47,764 (27.3%)	476,761 (27.3%)
Midtjylland	56,365 (24.5%)	563,194 (24.5%)	43,586 (24.9%)	435,121 (24.9%)
Nordjylland	24,240 (10.5%)	242,077 (10.5%)	19,031 (10.9%)	189,963 (10.9%)
Sjælland	33,665 (14.6%)	336,630 (14.7%)	25,315 (14.5%)	253,107 (14.5%)
Syddanmark	50,601 (22.0%)	505,209 (22.0%)	39,480 (22.5%)	393,134 (22.5%)
Immigration status				
First generation	6,263 (2.7%)	131,410 (5.7%)	3,918 (2.2%)	155,533 (8.9%)
Second generation	9,045 (3.9%)	208,059 (9.1%)	5,881 (3.4%)	237,565 (13.6%)

Characteristics of BNT162 recipients and unvaccinated peers included in analyses. Recipients of the first dose were included until 02 October 2021. Recipients of the second dose were included until 02 September 2021 to ensure a follow-up of minimum 60 days.

Table S12. Effectiveness of BNT162b2 vaccine among adolescents 12 thorough 17 years.

	BNT162b2 vaccine recipients		Unvaccinated comparators		Vaccine effectiveness (VE)	
	Events (n/N)	Risk, % (95% CI)	Events (n/N)	Risk, % (95% CI)	VE (95% CI)	IPW-VE (95% CI)
First dose (day 0-20)						
ITT	778/229799	0.34 (0.32, 0.36)	17544/2296231	0.76 (0.75, 0.78)	48 (44-51)	
Complete case**	778/229799	0.34 (0.32, 0.36)	15571/1429266	1.09 (1.07, 1.11)	62 (59-65)	62 (59-65)
Second dose (day 0-59)						
ITT	359/175176	0.20 (0.18, 0.23)	50977/1748086	2.92 (2.89, 2.94)	91 (90-92)	
Complete Case	359/175176	0.20 (0.18, 0.23)	47427/1184197	4.00 (3.97, 4.04)	93 (92-94)	93 (93-94)

Vaccine effectiveness was calculated as (1 – risk ratio) * 100%. Risk ratios were obtained using log-binomial regression adjusted for immigration status. Birth year, sex and municipality of residence was accounted for by matching vaccinated and unvaccinated individuals on these variables.
ITT: Follow up emulated the intention to treat principle, i.e. individuals were followed according to the exposure status at the start of follow up, regardless of changes in the exposure status (unvaccinated individuals being vaccinated during follow up).
Complete case analysis: Unvaccinated individuals who were vaccinated during follow up were excluded from the analysis.
IPW=IP-weighted: Inverse probability of censoring weighted, i.e. individuals who completed follow up were weighted based on selected covariates to also represent censored individuals.

Table S13. Rates of PCR-testing against SARS-CoV-2 in vaccinated and unvaccinated adolescents

	Tests (N)	Person time (months)	Monthly test rate (per 1000 individuals)
Vaccinated	120087	137334	874
Unvaccinated	1258490	1129408	1114

The number of PCR-tests for SARS-CoV-2 performed per 1000 persons per month during follow-up in unvaccinated and vaccinated adolescents aged 12 through 17 years.

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