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eMethods

TriNetX Database and Statistical Analysis Description of TriNetX database: The data used in this study were accessed from August to September 2023 from the TriNetX US Collaborative Network without the use of natural language processing or the Research USA Minimal Date Shift Network with date shifting of records limited to 0-7 days. This resource provides access to electronic health records (diagnoses, procedures, medications, laboratory values, genomic information) from over 100 million patients from 59 healthcare organizations, which is de-identified per criteria from the Health Insurance Portability and Accountability Act (HIPAA), Section §164.514(a) of the HIPAA Privacy Rule. MetroHealth System, Cleveland, Ohio, IRB has determined that research using TriNetX in ways such as described in this manuscript, is not Human Subject Research and therefore exempt from IRB review.

The TriNetX platform de-identifies and aggregates electronic health record (EHR) data from 59 contributing healthcare systems, most of which are large academic medical institutions with both inpatient and outpatient facilities at multiple locations, across all 50 states in the US.   Patient EHR data includes information from hospitals, primary care, and specialty treatment providers, covering diverse geographic locations, age groups, racial and ethnic groups, income levels and insurance types including various commercial insurances, governmental insurance (Medicare and Medicaid), self-pay/uninsured, worker compensation insurance, and military/VA insurance among others. Race and ethnicity data in TriNetX is derived from self-reports in the clinical EHR systems, which is then mapped to the following categories: (1) Race: Asian, American Indian or Alaskan Native, Black or African American, Native Hawaiian or Other Pacific Islander, White, Unknown race; and (2) Ethnicity: Hispanic or Latino, Not Hispanic or Latino, Unknown Ethnicity.

COVID-19 Cohort Inclusion and Exclusion Criteria Codes
Included if any of code below:
U07.1 COVI-19
J12.81 Pneumonia due to SARS-associated coronavirus
J12.82 Pneumonia due to coronavirus disease 2019
9088 (TNX curated) SARS coronavirus 2 and related RNA [Presence] – positive
Excluded if any code below one or more months before the first above code:
E88.01 Alpha-1-antitrypsin deficiency
B15-B19 Viral hepatitis
K70-K77 Diseases of the liver
9047 (TNX curated) Aspartate aminotransferase {Enzymatic activity/volume] in Serum or Plasma ≥ 110 U/L
9044 (TNX curated) Alanine aminotransferase [Enzymatic activity/volume] in Serum, Plasma or Blood ≥ 100 U/L
9050 (TNX curated) Bilirubin total [Mass/volume] in Serum, Plasma or Blood ≥2mg/dL

ORI Cohort Inclusion and Exclusion Criteria Codes

Included if any of code below:

J00-J06 Acute upper respiratory infections

J09-J18 Influenza and pneumonia

J20-J22 Other acute lower respiratory infections

Excluded if any code below one or more months before the first above code:

E88.01 Alpha-1-antitrypsin deficiency

B15-B19 Viral hepatitis

K70-K77 Diseases of the liver

9047 (TNX curated) Aspartate aminotransferase {Enzymatic activity/volume] in Serum or Plasma ≥ 110 U/L

9044 (TNX curated) Alanine aminotransferase [Enzymatic activity/volume] in Serum, Plasma or Blood ≥ 100 U/L

9050 (TNX curated Bilirubin total [Mass/volume] in Serum, Plasma or Blood ≥2mg/dL

Excluded if any code below occurred between January 20, 2020 and March 31, 2020

B97.29 Other coronavirus as the cause of diseases classified elsewhere

B34.2 Coronavirus infection, unspecified

J12.81 Pneumonia due to SARS-associated coronavirus

Excluded if any code below occurred anytime

J12.82 Pneumonia due to coronavirus disease 2019

U07.1 COVID-19

9088 (TNX curated) SARS coronavirus 2 and related RNA [Presence] - positive

Excluded if any code below occurred on or before October 29, 2021

9089 (TNX curated) SARS coronavirus 2 IgG IgM Ab [Presence] in Serum or Plasma – positive

94505-5 SARS-CoV-2 (COVID-19) IgG Ab [Units/volume] in Serum or Plasma by Immunoassay ≥0.1 [arbU]/ml, ever

94506-3 SARS-CoV-2 (COVID-19) IgM Ab [Units/volume] in Serum or Plasma by Immunoassay ≥0.1 [arbU]/ml, ever

94562-6 SARS-CoV-2 (COVID-19) IgA Ab [Presence] in Serum or Plasma by Immunoassay – positive, ever

94762-2 SARS-CoV-2 (COVID-19) Ab [Presence] in Serum or Plasma by Immunoassay – positive, ever

94769-7 SARS-CoV-2 (COVID-19) Ab [Units/volume] in Serum or Plasma by Immunoassay ≥0.1 [IU]/ml, ever

TNX curated 9088 is a composite code created by TriNetX and includes RNA detection tests for SARS-CoV-2 including any of the codes below:

> 94307-6: SARS-CoV-2 (COVID-19) N gene [Presence] in Specimen by Nucleic acid amplification using CDC primer-probe set N110

> 94308-4: SARS-CoV-2 (COVID-19) N gene [Presence] in Specimen by Nucleic acid amplification using CDC primer-probe set N213

> 94309-2: SARS-CoV-2 (COVID-19) RNA [Presence] in Specimen by NAA with probe detection2,104,487

> 94310-0: SARS-related coronavirus N gene [Presence] in Specimen by Nucleic acid amplification using CDC primer-probe set N311

> 94314-2: SARS-CoV-2 (COVID-19) RdRp gene [Presence] in Specimen by NAA with probe detection12,231

> 94315-9: SARS-related coronavirus E gene [Presence] in Specimen by NAA with probe detection10

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94316-7: SARS-CoV-2 (COVID-19) N gene [Presence] in Specimen by NAA with probe detection118,417

94500-6: SARS-CoV-2 (COVID-19) RNA [Presence] in Respiratory specimen by NAA with probe detection4,746,972

94502-2: SARS-related coronavirus RNA [Presence] in Respiratory specimen by NAA with probe detection11,974

94533-7: SARS-CoV-2 (COVID-19) N gene [Presence] in Respiratory specimen by NAA with probe detection51,554

94534-5: SARS-CoV-2 (COVID-19) RdRp gene [Presence] in Respiratory specimen by NAA with probe detection332,029

94559-2: SARS-CoV-2 (COVID-19) ORF1ab region [Presence] in Respiratory specimen by NAA with probe detection48,000

94565-9: SARS-CoV-2 (COVID-19) RNA [Presence] in Nasopharynx by NAA with non-probe detection84,044

94759-8: SARS-CoV-2 (COVID-19) RNA [Presence] in Nasopharynx by NAA with probe detection42,222

94760-6: SARS-CoV-2 (COVID-19) N gene [Presence] in Nasopharynx by NAA with probe detection13,728

94845-5: SARS-CoV-2 (COVID-19) RNA [Presence] in Saliva (oral fluid) by NAA with probe detection28,110

95406-5: SARS-CoV-2 (COVID-19) RNA [Presence] in Nose by NAA with probe detection8,078

95409-9: SARS-CoV-2 (COVID-19) N gene [Presence] in Nose by NAA with probe detection127

96123-5: SARS-CoV-2 (COVID-19) RdRp gene [Presence] in Upper respiratory specimen by NAA with probe detection

LOINC 94558-4: SARS-CoV-2 (COVID-19) Ag [Presence] in Respiratory specimen by Rapid immunoassay

LOINC 94763-0: SARS-CoV-2 (COVID-19) Ag [Presence] in Specimen by Organism specific culture

LOINC 94558-4: SARS-CoV-2+SARS-CoV-2 (COVID-19) Ag [Presence] in Respiratory specimen by Rapid immunoassay

LOINC 96119-3: SARS-CoV-2 (COVID-19) Ag [Presence] in Upper respiratory specimen by Immunoassay

LOINC 96119-3: SARS-CoV-2 (COVID-19) Ag [Presence] in Upper respiratory specimen by Rapid immunoassay

TNX curated 9047 is a composite code for Aspartate aminotransferase {Enzymatic activity/volume] in Serum or Plasma includes any of the codes below:
LOINC 1920-8: Aspartate aminotransferase [Enzymatic activity/volume] in Serum or Plasma
LOINC 30239-8: Aspartate aminotransferase [Enzymatic activity/volume] in Serum or Plasma by With P-5'-P

TNX curated 9044 is a composite code for Alanine aminotransferase [Enzymatic activity/volume] in Serum, Plasma or Blood includes any of the codes below:
LOINC 1742-6: Alanine aminotransferase [Enzymatic activity/volume] in Serum or Plasma
LOINC 1743-4: Alanine aminotransferase [Enzymatic activity/volume] in Serum or Plasma by With P-5'-P
LOINC 1744-2: Alanine aminotransferase [Enzymatic activity/volume] in Serum or Plasma by No addition of P-5'-P
LOINC 76625-3: Alanine aminotransferase [Enzymatic activity/volume] in Blood
LOINC 77144-4: Alanine aminotransferase [Enzymatic activity/volume] in Serum, Plasma or Blood

TNX curated 9050 is a composite code for Bilirubin total [Mass/volume] in Serum, Plasma or Blood includes any of the codes below:
LOINC 1975-2: Bilirubin.total [Mass/volume] in Serum or Plasma
LOINC 42719-5: Bilirubin.total [Mass/volume] in Blood

TNX curated 9089 is a composite code for SARS coronavirus 2 IgG IgM Ab [Presence] in Serum or Plasma includes any of the codes below:
LOINC 94507-1: SARS-CoV-2 (COVID-19) IgG Ab [Presence] in Serum, Plasma or Blood by Rapid immunoassay
LOINC 94508-9: SARS-CoV-2 (COVID-19) IgM Ab [Presence] in Serum, Plasma or Blood by Rapid immunoassay
LOINC 94547-7: SARS-CoV-2 (COVID-19) IgG+IgM Ab [Presence] in Serum or Plasma by Immunoassay
LOINC 94563-4: SARS-CoV-2 (COVID-19) IgG Ab [Presence] in Serum or Plasma by Immunoassay
LOINC 94564-2: SARS-CoV-2 (COVID-19) IgM Ab [Presence] in Serum or Plasma by Immunoassay
LOINC 94761-4: SARS-CoV-2 (COVID-19) IgG Ab [Presence] in DBS by Immunoassay
LOINC 99596-9: SARS-CoV-2 (COVID-19) N protein IgG Ab [Presence] in Serum or Plasma by Immunoassay
LOINC 99597-7: SARS-CoV-2 (COVID-19) S protein IgG Ab [Presence] in Serum or Plasma by Immunoassay

Matching codes:
Age: Current age
AI: Age at index
M: Male
F: Female
UN: Unknown gender
2186-5: Not Hispanic or Latino
2134-2: Hispanic or Latino
UN: Unknown ethnicity
2106-3: White
2054-5: Black or African American
2028-9: Asian
1002-5: Native American/Alaska native
2076-8: Native Hawaiian or Other Pacific Islander
2131-1: Unknown race
Z23: Encounter for immunization
Z68.5: Body mass index [BMI] pediatric
Z68.51: Body mass index [BMI] pediatric, less than 5th percentile for age
Z68.52: Body mass index [BMI] pediatric, 5th percentile to less than 85th percentile for age
Z68.53: Body mass index [BMI] pediatric, 85th percentile to less than 95th percentile for age
Z68.54: Body mass index [BMI] pediatric, greater than or equal to 95th percentile for age
1013829: Preventive medicine services
91300: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]) vaccine, mRNA-LNP, spike protein, preservative free, 30 mcg/0.3mL dosage, diluent reconstituted, for intramuscular use

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eTable 1. Baseline Characteristics of Study Population Before and After Matching (Age 1-4 Years)

	Unmatched cohort, No. (%)			Matched cohort, No. (%)		
	COVID-19 n=119,455	ORI n=601,209	SMD	COVID-19 n=119,379	ORI n=119,379	SMD
Age at Index in years, mean (SD)	2.33±1.20	2.18±1.14	0.12	2.32±1.19	2.31±1.14	0.003
Sex						
Male	63,621 (53.3)	321,076 (53.4)	<0.01	63,588 (53.3)	63,557 (53.2)	<0.001
Female	55,763 (46.7)	279,941 (46.6)	<0.01	55,727 (46.7)	55,758 (46.7)	<0.001
Unknown	71 (0.1)	192 (<0.1)	0.01	64 (0.1)	64 (0.1)	<0.001
Ethnicity						
Not Hispanic	73,625 (61.6)	370,871 (61.7)	<0.01	73,576 (61.6)	73,550 (61.6)	<0.001
Hispanic	20,717 (17.3)	104,616 (17.4)	<0.01	20,696 (17.3)	20,719 (17.3)	<0.001
Unknown	25,113 (21.0)	125,722 (20.9)	<0.01	25,107 (21.0)	25,110 (21.0)	<0.001
Race						
White	61,653 (51.6)	314,847 (52.4)	0.02	61,610 (51.6)	61,579 (51.6)	<0.001
Black	23.707 (19.8)	116,257 (19.3)	0.01	23,688 (19.8)	23,674 (19.8)	<0.001
Asian	5052 (4.2)	23,633 (3.9)	0.01	5050 (4.2)	5091 (3.3)	0.002
Native American or Alaska Native	597 (0.5)	3362 (0.6)	0.01	597 (0.5)	587 (0.5)	0.001
Native Hawaiian or Other Pacific Islander	512 (0.4)	2900 (0.5)	0.01	512 (0.4)	513 (0.4)	<0.001
Unknown Race	27,934 (23.4)	140,210 (23.3)	<0.01	27,922 (23.4)	27,935 (23.4)	<0.001
BMI, pediatric						
measured	10,503 (8.8)	230,511 (38.3)	0.01	10,480 (8.8)	10,452 (8.8)	0.001
<5th percentile	998 (0.8)	4712 (0.8)	0.02	995 (0.8z0	934 (0.8)	0.006
5th to <85th percentile	7566 (6.3)	41,029 (6.8)	<0.01	7561 (6.3)	7537 (6.3)	0.001
85th to <95th percentile	1723 (1.4)	8441 (1.4)	<0.01	1718 (1.4)	1695 (1.4)	0.002
≥95th percentile	1969 (1.6)	8949 (1.5)	0.01	1954 (1.6)	1961 (1.6)	0.001
Preventive medicine services	44,338 (37.1)	239,056 (39.8)	0.05	44,323 (37.1)	44,460 (37.2)	0.002

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Encounter for immunization	41,480 (34.7)	230,511 (38.3)	0.08	41,463 (34.7)	41,516 (34.8)	0.001
SARS-CoV-2 vaccination	235 (0.2)	1580 (0.3)	0.01	235 (0.2)	201 (0.2)	0.007

Abbreviations: ORI, other respiratory infection; SMD, standard mean difference; SD, standard deviation

eTable 2. Baseline Characteristics of Study Population Before and After Matching with Inpatient Stay (Age 1-10 Years)

	Unmatched cohort, No. (%)			Matched cohort, No. (%)		
	COVID-19 n=10,257	ORI n=44,970	SMD	COVID-19 n=10,256	ORI n=10,256	SMD
Age at Index in years, mean (SD)	4.59±3.06	3.56±2.69	0.36	4.59±3.06	4.55±3.04	0.013
Sex						
Male	5628 (54.9)	24,930 (55.4)	0.01	5628 (54.9)	5608 (54.7)	0.004
Female	4626 (45.1)	20,034 (44.6)	0.01	4625 (45.1)	4647 (45.3)	0.004
Unknown	10	10		10	10	
Ethnicity						
Not Hispanic	6612 (64.5)	30,457 (67.7)	0.07	6612 (64.5)	6595 (64.3)	0.004
Hispanic	2095 (20.4)	7346 (16.3)	0.11	2094 (20.4)	2119 (20.7)	0.006
Unknown	1550 (15.1)	7167 (15.9)	0.02	1550 (15.1)	1542 (15.0)	0.002
Race						
White	5164 (50.3)	24,252 (53.9)	0.07	5164 (50.4)	5212 (50.8)	0.009
Black	2151 (21.0)	9078 (20.2)	0.02	2150 (21.0)	2161 (21.1)	0.003
Asian	330 (3.2)	1407 (3.1)	0.01	330 (3.2)	311 (3.0)	0.011
Native American or Alaska Native	92 (0.9)	494 (1.1)	0.02	92 (0.9)	68 (0.7)	0.027
Native Hawaiian or Other Pacific Islander	25 (0.2)	119 (0.3)	<0.01	25 (0.2)	24 (0.2)	0.002
Unknown Race	2495 (24.3)	9620 (21.4)	0.07	2495 (24.3)	2480 (24.2)	0.003
BMI, pediatric						
measured	1352 (13.2)	8119 (18.1)	0.13	1352 (13.2)	1310 (12.8)	0.012
<5th percentile	184 (1.8)	800 (1.8)	<0.01	184 (1.8)	150 (1.5)	0.026
5th to <85th percentile	860 (8.4)	5621 (12.5)	0.13	860 (8.4)	835 (8.1)	0.009
85th to <95th percentile	326 (3.2)	1841 (4.1)	0.05	326 (3.2)	306 (3.0)	0.011
≥95th percentile	428 (4.2)	2067 (4.6)	0.05	326 (3.2)	306 (3.0)	0.011
Preventive medicine services	3247 (31.7)	16,022 (35.6)	0.08	3246 (31.6)	3284 (32.0)	0.008
Encounter for immunization	2710 (26.4)	14,572 (32.4)	0.13	2710 (26.4)	2704 (26.4)	0.001
SARS-CoV-2 vaccination	52 (0.5)	290 (0.6)	0.02	52 (0.5)	35 (0.3)	0.026

Abbreviations: ORI, other respiratory infection; SMD, standard mean difference; SD, standard deviation

eTable 3. Baseline Characteristics of Study Population Before and After Matching with Inpatient Stay (Age 1-4 Years)

	Unmatched cohort, No. (%)			Matched cohort, No. (%)		
	COVID-19 n=5575	ORI n=30,807	SMD	COVID-19 n=5574	ORI n=5574	SMD
Age at Index in years, mean (SD)	2.12±1.13	1.96±1.07	0.14	2.12±1.13	2.12±1.12	0.003
Sex						
Male	3099 (55.6)	17,438 (56.6)	0.02	3098 (55.6)	3085 (55.3)	0.004
Female	2475 (44.4)	13,365 (43.4)	0.02	2475 (44.4)	2489 (44.7)	0.005
Unknown	10	10		10	0	
Ethnicity						
Not Hispanic	3512 (63.0)	20,511 (66.6)	0.08	3512 (63.0)	3498 (62.8)	0.005
Hispanic	1133 (20.3)	4962 (16.1)	0.11	1132 (20.3)	1146 (20.6)	0.006
Unknown	930 (16.7)	5334 (17.3)	0.02	930 (16.7)	930 (16.7)	<0.001
Race						
White	2709 (48.6)	16,096 (52.2)	0.07	2709 (48.6)	2736 (49.1)	0.010
Black	1133 (20.0)	6129 (19.9)	<0.01	1112 (20.0)	1106 (19.8)	0.003
Asian	201 (3.6)	1030 (3.3)	0.01	201 (3.6)	209 (3.8)	0.008
Native American or Alaska Native	47 (0.8)	363 (1.2)	0.03	47 (0.2)	42 (0.8)	0.010
Native Hawaiian or Other Pacific Islander	13 (0.2)	83 (0.3)	0.01	13	10	
Unknown Race	1492 (26.8)	7106 (23.1)	0.09	1492 (26.8)	1476 (26.5)	0.006
BMI, pediatric						
measured	412 (7.4)	3143 (10.2)	0.10	412 (7.4)	375 (6.7)	0.026
<5th percentile	75 (1.3)	382 (1.2)	0.01	75 (1.3)	53 (1.0)	0.037
5th to <85th percentile	272 (4.9)	2237 (7.3)	0.10	272 (4.9)	260 (4.7)	0.010
85th to <95th percentile	76 (1.4)	537 (1.7)	0.03	76 (1.4)	79 (1.4)	0.005
≥95th percentile	78 (1.4)	561 (1.8)	0.03	78 (1.4)	66 (1.2)	0.019
Preventive medicine services	1544 (27.7)	9491 (30.8)	0.07	1543 (27.7)	1559 (28.0)	0.006
Encounter for immunization	1361 (24.4)	8901 (28.9)	0.08	1361 (24.4)	1367 (24.5)	0.002
SARS-CoV-2 vaccination	10	96		10	10	

Abbreviations: ORI, other respiratory infection; SMD, standard mean difference; SD, standard deviation

eTable 4. Comparison of clinical outcomes during 1 to 6 months after COVID-19 vs ORI among matched cohorts of patients aged 1-10 years (01/01/2020 – 12/31/2022), not excluding those with liver abnormalities in the acute phase

n, All 1-4 = 119,379 n, All 1-10 = 260,132 n, Inpt 1-4 = 5575 n, Inpt 1-10 = 10,256		Age Group (years)	COVID-19 Cohort No.	ORI Cohort No.	RR (95%CI)
Elevated AST[a] or ALT[b]	All	1-4	245	82	2.99 (2.33-3.84)
		1-10	472	144	3.28 (2.72-3.95)
	Inpt	1-4	156	44	3.45 (2.54-4.94)
		1-10	274	70	3.91 (3.02-5.08)
Elevated TBil[c]	All	1-4	74	21	3.52 (2.17-5.72)
		1-10	148	31	4.77 (3.24-7.03)
	Inpt	1-4	41	12	3.42 (1.80-6.49)
		1-10	72	16	4.50 (2.62-7.73)
Diseases of the liver (K70-K77) OR viral hepatitis (B15-B19)	All	1-4	71	29	2.45 (1.59-3.77)
		1-10	170	85	2.00 (1.54-2.60)
	Inpt	1-4	40	13	3.08 (1.65-5.75)
		1-10	72	15	4.80 (2.75-8.37)
Diseases of the liver (K70-K77)	All	1-4	60	17	3.53 (2.06-6.05)
		1-10	156	69	2.26 (1.70-3.00)
	Inpt	1-4	39	13	3.00 (1.60-5.61)
		1-10	69	14	4.93 (2.78-8.75)
Other inflammatory disease of the liver (K75)	All	1-4	16	10	1.60 (0.73-3.53)
		1-10	31	11	2.82 (1.42-5.61)
	Inpt	1-4	14	10	1.40 (0.62-3.15)
		1-10	23	10	2.30 (1.10-4.83)
Other diseases of the liver (K76)	All	1-4	40	13	3.08 (1.65-5.75)
		1-10	120	60	2.00 (1.47-2.73)
	Inpt	1-4	24	10	2.40 (1.15-5.01)
		1-10	40	10	4.60 (2.32-9.11)
Hepatitis of unspecified etiology[d]	All	1-4	20	10	2.00 (0.94-4.27)
		1-10	32	13	2.83 (1.29-4.69)
	Inpt	1-4	17	10	1.70 (0.78-3.71)
		1-10	22	10	2.20 (1.04-4.64)

Abbreviations: ORI, other respiratory infection; RR, risk ratio; CI, confidence interval; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBil, total bilirubin; Inpt, inpatient. Cohorts matched on factors listed in Table 1. Patients with pre-existing disease are excluded from the cohorts; however, patients with the outcome during the acute period (from 1 months before to month after COVID-19 or ORI indexed encounter diagnosis) are NOT excluded from the analysis.

[a] AST ≥110 units per liter

[b] ALT ≥100 units per liter

[c] TBil ≥2 milligrams per deciliter

[d] Surveillance codes include B17.8, B17.9, B19.0, B19.9, K71.6, K72.0, K72.9, K75.2, K75.9

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eTable 5. Comparison of clinical outcomes during 1 to 6 months after COVID-19 vs ORI among matched cohorts of patients aged 1-10 years (01/01/2020 – 12/31/2022), not excluding those with previous liver abnormalities					
n, All 1-4 = 129,111 n, All 1-10 = 279,161 n, Inpt 1-4 = 6520 n, Inpt 1-10 = 11,995		Age Group (years)	COVID-19 Cohort No.	ORI Cohort No.	RR (95%CI)
Elevated AST[a] or ALT[b]	All	1-4	468	127	3.68 (3.03-4.48)
		1-10	930	267	3.48 (3.04-3.99)
	Inpt	1-4	320	77	4.16 (3.25-5.32)
		1-10	589	171	3.44 (2.91-4.08)
Elevated TBil[c]	All	1-4	161	45	3.58 (2.57-4.98)
		1-10	383	117	3.27 (2.66-4.03)
	Inpt	1-4	92	22	4.18 (2.63-6.65)
		1-10	204	74	2.76 (2.12-3.59)
Diseases of the liver (K70-K77) OR viral hepatitis (B15-B19)	All	1-4	159	55	2.89 (2.13-3.93)
		1-10	367	165	2.22 (1.85-2.67)
	Inpt	1-4	95	22	4.32 (2.72-6.86)
		1-10	158	49	3.22 (2.34-4.44)
Viral hepatitis (B15-B19)	All	1-4	32	13	2.46 (1.29-4.69)
		1-10	42	17	2.47 (1.41-4.34)
	Inpt	1-4	*	*	*
		1-10	*	*	*
Diseases of the liver (K70-K77)	All	1-4	132	43	3.07 (2.18-4.33)
		1-10	333	151	2.21 (1.82-2.67)
	Inpt	1-4	92	22	4.18 (2.63-6.65)
		1-10	153	49	3.12 (2.27-4.30)
Hepatic failure, not elsewhere classified (K72)	All	1-4	24	10	2.40 (1.15-5.02)
		1-10	41	21	1.95 (1.15-3.30)
	Inpt	1-4	18	11	1.64 (0.77-3.46)
		1-10	22	12	1.83 (0.91-3.70)
Other inflammatory disease of the liver (K75)	All	1-4	30	10	3.00 (1.47-6.14)
		1-10	70	16	4.38 (2.54-7.53)
	Inpt	1-4	23	10	2.30 (1.10-4.83)
		1-10	41	11	3.73 (1.92-7.25)
Other diseases of the liver (K76)	All	1-4	89	32	2.78 (1.86-4.16)
		1-10	242	124	1.95 (1.57-2.42)
	Inpt	1-4	61	10	6.10 (3.13-11.90)
		1-10	103	34	3.03 (2.06-4.46)
Hepatitis of unspecified etiology[d]	All	1-4	44	10	4.40 (2.21-8.74)
		1-10	66	27	2.44 (1.56-3.83)
	Inpt	1-4	34	11	3.09 (1.57-6.10)
		1-10	44	15	2.93 (1.63-5.27)

Abbreviations: ORI, other respiratory infection; RR, risk ratio; CI, confidence interval; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBil, total bilirubin; Inpt, inpatient. Cohorts matched on factors listed in Table 1. Patients with pre-existing disease are NOT excluded from the cohorts;

patients with the outcome during the acute period (from 1 months before to month after COVID-19 or ORI indexed encounter diagnosis) are also NOT excluded from the analysis.

[a] AST ≥110 units per liter

[b] ALT ≥100 units per liter

[c] TBil ≥2 milligrams per deciliter

[d] Surveillance codes include B17.8, B17.9, B19.0, B19.9, K71.6, K72.0, K72.9, K75.2, K75.9

*Indicates counts too few to report

eTable 6. Comparison of elevated laboratory values during 1 to 6 months after COVID-19 vs ORI among matched cohorts of pediatric patients with laboratory values measured during the acute period of infection (01/01/2020 – 12/31/2022)

n, (1-4) = 5513 n, (1-10) = 11,210	Age Group	COVID-19 Cohort No.	ORI Cohort No.	RR (95% CI)
Elevated AST[a] or ALT[b]	1-4	82	37	2.23 (1.50-3.27)
	1-10	334	107	3.12 (2.51-3.88)
Elevated TBil[c]	1-4	19	10	3.61 (1.35-9.66)
	1-10	97	38	2.55 (1.76-3.71)

Abbreviations: ORI, other respiratory infection; HR, hazard ratio; CI, confidence interval; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBil, total bilirubin; Inpt, inpatient. Cohorts matched on factors listed in Table 1. Patients with elevated labs from 0 to 1 months after respiratory illness are NOT excluded from this analysis.

[a] AST ≥110 units per liter

[b] ALT ≥100 units per liter

[c] TBil ≥2 milligrams per deciliter

eTable 7. Comparison of pre-existing conditions among cases with hepatic complications[a] after COVID-10 vs ORI aged 1 – 10 years (01/01/2020 – 12/31/2022)						
	All Cases			Cases with Inpatient Stay		
	COVID-19 (%)	ORI (%)	SMD	COVID-19 (%)	ORI (%)	SMD
Age at Index in years, mean (SD)	5.51±3.24	4.42±3.21	0.34	4.70±3.02	4.29±3.20	0.13
Sex						
Male	61	58	0.06	57	56	0.02
Female	39	42	0.06	43	44	0.02
Unknown	N/A	N/A	N/A	N/A	N/A	N/A
Ethnicity						
Not Hispanic	63	59	0.07	63	75	0.26
Hispanic	27	25	0.05	19	11	0.22
Unknown	14	26	0.16	18	14	0.11
Race						
White	49	60	0.22	42	56	0.27

Black	21	12	0.24	27	17	0.24
Asian	*	*	*	*	*	*
Native American or Alaska Native	*	*	*	*	*	*
Native Hawaiian or Other Pacific Islander	*	*	*	*	*	*
Unknown Race	24	23	0.02	27	21	0.13
BMI, pediatric						
measured	31	11	0.50	16	26	0.26
<5th percentile	1	1	<0.01	*	*	*
5th to <85th percentile	10	6	0.14	*	*	*
85th to <95th percentile	*	*	*	*	*	*
≥95th percentile	20	7	0.38	*	*	*
Preventive medicine services	31	20	0.26	22	27	0.12
Encounter for immunization	34	19	0.36	24	35	0.24
SARS-CoV-2 vaccination	*	*	*	*	*	*
A00-B99 Certain infectious and parasitic diseases	46	27	0.40	46	50	0.08
C00-D49 Neoplasm	15	8	0.22	20	12	0.22
D50-D89 Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	34	13	0.49	43	30	0.29
E00-E89 Endocrine, nutritional and metabolic diseases	68	40	0.57	54	47	0.15
F01-F99 Mental, Behavioral and Neurodevelopmental disorders	31	18	0.31	33	37	0.08
G00-G99 Diseases of the nervous system	33	16	0.39	29	41	0.25
H00-H59 Diseases of the eye and adnexa	34	14	0.49	30	38	0.17
H60-H95 Diseases of the ear and mastoid process	43	21	0.47	36	37	0.01
I00-I99 Diseases of the circulatory system	24	15	0.22	30	38	0.17
J00-J99 Diseases of the respiratory system	59	31	0.59	52	70	0.39
K00-K95 Diseases of the digestive system	51	36	0.32	52	62	0.20
L00-L99 Diseases of the skin and subcutaneous tissue	43	24	0.40	42	43	0.01
M00-M99 Diseases of the musculoskeletal system and connective tissue	30	15	0.36	29	33	0.09
N00-N99 Diseases of the genitourinary system	24	15	0.24	24	26	0.05
P00-P96 Certain conditions originating in the perinatal period	13	16	0.08	16	30	0.36

Supplemental material

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Q00-Q99 Congenital malformations, deformations and chromosomal abnormalities	27	27	<0.01	31	48	0.34
S00-T88 Injury, poisoning and certain other consequences of external causes	40	27	0.28	43	46	0.05
V00-Y99 External causes of morbidity	18	8	0.28	18	19	0.03

Abbreviations: ORI, other respiratory infection; SMD, standard mean difference; SD, standard deviation

Shading highlights the cohort with the higher proportion when SMD is ≥ 0.1

[a] Any encounter diagnosis of K70-K77 or B15-B19 during the 1-6 month follow-up period after respiratory infection

*Indicates counts too small to calculate %