Covid-19 in Kids

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Disclaimers

1. We have no conflicts of interest, financial or otherwise, related to this talk

2. We are not infectious disease physicians…we are not epidemiologists

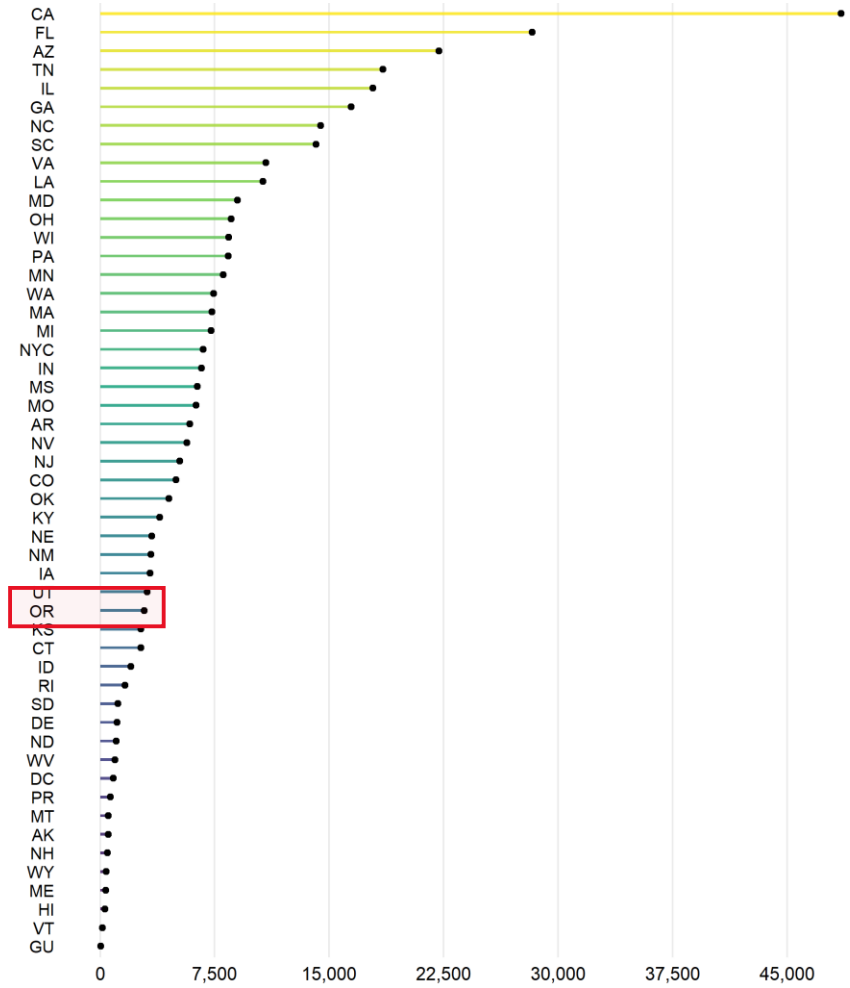
…better, we're ED docs. We'll just wing it!!!

Outline

- Epidemiology of COVID in kids
- Transmissibility of COVID in kids
- Acute Infection
  - What are the symptoms and how bad is it in kids?
  - Testing and its implications
  - Collateral COVID concerns
- Multisystem Inflammatory Syndrome in Children
  - What is this? How's it different than acute infection and how do I spot it?

Cumulative COVID-19 Child Cases 8.6.2020

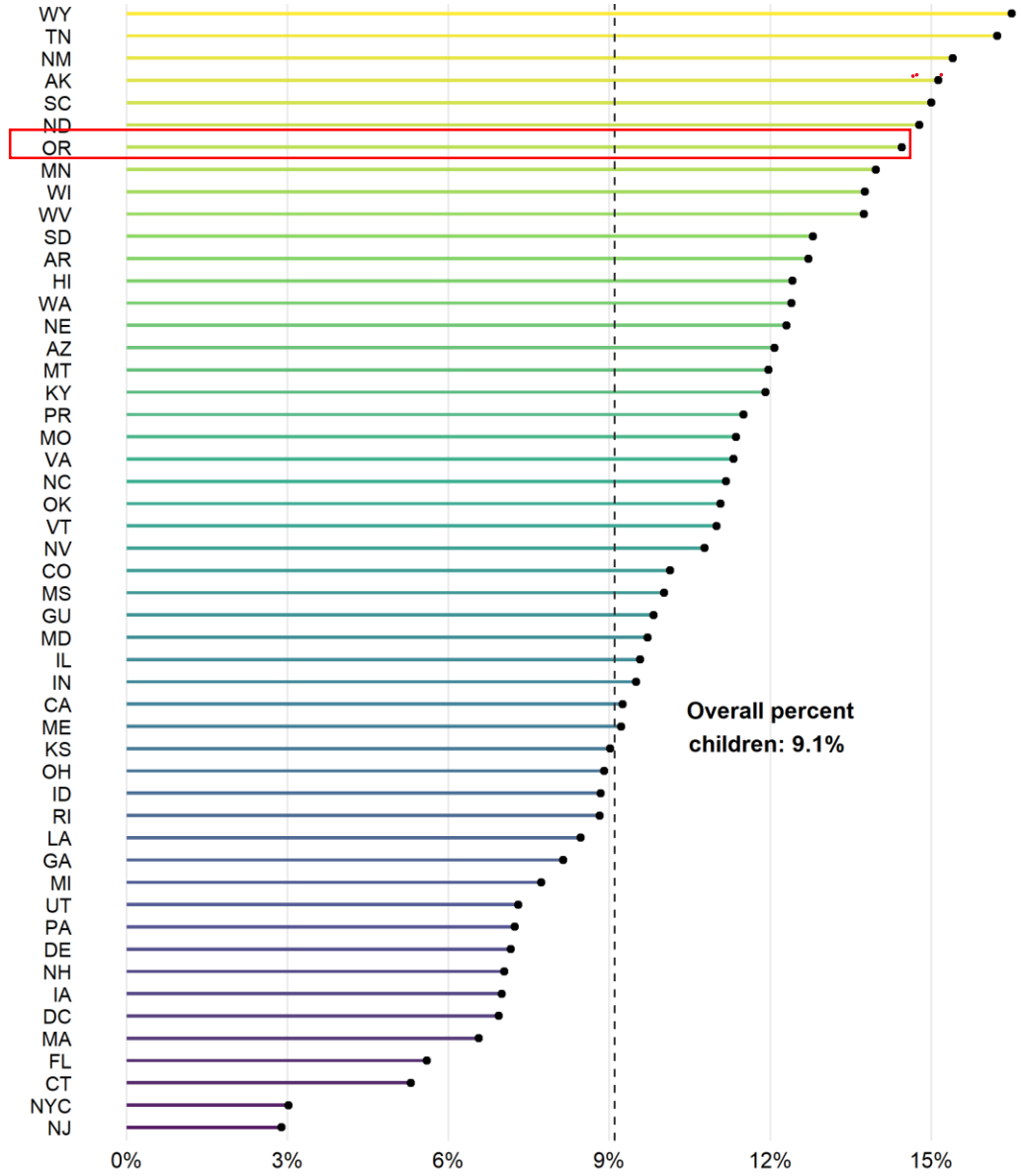
- 380,174 total child COVID-19 cases
- Seven states with 15,000+ cumulative child cases
- Oregon 2,887 child cases
- Half of states reported 5,000+ child cases



Analysis by American Academy of Pediatrics and Children's Hospital Association

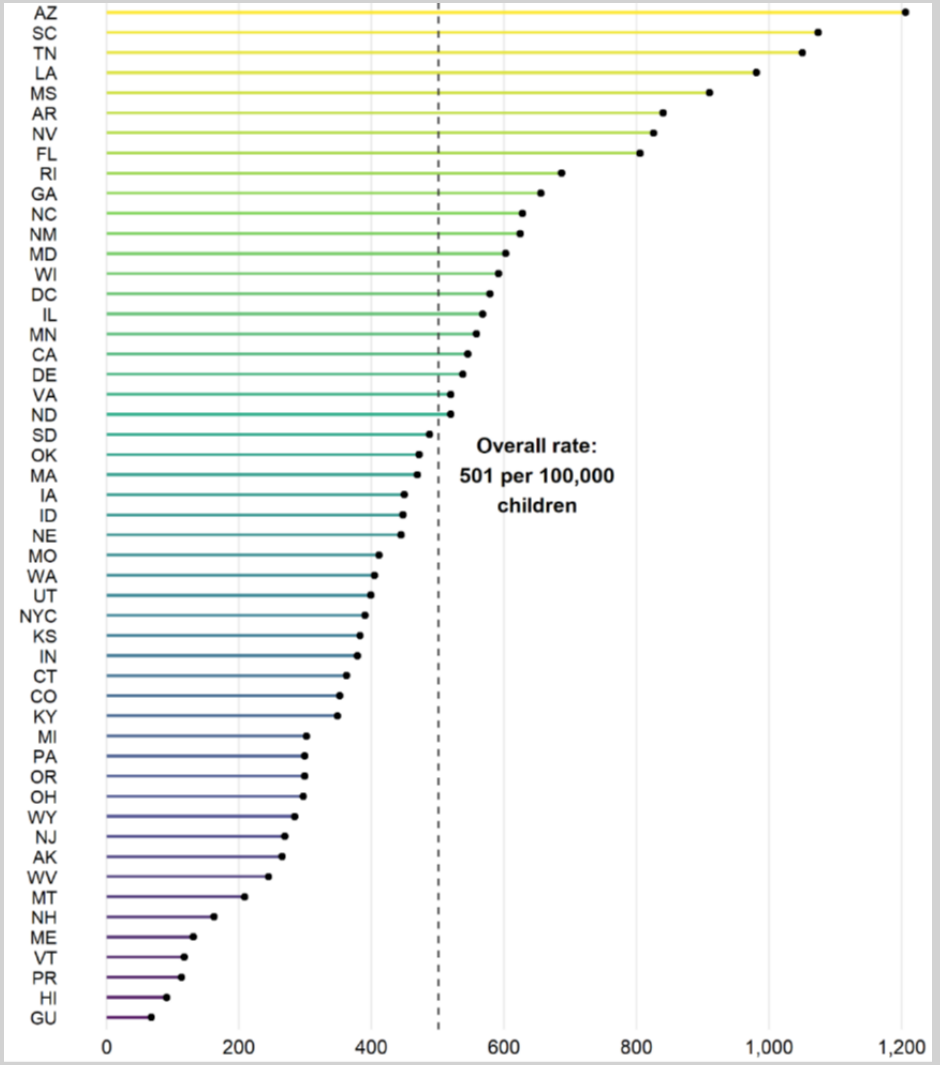
Percent of Cumulative COVID-19 Cases that were Children 8.6.2020

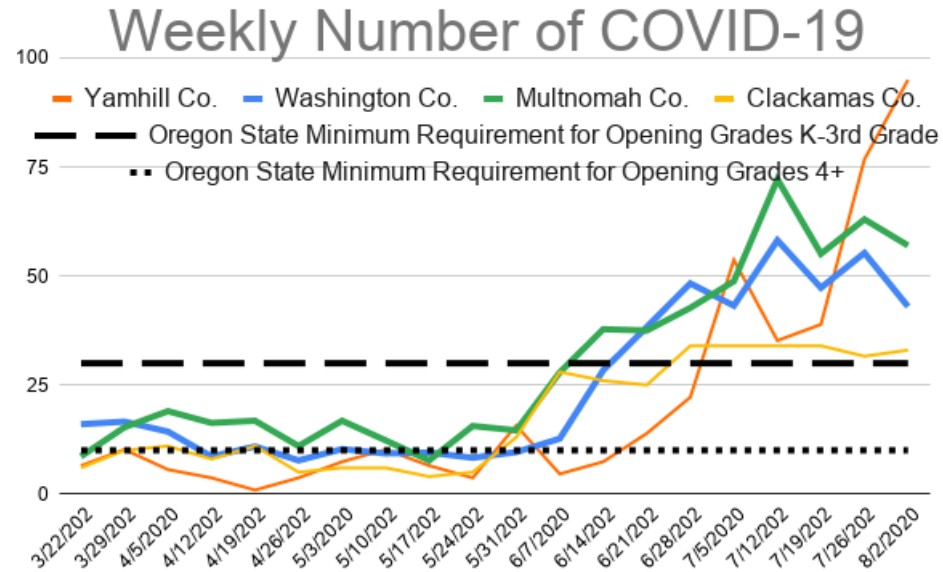
- Children represented 9.1% of all available cases in United States
- 14.5% of pediatric cases were children in Oregon



Cumulative COVID-19 cases per 100,000 children 8.6.2020

- US rate: 501 child COVID-19 cases per 100,000 children
- Oregon: 299 cases per 100,000 children





OREGON DEPARTMENT OF EDUCATION

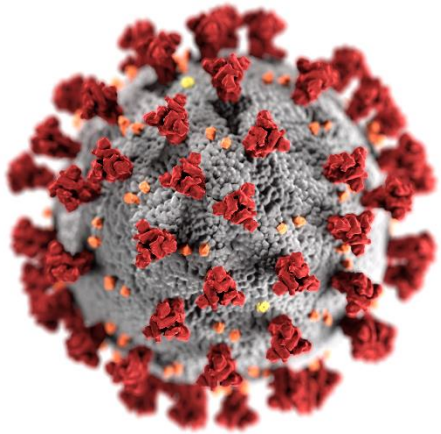
Oregon Health Authority

Ready Schools, Safe Learners: Community COVID-19 Metrics

School re-opening?

Kristine B. Rabii, MSc., CIC

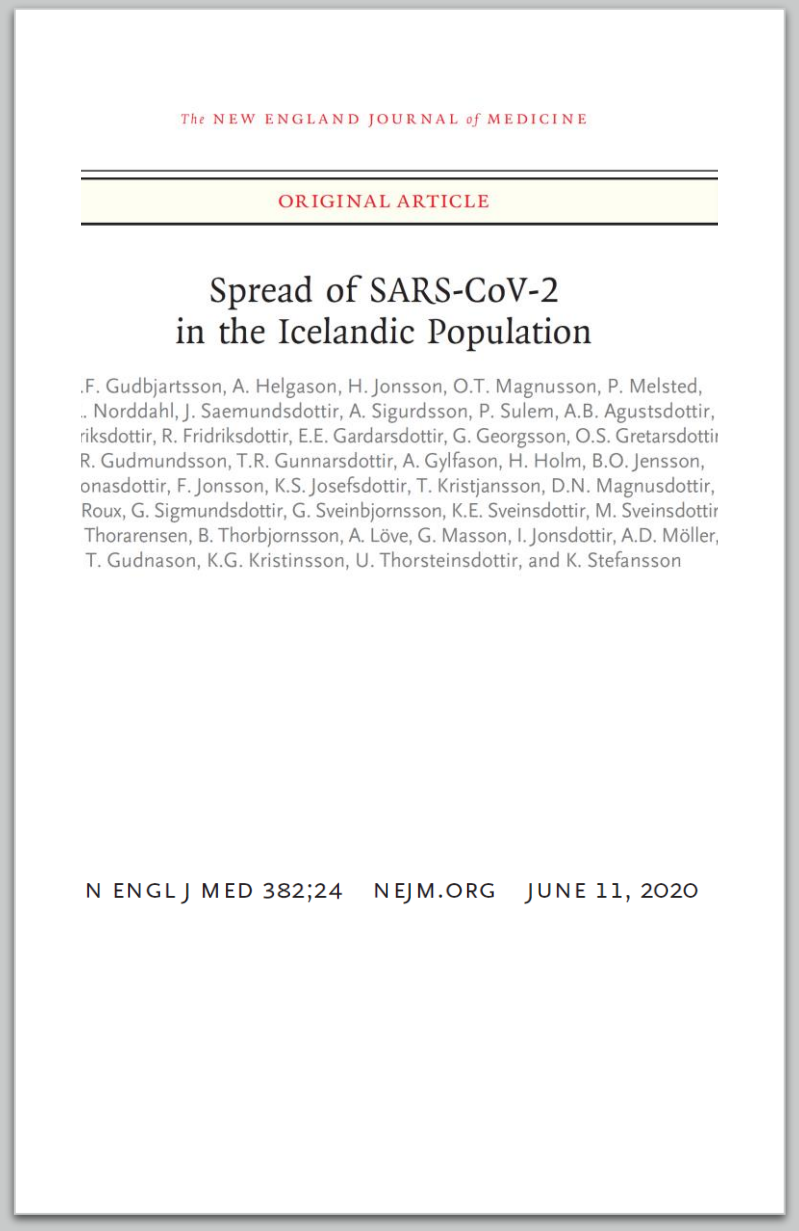
Transmissibility



Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study

*Kristine Macartney, Helen E Quinn, Alexis J Pillsbury, Archana Koirala, Lucy Deng, Noni Winkler, Anthea L Katelaris, Matthew V N O'Sullivan, Craig Dalton, Nicholas Wood, and the NSW COVID-19 Schools Study Team**

Lancet Child Adolesc Health 2020



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Spread of SARS-CoV-2 in the Icelandic Population

.F. Gudbjartsson, A. Helgason, H. Jonsson, O.T. Magnusson, P. Melsted, .. Norddahl, J. Saemundsdottir, A. Sigurdsson, P. Sulem, A.B. Agustsdottir, riksdottir, R. Fridriksdottir, E.E. Gardarsdottir, G. Georgsson, O.S. Gretarsdottir R. Gudmundsson, T.R. Gunnarsdottir, A. Gylfason, H. Holm, B.O. Jensson, onasdottir, F. Jonsson, K.S. Josefsdottir, T. Kristjansson, D.N. Magnusdottir, Roux, G. Sigmundsdottir, G. Sveinbjornsson, K.E. Sveinsdottir, M. Sveinsdottir Thorarensen, B. Thorbjornsson, A. Löve, G. Masson, I. Jonsdottir, A.D. Möller, T. Gudnason, K.G. Kristinsson, U. Thorsteinsdottir, and K. Stefansson

N ENGL J MED 382;24 NEJM.ORG JUNE 11, 2020

- Random Sampling:
  - Zero cases in < 10 year-old children
- High Risk Sample:
  - Case rate for children were half those in adults (7% vs 14%)

Articles

Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study

*Marina Pollán, Beatriz Pérez-Gómez, Roberto Pastor-Barriuso, Jesús Oteo, Miguel A Hernán, Mayte Pérez-Olmeda , Jose L Sanmartín, Aurora Fernández-García, Israel Cruz, Nerea Fernández de Larrea, Marta Molina, Francisco Rodríguez-Cabrera, Mariano Martín, Paloma Merino-Amador, Jose León Paniagua, Juan F Muñoz-Montalvo, Faustino Blanco, Raquel Yotti, on behalf of the ENE-COVID Study Group**

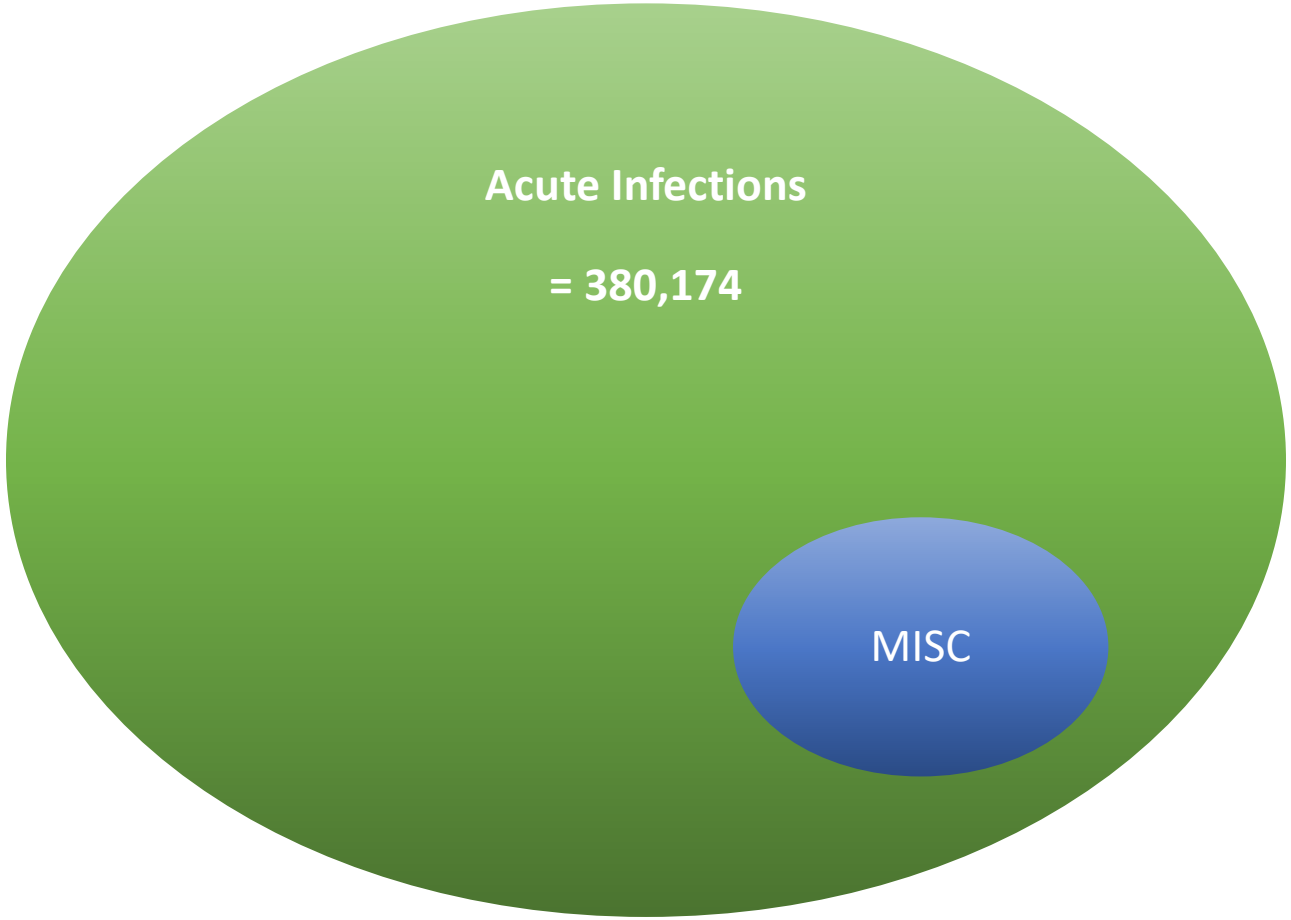
- Antibody prevalence in community from April 27th – May 11th
  - 3.1% of children < 10 years of age vs 5% overall

Lancet, July 6, 2020

Children are unlikely to have been the primary source of household SARS-CoV-2 infections

Children generally get COVID from Adults

Acute COVID-19 Infection in Children



Who was getting infected and how bad was it?

Table 1 Disease severity

Asymptomatic: all the following must be present

1. No signs or symptoms
2. AND negative chest X-ray
3. AND absence of criteria for other cases

Mild: any of the following (AND absence of criteria for more severe cases)

1. Symptoms of upper respiratory tract infection
2. AND absence of pneumonia at chest X-ray

Moderate: all the following (AND absence of criteria for more severe cases)

1. Cough AND (sick appearing OR pneumonia at chest X-ray)

Severe: any of the following (AND absence of criteria as for critical case)

2. Oxygen saturation < 92%
3. OR difficult breathing or other signs of severe respiratory distress (apnea, gasping, head nodding)
4. OR need for any respiratory support

Critical: Any of the following

1. Patient in ICU
2. OR intubated
3. OR multiorgan failure
4. OR shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, acute kidney injury.

Adapted from Dong Y et al. [4]

Table 1 Characteristics of Children' COVID-19 Cases in China

Characteristics	All cases	Different Category		
		Confirmed	Suspected	*P* Value
Median age (Interquartile range)	7.00 (11.0)	10.00(11.0)	6.00(10.0)	<0.001
Age group				
<1	379(17.7)	86(11.8)	293(20.8)	
1-5	493(23.0)	137(18.7)	356(25.2)	
6-10	523(24.4)	171(23.4)	352(24.9)	<0.001
11-15	413(19.3)	180(24.6)	233(16.5)	
>15	335(15.6)	157(21.5)	178(12.6)	
Gender				
Boy	1213(56.6)	420(57.5)	793(56.2)	0.567
Girl	930(43.4)	311(42.5)	619(43.8)	
Severity of illness				
Asymptomatic	94(4.4)	94(12.9)	0(0.0)	
Mild	1091(50.9)	315(43.1)	776(54.9)	
Moderate	831(38.8)	300(41.0)	531(37.6)	
Severe	112(5.2)	18(2.5)	94(6.7)	<0.001
Critical	13(0.6)	3(0.4)	10(0.7)	
Missing	2(0.1)	1(0.1)	1(0.1)	
Days from symptom onset to diagnosis				
Median days (Interquartile range)	2(4.0)	3(4.0)	2(4.0)	<0.001
Range	0-42	0-42	0-36	
Province				
Hubei	984(45.9)	229(31.3)	755(53.5)	
Surrounding areas*	397(18.5)	155(21.2)	242(17.1)	<0.001
Others	762(35.6)	347(47.5)	415(29.4)	
Total	2143	731(34.1)	1412(65.9)	

Data are presented with median (Interquartile range) and n (%).
*Surrounding areas are the provinces and Municipality bordering Hubei, they are Anhui, Henan, Hunan, Jiangxi, Shaanxi and Chongqing.

What Symptoms are Patients Presenting With and Can that Severity be Accurate?

Table 1. Epidemiologic Characteristics, Clinical Features, and Outcomes in the Italian CONFID

Characteristics	CONFIDENCE Study (N=100)
Median age (range) — yr	3.3 (0–17.5)
Age distribution — no. (%)	
<1 yr	40 (40.0)
1 to <6 yr	15 (15.0)
6–10 yr	21 (21.0)
>10 yr	24 (24.0)
Sex — no./total no. (%)	
Female	43/100 (43.0)
Male	57/100 (57.0)
Coexisting conditions — no./total no. (%)	27/100 (27.0)
Exposure to SARS-CoV-2 — no./total no. (%)	
Family cluster	45/100 (45.0)
Other exposure	48/100 (48.0)
Unknown exposure	7/100 (7.0)
Signs and symptoms in patients for whom data were available — no./total no. (%)	100/100 (100.0)
Symptomatic on presentation in emergency department — no./total no. (%)	79/100 (79.0)
Fever, cough, or shortness of breath — no./total no. (%)	28/54 (51.8)
Fever — no./total no. (%)	54/100 (54.0)
Temperature — no./total no. (%)§	
≤37.5°C	46/100 (46.0)
37.6–38.0°C	15/100 (15.0)
38.1–39.0°C	28/100 (28.0)
>39.0°C	11/100 (11.0)
Symptoms — no./total no. (%)	
Cough	44/100 (44.0)
Shortness of breath	11/100 (11.0)
No feeding or difficulty feeding	23/100 (23.0)
Rhinorrhea	22/100 (22.0)
Drowsiness	11/100 (11.0)
Nausea or vomiting	10/100 (10.0)
Fatigue	9/100 (9.0)
Diarrhea	9/100 (9.0)
Dehydration	6/100 (6.0)
Abdominal pain	4/100 (4.0)
Headache	4/100 (4.0)
Sore throat	4/100 (4.0)
Rash	3/100 (3.0)
Cyanosis	1/100 (1.0)
Apnea	1/100 (1.0)
Tachypnea¶	NA
Tachycardia‖	NA
Oxygen saturation <92% as measured by pulse oximetry — no./total no. (%)	1/100 (1.0)
Outcome — no./total no. (%)	
Admitted	67/100 (67.0)
Admitted for signs and symptoms	38/100 (38.0)
Admitted and awaiting swab results	4/100 (4.0)
Admitted for isolation	25/100 (25.0)
Survived — no./total no. (%)	100/100 (100.0)
Died — no./total no. (%)	0

N Parri et al. N Engl J Med 2020;383:187-190.

European Journal of Pediatrics (2020) 179:1029–1046
https://doi.org/10.1007/s00431-020-03684-7

REVIEW

SARS-COV-2 infection in children and newborns: a systematic review

Ilaria Liguoro[1] · Chiara Pilotto[1] · Margherita Bonanni[1] · Maria Elena Ferrari[1] · Anna Pusiol[1] · Agostino Nocerino[2] · Enrico Vidal[1] · Paola Cogo[1]

Received: 15 April 2020 / Revised: 7 May 2020 / Accepted: 9 May 2020 / Published online: 18 May 2020

- N = 7480 kids from 62 studies, 3 reviews
- Age = 7.6 years
- Italian 3293 (44.1%), USA 2572 (34.4%), Chinese 1358 (18.2%)
- 15.1% asymptomatic, 82.1% mild or moderate illness. 2% severe, 0.6% critically ill, 0.08% (6 pts) died
- Most common symptoms:
  - Fever (51.6%)
  - Cough (47.3%)
  - Sore throat (17.9%)
  - Runny nose (7.7%)
  - Dyspnea (7.7%)
  - Diarrhea (9.7%)
  - Vomiting (7.2%)
  - Fatigue (10.6%)

Best so far

Laboratory and Radiographic Findings

Table 3 Lab investigations in children with documented SARS-CoV-2 infection

Author	*N*	Low WBC*	High WBC*	Lymphopenia/ neutropenia*	Low Plt*	High Plt*	High CRP-PCT*	High CPK*	High transaminase*
Total	655	100	80	81	7	14	190	37	69
%		17.1[a]	13.7[a]	13.3[b]	5.1[c]	10.3[c]	31.1[d]	14.5[e]	12.4[f]

Table 4 Radiological findings in children with documented SARS-CoV-2 infection

Author	*N*	Abnormal radiological findings	Chest X-ray	CT scan	GGO	Local patchy	Bilateral patchy	Normal
Total	674	331	59	495	169	117	102	198
%		49.1	8.8[a]	73.9[a]	29.4[b]	26.6[c]	23.2[c]	32.7[d]

What about little babies???

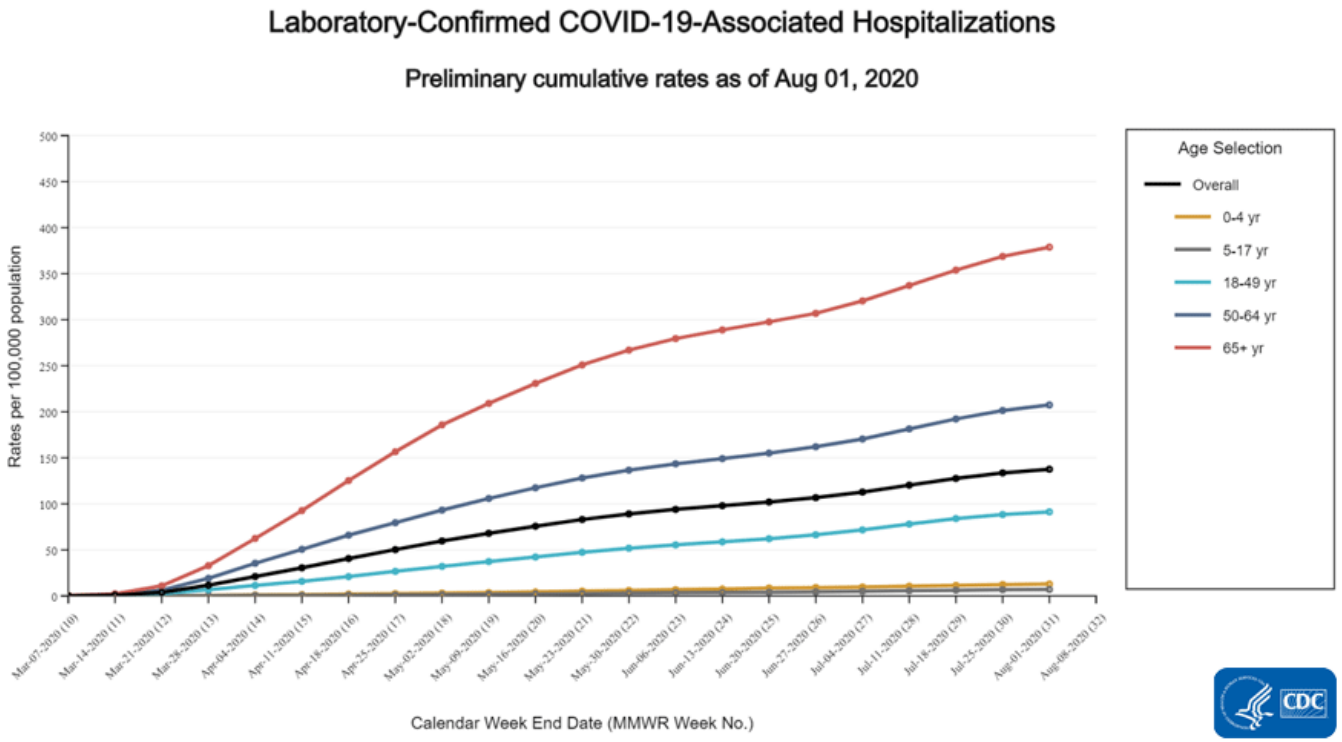
Table 6 Clinical features and laboratory results in newborns and infants ≤ 3 months of age with documented SARS-CoV-2 infection

Author	*N*	Clinical features				Symptoms					Family contact	Labs						
		Asymptomatic	Mild	Moderate	Severe	Fever	Cough	Dyspneic	Vomiting	Feeding intolerance		High WBC	Low L	Low Plt	High Plt	High CRP-PCT	High CPK	High transaminase
Total	25 (17 m)	5	12	5	3	8	2	10	3	6	21	5	4	2	1	3	5	4
%		20.0	48.0	20.0	12.0	32	8	40	12	24	84	20	16	8	4	12	20	16

Table 7 Radiological findings and treatments used in newborns and infants ≤3 months of age with documented SARS-CoV-2 infection

Author	*N*	Radiology findings							Treatment					
		Abnormal	Chest X-ray	CT-scan	GGO	Local patchy	Bilateral patchy	Normal	PICU	MV	Symptomatic alone	Antibiotic	IVIg	IFN
Total	25 (15 m)	12	16	2	1	5	3	7	2	1	2	12	1	2
%		48	64	8	4	20	12	28	8	4	8	48	4	8

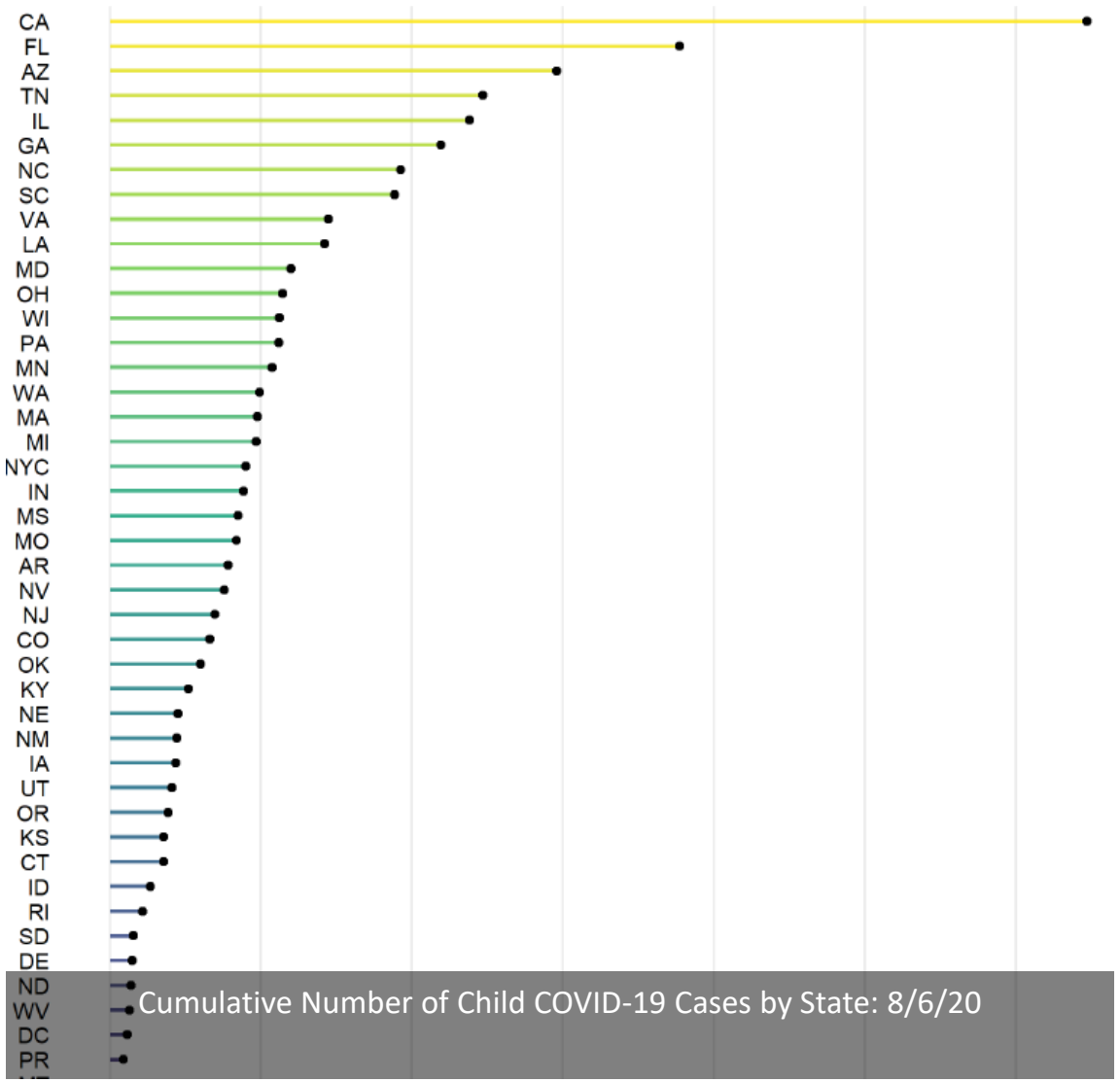
HOSPITALIZATION RATES BY AGE

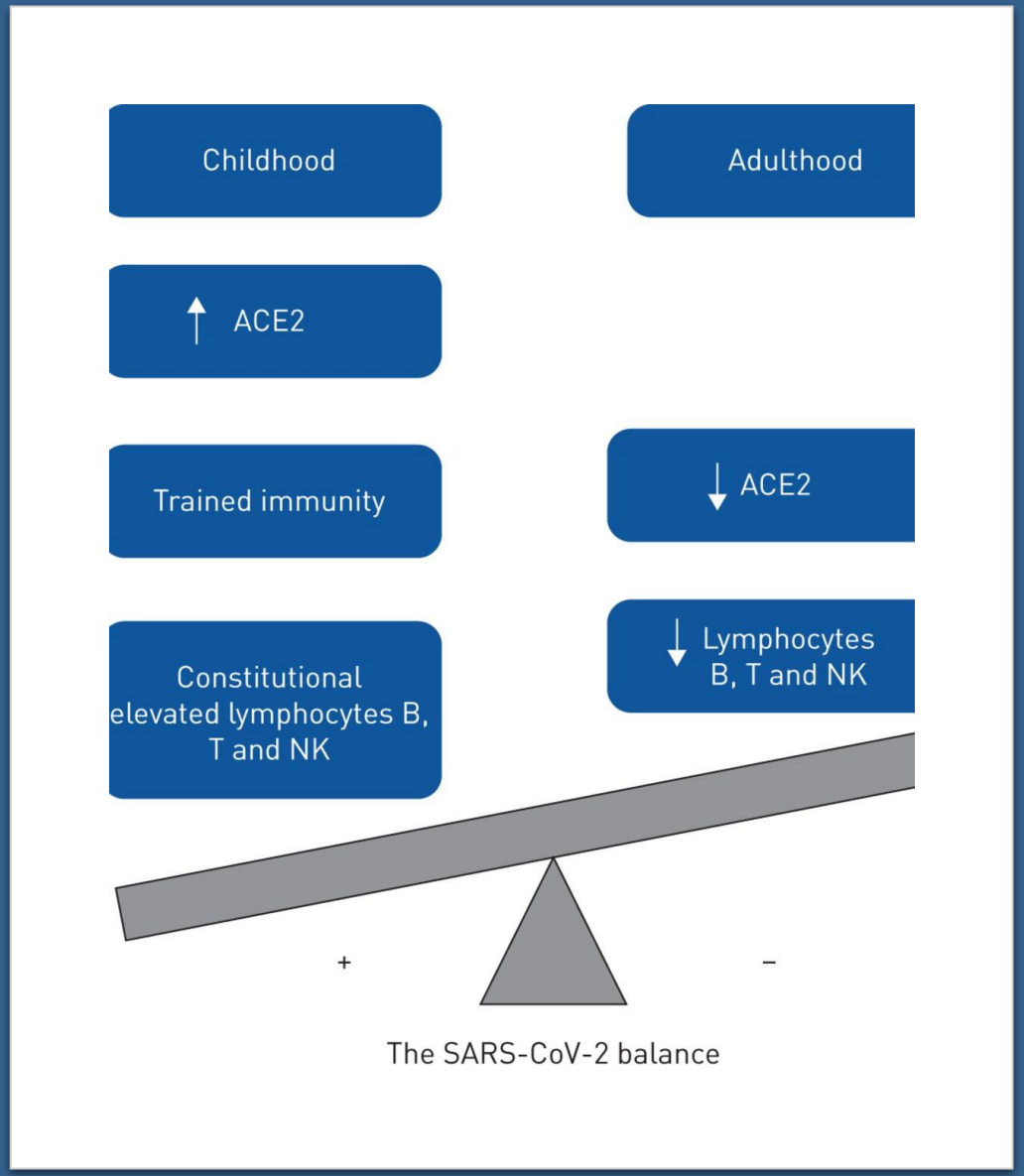


Age Group	Cumulative Rate per 100,000 population
Overall	137.6
0-4 years	12.9
5-17 years	7.0
18-49 years	91.3
50-64 years	207.4
65+ years	378.8

Oregon

- Child population: 965,480
- Cases: 2,887
- Cumulative Total Cases: 19,979
- Percent Children of Total Cases: 14.5%
- Child hospitalizations: 41
- Total Hospitalizations: 1,726
- % children of total hospitalizations: 2.4%
- % of children hospitalized: 1.4%

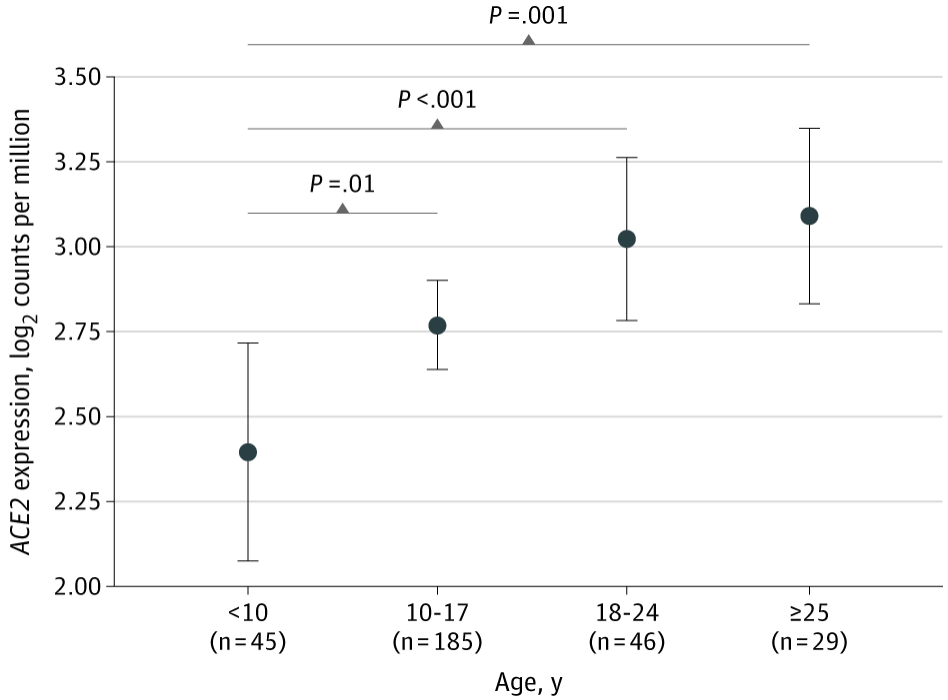




The SARS-CoV-2 balance

Physiological advantages of children against COVID-19?

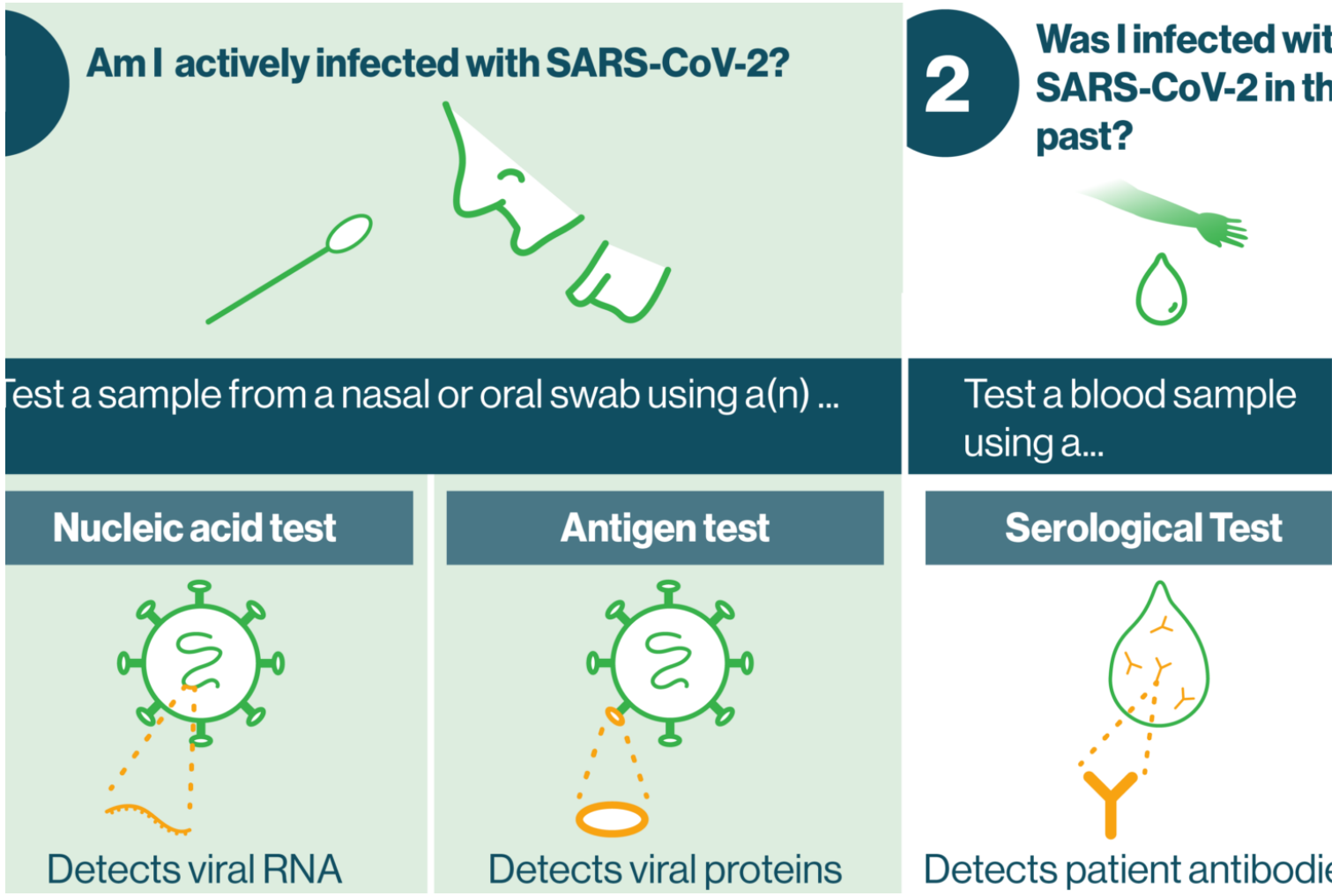
Cristiani et al., European Respiratory Journal 2020



Nasal ACE2 Levels and COVID-19 in Children

Who should be tested?

- Current CDC recommendations for testing people who:
  - Have signs or symptoms of COVID-19
  - Have no symptoms but recently had contact with someone known or suspected to have COVID-19
  - Have no symptoms and no known contact with someone known or suspected to have COVID-19 but still may be tested for early identification in special settings
  - Have had confirmed COVID-19 but no longer have symptoms
  - May be tested by public health officials to track spread of the virus that causes COVID-19



How do we test for COVID, and how good are these?

Implications for practice and policy?

- A positive RT-PCR test for covid-19 test has more weight than a negative test because of the test's high specificity but moderate sensitivity
- A single negative covid-19 test should not be used as a rule-out in patients with strongly suggestive symptoms
- Clinicians should share information with patients about the accuracy of covid-19 tests

Discussing Covid-19 testing to families

- No test is 100% accurate
- If your swab test comes back positive for covid-19 then we can be very confident that you do have covid-19
- However, people with covid-19 can be missed by these swab tests. If you have strong symptoms of covid-19, it is safest to self-isolate, even if the swab test does not show covid-19

COVID Collateral Concerns

- Be alert for non-accidental trauma
- Increased anxiety and depression
- Delayed presentation for care
- Decline in vaccination rates

Physical child abuse demands increased awareness during health and socioeconomic crises like COVID-19

VIEWPOINT

Coronavirus Disease 2019 (COVID-19) and Mental Health for Children and Adolescents

Journal of Paediatrics and Child Health

doi:10.1111/jpc.15059

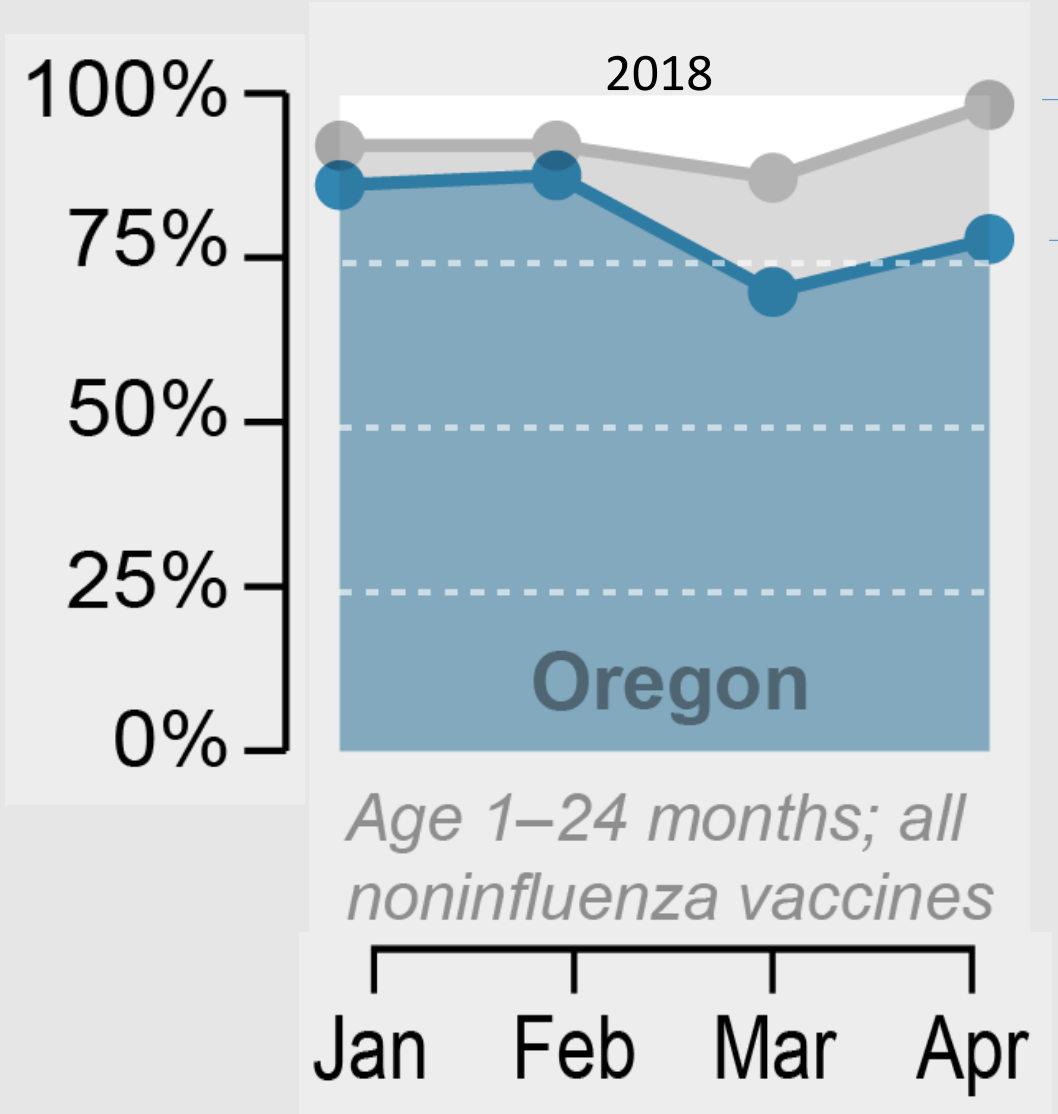
INSTRUCTIVE CASE

PANDEMIC: Presentation of non-Covid cases – Delay in emergencies in children

Bronwyn D Power, Rachel F Power, John Twomey, Zahir Afridi and Orla M Neylon

Department of Paediatrics, University Hospital Limerick, Limerick, Ireland

Oregon Monthly Vaccinations

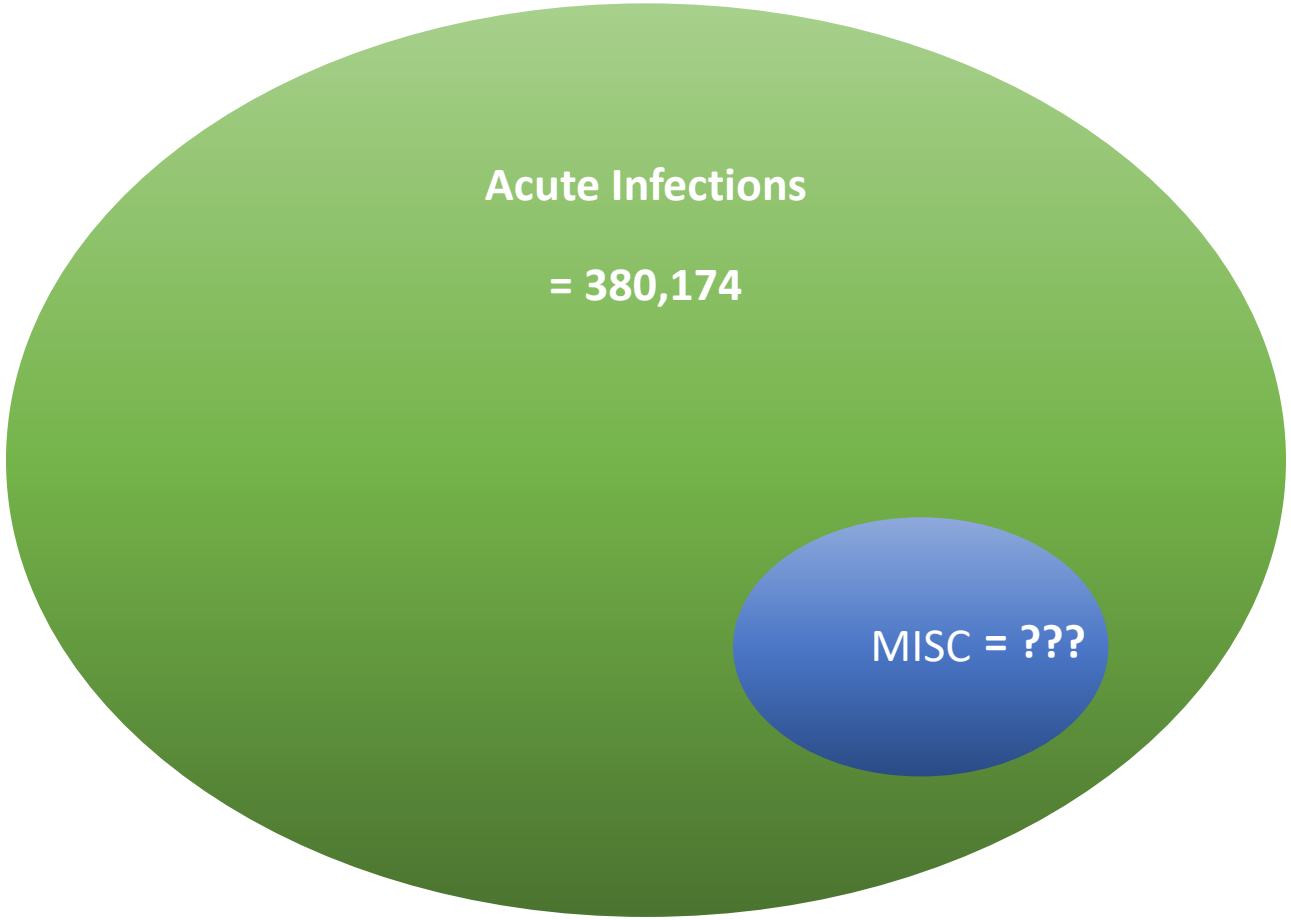


2019

2020

~ 25% decrease in vaccinations compared with 2019

Last and actually least (numerically anyway…)
Multisystem Inflammatory Syndrome in Children



Initial identification

- In mid-April 2020, 8 patients with severe inflammatory syndrome with features similar to atypical Kawasaki disease, Kawasaki disease shock syndrome, or toxic shock syndrome
- Fever, rash, conjunctivitis, peripheral edema, extremity pain, GI symptoms. Only 1 had respiratory symptoms
- All progressed to warm shock requiring volume and vasoactives
- Elevated inflammatory markers
- 7/8 with significant cardiac involvement
- 1 died due to arrythmia with refractory shock, CVA

Correspondence

Hyperinflammatory shock in children during COVID-19 pandemic

South Thames Retrieval Service in London, UK, provides paediatric intensive care support and retrieval to 2 million children in South East England. During a period of 10 days in mid-April, 2020, we noted an unprecedented cluster of eight children with hyperinflammatory shock, showing features similar to atypical Kawasaki disease, Kawasaki disease shock syndrome,[1] or toxic shock syndrome (typical number is one or two children per week). This case cluster formed the basis of a national alert.

All children were previously fit and well. Six of the children were of Afro-Caribbean descent, and five of the children were boys. All children except one were well above the 75th centile

Published Online May 6, 2020 https://doi.org/10.1016/S0140-6736(20)31094-1

	Age; weight; BMI; comorbidities	Clinical presentation: initial	Clinical presentation: PICU referral	Organ support treatment	Pharmacological treatment	Imaging results	Laboratory results	Microbiology results	PICU length of stay; outcome
Patient 1	14 years; 95 kg; Afro-Caribbean; no comorbidities	4 days >40°C; 3 days diarrhoea, non-bloody abdominal pain; headache	BP 80/40 mm Hg; HR 120 beats per min; RR 40 breaths per min; work of breathing; SaO2 99% NIO2	NIV, RRT, VA-ECMO	Dopamine, noradrenaline, epinephrine, adrenaline, milrinone, hydrocortisone, IVIG, cefotaxime, clindamycin	RV dysfunction/ elevated RVSP, ileitis, GB oedema and dilated biliary tree, lung consolidations and diffuse nodules	Ferritin 4220 µg/L; D-dimers 13·4 mg/L; troponin 675 ng/L; proBNP >35 000; CRP 556 mg/L; albumin 20 g/L; platelets 125×10⁹	SARS-CoV-2 positive (post mortem)	6 days; demise (right MCA and ACA ischaemic infarction)
Patient 2	8 years; 30 kg; 5 days >39°C; BMI 18 kg/m²; no comorbidities	non-bloody Afro-diarrhoea, abdominal pain; conjunctivitis; rash; mild	BP 81/37 mm Hg; NIV HR 165 beats per min; RR 40 breaths per		Noradrenaline, adrenaline, IVIG, infliximab, methylprednisolone, ceftriaxone, clindamycin	Mild biventricular dysfunction, severely dilated coronaries; ascites; pleural effusions	Ferritin 277 µg/L; D-dimers 4·8 mg/L; troponin 25 ng/L; CRP 285 mg/L; procalcitonin 8·4 µg/L; albumin 18 g/L; platelets 61×10⁹	SARS-CoV-2 negative; likely COVID-19 exposure from mother	4 days; alive
Patient 3	4 years; 18 kg; 4 days >39°C; BMI 17 kg/m²; no comorbidities	diarrhoea and vomiting; abdominal pain; rash; conjunctivitis	BP 90/30 mm Hg; NIV HR 170 beats per min; RR 35 breaths per min; SVIA		Noradrenaline, adrenaline, IVIG, ceftriaxone, clindamycin	Ascites; pleural effusions	Ferritin 574 µg/L; D-dimers 11·7 mg/L; troponin 45 ng/L; CRP 322 mg/L; procalcitonin 10·3 µg/L; albumin 22 g/L; platelets 188×10⁹	Adenovirus positive; HERV positive	4 days; alive
Patient 4	13 years; 64 kg; BMI 33 kg/m²; Afro-Caribbean; no comorbidities	5 days >39°C; non-bloody diarrhoea; abdominal pain; conjunctivitis	BP 77/41 mm Hg; HR 127 beats per min; RR 24 breaths per min; SVIA	HFNC	Noradrenaline, milrinone, IVIG, ceftriaxone, clindamycin	Moderate to severe LV dysfunction; ascites	Ferritin 631 µg/L; D-dimers 3·4 mg/L; troponin 250 ng/L; proBNP 13427 ng/L; CRP 307 mg/L; procalcitonin 12·1 µg/L; albumin 21 g/L; platelets 146×10⁹	SARS-CoV-2 negative	5 days; alive
Patient 5	6 years; 22 kg; BMI 14 kg/m²; Asian; autism, ADHD	4 days >39°C; odynophagia; rash; conjunctivitis	BP 85/43 mm Hg; NIV HR 150 beats per min; RR 50 breaths per min; SVIA		Milrinone, IVIG, methylprednisolone, aspirin, ceftriaxone	Dilated LV, AVR, pericoronary hyperechogenicity	Ferritin 550 µg/L; D-dimers 13·1 mg/L; troponin 47 ng/L; NT-proBNP 7004 ng/L; CRP 183 mg/L; albumin 34 g/L; platelets 165×10⁹	SARS-CoV-2 positive; likely COVID-19 exposure from father	4 days; alive
Patient 6	6 years; 26 kg; BMI 15 kg/m²; Afro-Caribbean; no comorbidities	5 days >39°C; myalgia; 3 days diarrhoea and vomiting; abdominal pain; rash; odynophagia; headache; conjunctivitis	BP 77/46 mm Hg; NIV HR 120 beats per min; RR 40 breaths per min; SVIA		Dopamine, noradrenaline, milrinone, IVIG, methylprednisolone, aspirin, ceftriaxone, clindamycin	Mild LV systolic impairment	Ferritin 1028 µg/L; D-dimers 9·9 mg/L; troponin 45 ng/L; NT-proBNP 9576 ng/L; CRP 169 mg/L; procalcitonin 11·6 µg/L; albumin 25 g/L; platelets 158	SARS-CoV-2 negative; confirmed COVID-19 exposure from grandfather	8 days; alive
Patient 7	12 years; 50 kg; BMI 20 kg/m²; Afro-Caribbean	4 days >39°C; 2 days diarrhoea and vomiting; abdominal pain; rash; odynophagia; headache	BP 80/48 mm Hg; NIV HR 125 beats per min; RR 47 breaths per min; SaO2 98%; HFNC FiO2 0·35		Noradrenaline, adrenaline, milrinone, IVIG, methylprednisolone, heparin, ceftriaxone, clindamycin, metronidazole	Severe biventricular impairment; ileitis; ascites; pleural effusions	Ferritin 958 µg/L; D-dimer 24·5 mg/L; troponin 813 ng/L; NT-proBNP >35 000 ng/L; CRP 251 mg/L; procalcitonin 725 µg/L; albumin 24 g/L; platelets 273×10⁹	SARS-CoV-2 negative	4 days; alive
Patient 8	8 years; 50 kg; BMI 25 kg/m²; female; Afro-Caribbean; no comorbidities	4 days >38°C; odynophagia; no 2 days diarrhoea and vomiting; abdominal pain	BP 82/41 mm Hg; NIV HR 130 beats per min; RR 35 breaths per min; SaO2 97% NIO2		Dopamine, noradrenaline, milrinone, IVIG, aspirin, ceftriaxone, clindamycin	Moderate LV dysfunction	Ferritin 460 µg/L; D-dimers 4·3 mg/L; troponin 120 ng/L; CRP 347 mg/L; procalcitonin 7·42 µg/L; albumin 22 g/L; platelets 296×10⁹	SARS-CoV-2 negative; likely COVID-19 exposure from parent	7 days; alive

ACAs=anterior cerebral artery. ADHD=attention deficit hyperactivity disorder. AVR=atrioventricular valve regurgitation. BMI=body-mass index. BP=blood pressure. COVID-19=coronavirus disease 2019. CRP=C-reactive protein. FiO2=fraction of inspired oxygen. HFNC=high-flow nasal cannula. HR=heart rate. IVIG=human intravenous immunoglobulin. LV=left ventricle. MCA=middle cerebral artery. NIV=non-invasive ventilation. NT-proBNP=N-terminal pro-B-type natriuretic peptide. PICU=paediatric intensive care unit. RR=respiratory rate. RRT=renal replacement therapy. RV=right ventricle. RVSP=right ventricular systolic pressure. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. SaO2=oxygen saturation. SVIA=self-ventilating in air. VA-ECMO=veno-arterial extracorporeal membrane oxygenation.

Table: Demographics, clinical findings, imaging findings, treatment, and outcome from PICU

Best So Far

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multisystem Inflammatory Syndrome in U.S. Children and Adolescents

L.R. Feldstein, E.B. Rose, S.M. Horwitz, J.P. Collins, M.M. Newhams, M.B.F. Son, J.W. Newburger, L.C. Kleinman, S.M. Heidemann, A.A. Martin, A.R. Singh, S. Li, K.M. Tarquinio, P. Jaggi, M.E. Oster, S.P. Zackai, J. Gillen, A.J. Ratner, R.F. Walsh, J.C. Fitzgerald, M.A. Keenaghan, H. Alharash, S. Doymaz, K.N. Clouser, J.S. Giuliano, Jr., A. Gupta, R.M. Parker, A.B. Maddux, V. Havalad, S. Ramsingh, H. Bukulmez, T.T. Bradford, L.S. Smith, M.W. Tenforde, C.L. Carroll, B.J. Riggs, S.J. Gertz, A. Daube, A. Lansell, A. Coronado Munoz, C.V. Hobbs, K.L. Marohn, N.B. Halasa, M.M. Patel, and A.G. Randolph, for the Overcoming COVID-19 Investigators and the CDC COVID-19 Response Team*

Case definition

- Age < 21 years
- fever > 38 or report of subjective fever lasting >24 hours
- Laboratory e/o inflammation
- Serious illness leading to hospitalization
- Multisystem organ involvement (at least 2)
- Lab confirmed SARS-COV2 infection (positive PCR or ab test) or epidemiological link to person with COVID-19 (preceding 4 weeks)
- No alternative plausible diagnosis

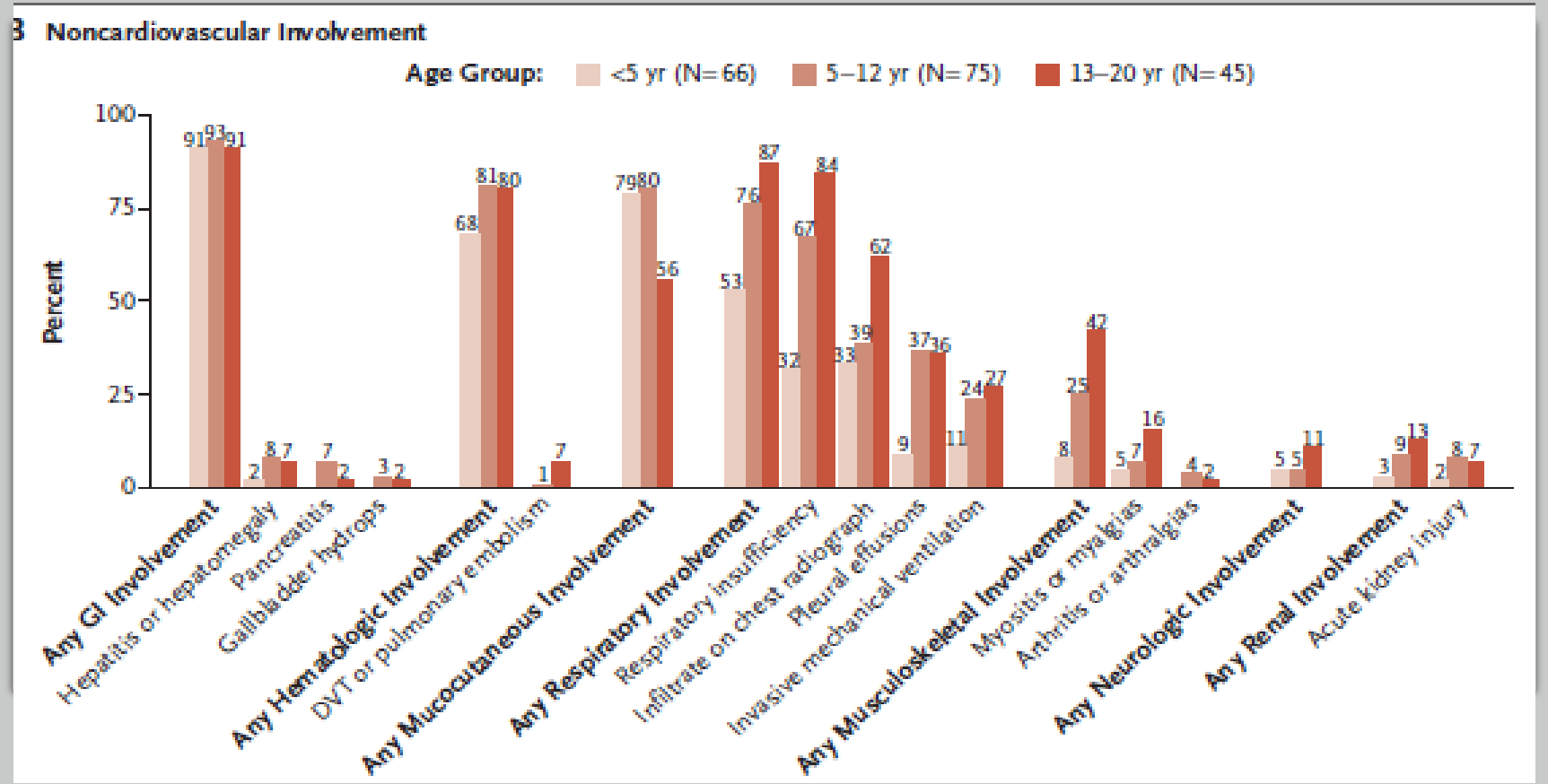
The Patients

- N = 186 patients
- Median age 8.3 (3.3-12.5)
- Race and ethnic group = 19% white, 25% black, 31% Hispanic or Latino, 5% other, 22% unknown
- 73% previously healthy
- 29% obese
- 70% PCR or serology positive
- 71% 4 or more system involvement
- 80% required ICU, 4% required ECMO
- 2% (4 patients) died

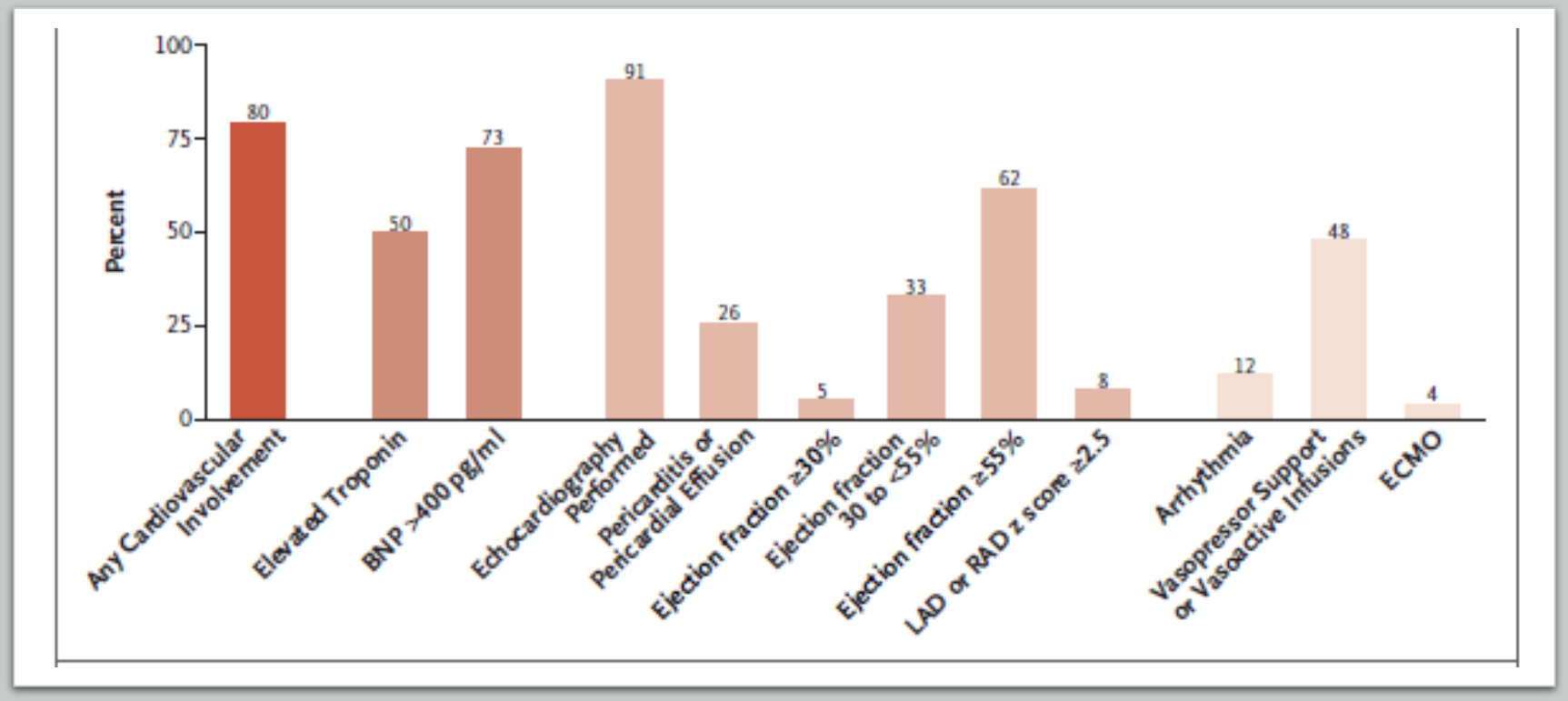
Table 1. Demographic and Clinical Characteristics of the Patients According to SARS-CoV-2 Infection Status.

Characteristic	Laboratory Confirmation of SARS-CoV-2 Infection (N=131)		Epidemiologic Link to Person with Covid-19 (N=55)*	All Patients (N=186)
	RT-PCR Positive (N=73)†	Antibody Test Positive, RT-PCR Negative or Unknown (N=58)		
Male sex — no. (%)	43 (59)	36 (62)	36 (65)	115 (62)
Median age (interquartile range) — yr	9.1 (4.8–14.2)	9.1 (4.1–11.7)	3.9 (1.4–11.6)	8.3 (3.3–12.5)
Age group — no. (%)				
<1 yr	6 (8)	0	7 (13)	13 (7)
1–4 yr	13 (18)	19 (33)	21 (38)	53 (28)
5–9 yr	21 (29)	14 (24)	11 (20)	46 (25)
10–14 yr	17 (23)	18 (31)	10 (18)	45 (24)
15–20 yr	16 (22)	7 (12)	6 (11)	29 (16)
Race and ethnic group — no. (%)‡				
White, non-Hispanic	13 (18)	8 (14)	14 (25)	35 (19)
Black, non-Hispanic	17 (23)	18 (31)	11 (20)	46 (25)
Hispanic or Latino	29 (40)	12 (21)	16 (29)	57 (31)
Other race, non-Hispanic	4 (5)	1 (2)	4 (7)	9 (5)
Unknown	11 (15)	19 (33)	11 (20)	41 (22)
Underlying conditions				
Previously healthy — no. (%)§	49 (67)	43 (74)	43 (78)	135 (73)
At least one underlying condition, excluding obesity — no. (%)	24 (33)	15 (26)	12 (22)	51 (27)
Respiratory — no. (%)	16 (22)	12 (21)	5 (9)	33 (18)
Cardiac — no. (%)	2 (3)	2 (3)	1 (2)	5 (3)
Immunocompromising or autoimmune — no. (%)	6 (8)	1 (2)	3 (5)	10 (5)
Other — no. (%)¶	15 (21)	3 (5)	2 (4)	20 (11)
Clinically diagnosed obesity — no./total no. (%)‖	8/62 (13)	3/55 (5)	1/36 (3)	12/153 (8)
BMI-based obesity — no./total no. (%)**	21/62 (34)	15/55 (27)	9/36 (25)	45/153 (29)
Organ-system involvement — no. (%)				
Two systems	5 (7)	1 (2)	12 (22)	18 (10)
Three systems	14 (19)	10 (17)	12 (22)	36 (19)
Four or more systems	54 (74)	47 (81)	31 (56)	132 (71)
Detection of additional virus — no. (%)††	6 (8)	2 (3)	1 (2)	9 (5)
Highest level of care — no. (%)				
Ward	11 (15)	5 (9)	22 (40)	38 (20)
Intensive care unit	62 (85)	53 (91)	33 (60)	148 (80)
Extracorporeal membrane oxygenation	6 (8)	1 (2)	1 (2)	8 (4)
Outcome — no. (%)				
Still hospitalized as of May 20, 2020	26 (36)	19 (33)	7 (13)	52 (28)
Discharged alive	44 (60)	39 (67)	47 (85)	130 (70)
Died	3 (4)	0	1 (2)	4 (2)

Organ System Involvement



Cardiovascular Involvement

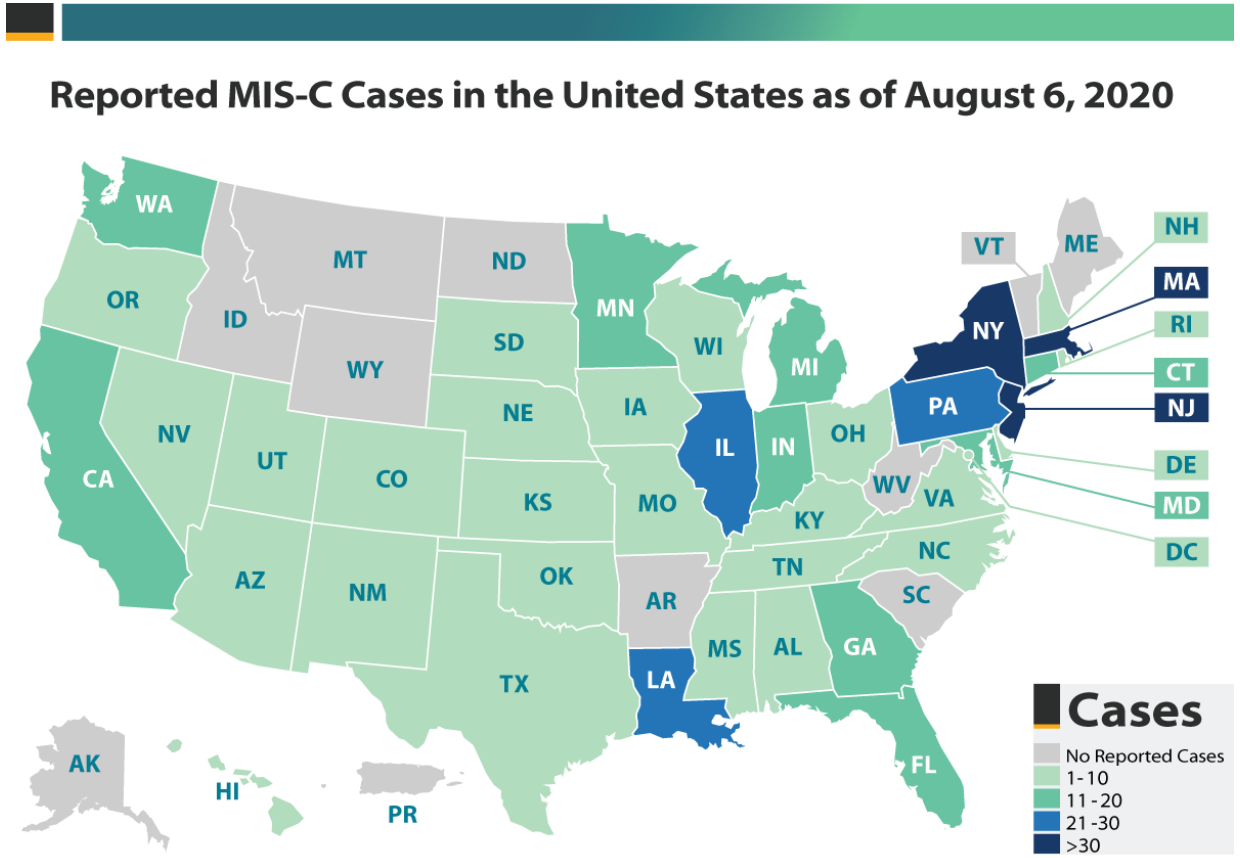


Kawasaki disease by another name?

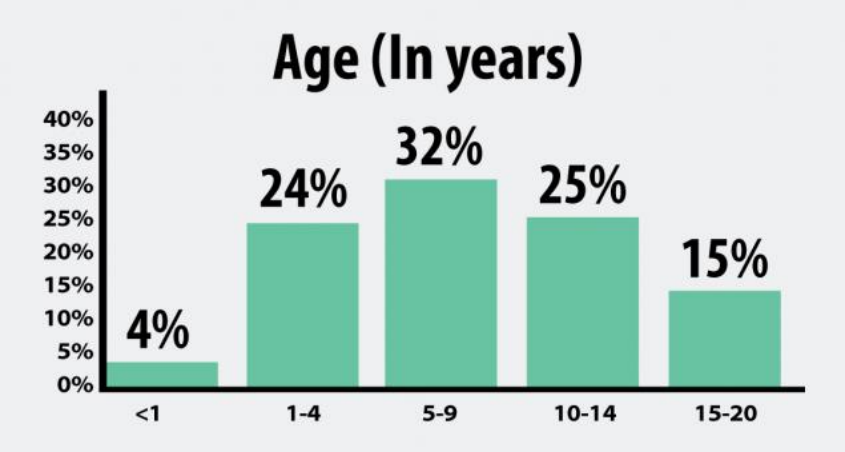
- 60% of patients would NOT have met criteria for complete or incomplete
- Kids with KD-like features more likely to be under 5

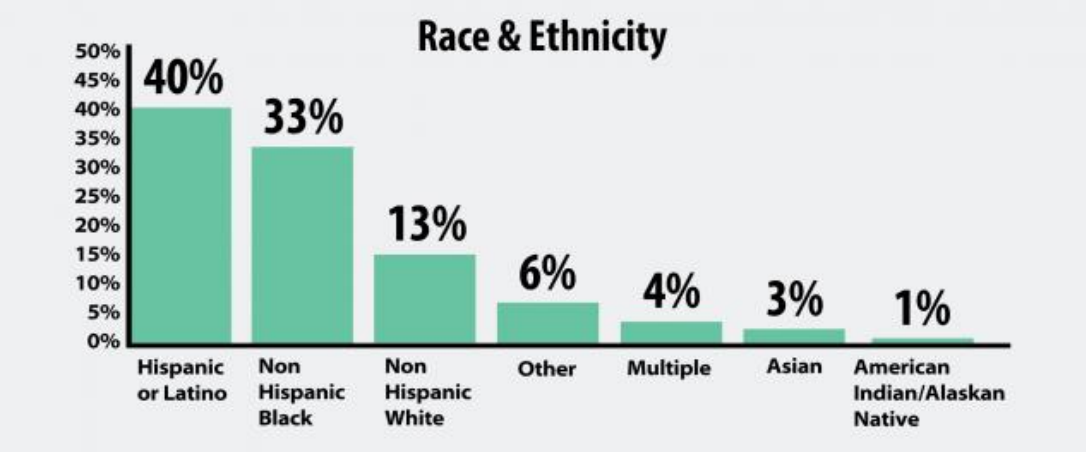
	Kawasaki's disease	MIS-C
Average age (yrs.)	3.4	8.3
CV shock requiring vasoactives?	~5%	~50% (most older kids)
CA aneurysms	25%	8%

Follow the data!



Who were these kids?





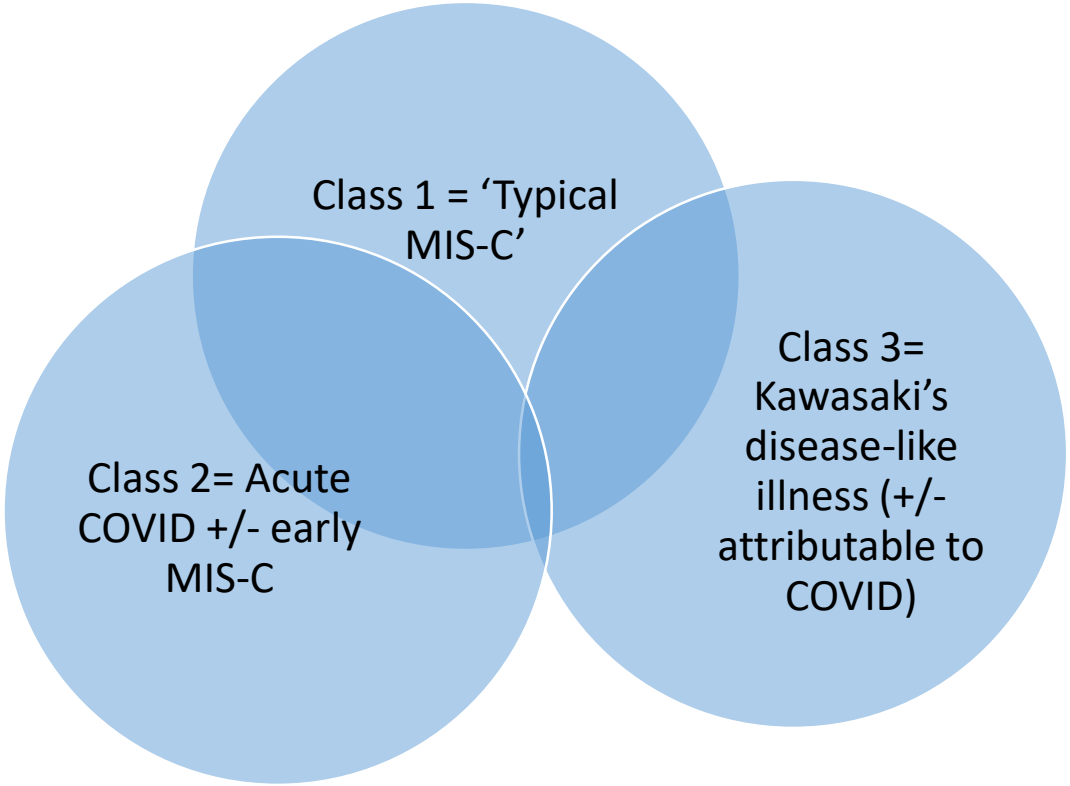
How’d they present?

Signs and Symptoms	
Abdominal pain	61.9%
Vomiting	61.8%
Skin rash	55.3%
Diarrhea	53.2%
Hypotension	49.5%
Conjunctival injection	48.4%
Organ System Involvement	
Gastrointestinal	90.9%
Cardiovascular	86.5%
Derm/mucocutaneous	70.9%
Complications	
Cardiac dysfunction	40.6%
Shock	35.4%
Myocarditis	22.8%
Coronary artery change	18.6%
Acute kidney injury	18.4%
Outcomes	
Required ICU	63.9%
Died	1.8%

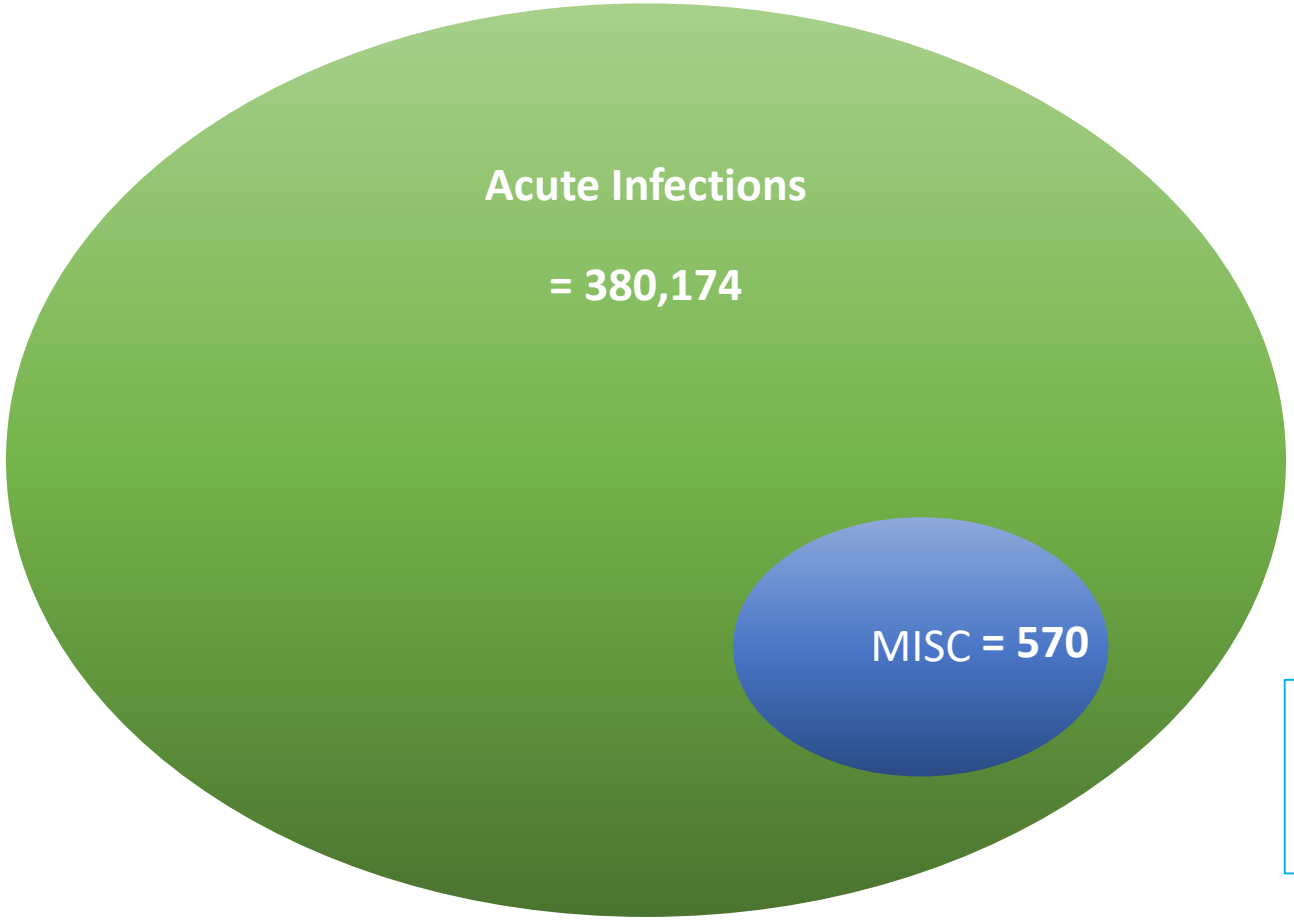
Are these really the same thing?

- Class 1:
  - 203 (35.6%) patients consistent with previous MISC description, including shock, cardiac dysfunction, abdominal pain, and markedly elevated inflammatory markers. 98% had positive SARS-COV-2 serology
- Class 2:
  - 169 (29.6%) with cough, SOB, PNA, ARDS-acute COVID or acute COVID + MISC combo?. 84% with PCR positive
- Class 3:
  - 198 (34.7%) median age 6 (youngest), more likely to have rash or mucocutaneous lesions, higher prevalence of coronary art aneurysms or dilatations than class 2 but not class 1. 63.1 serology only, 33.8 with both serology and PCR

What does this mean?



Last and actually least (numerically anyway…) Multisystem Inflammatory Syndrome in Children



= 0.15%
or 1 in 670 acute infections

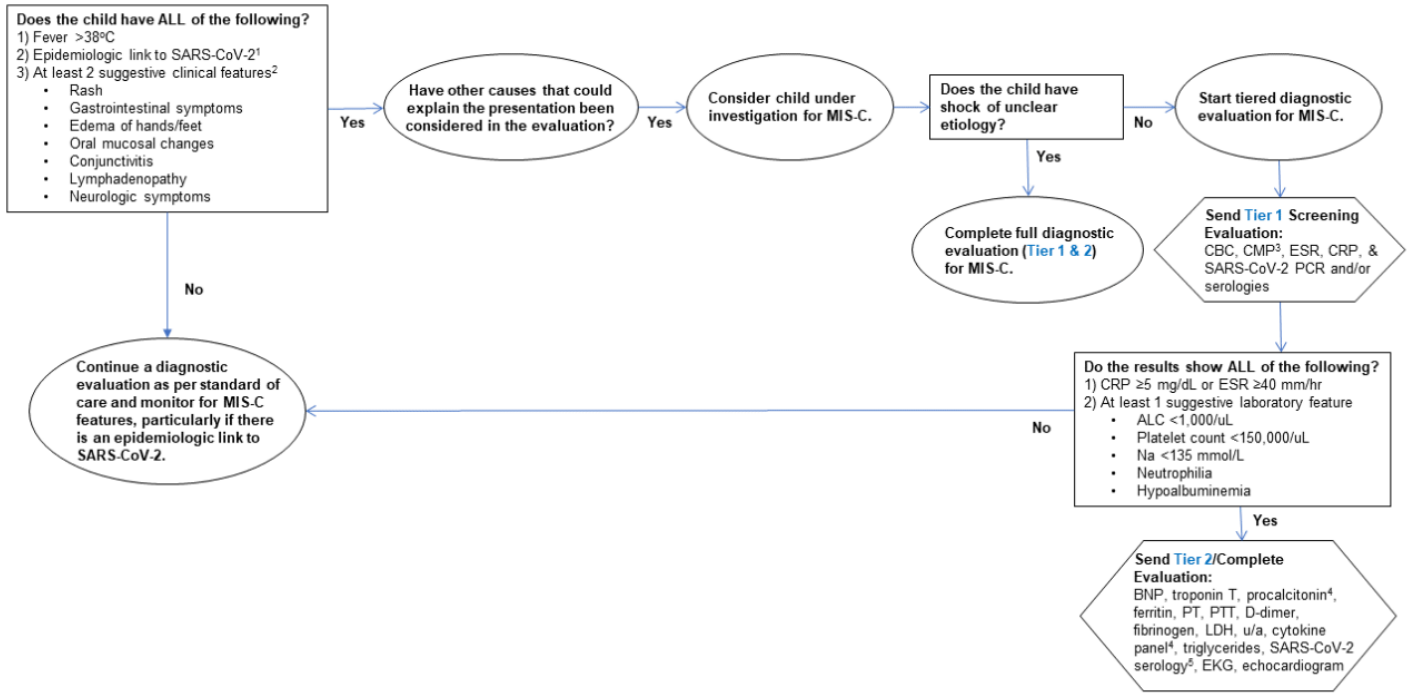


Figure 1. Diagnostic Pathway for MIS-C

[1]An epidemiologic link to SARS-CoV-2 infection is defined as a child with ANY of the following criteria: positive SARS-CoV-2 polymerase chain reactio (PCR), positive SARS-CoV-2 serologies, preceding illness resembling COVD-19, or close contact with confirmed or suspected COVID-19 cases in the p weeks.

[2]Rash, (polymorphic, maculopapular, or petechial, but not vesicular); GI symptoms, (diarrhea, abdominal pain, or vomiting); oral mucosal changes, (and/or cracked lips, strawberry tongue, or erythema of the oropharyngeal mucosa); conjunctivitis, (bilateral conjunctival injection without exudate) neurologic symptoms, (altered metal status, encephalopathy, focal neurologic deficits, meningismus, or papilledema).

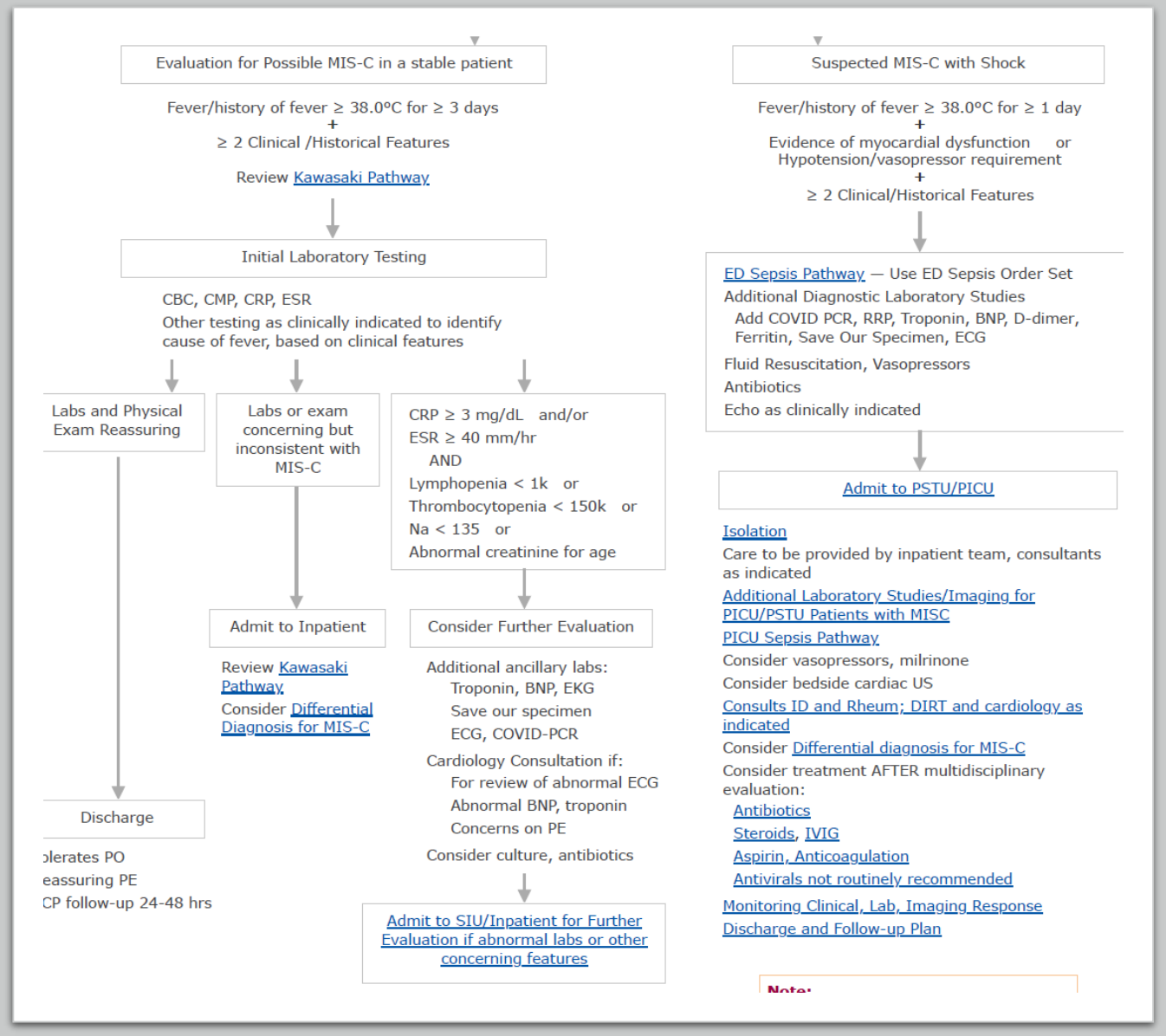
[3]Complete metabolic panel: Na, K, CO2, Cl, BUN, Cr, glucose, Ca, albumin, total protein, AST, ALT, ALP, Bilirubin.

[4]Send procalcitonin and cytokine panel, if available.

[5]If not sent in tier 1 evaluation. If possible, send SARS-CoV-2 IgG, IgM, IgA.

Q: What do we do in the meantime?

A: Screen!



One Institutional Approach

Summary

- Transmission
  - Young children have not driven the household transmission of COVID-19 and seldom led to outbreaks
- Testing
  - Positive tests for covid-19 are clinically useful, negative tests need to be interpreted with caution
- Don’t forget general pediatric concerns!
- Acute infection
  - Characterized by fever, cough, URI, GI symptoms
  - Large majority is asymptomatic, mild, or moderate, and hospitalization is rare
- MISC
  - Fever, GI symptoms, rash, conjunctival injection predominate
  - Hypotension in almost 50% of patients with major cardiac morbidity
  - Possibly 3 phenotypes but jury is out
  - It’s rare

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Thank you!