

COVID-19 in adolescents and children

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Disclosures:

I have no disclosures.

I will reference drugs and treatments that are not FDA approved for children.

Objectives:

1. Understand the incidence of pediatric COVID-19 compared to that of adults
2. Acknowledge the knowledge gaps that exist in the management of pediatric COVID-19
3. Identify MIS-C and the challenges with its diagnosis

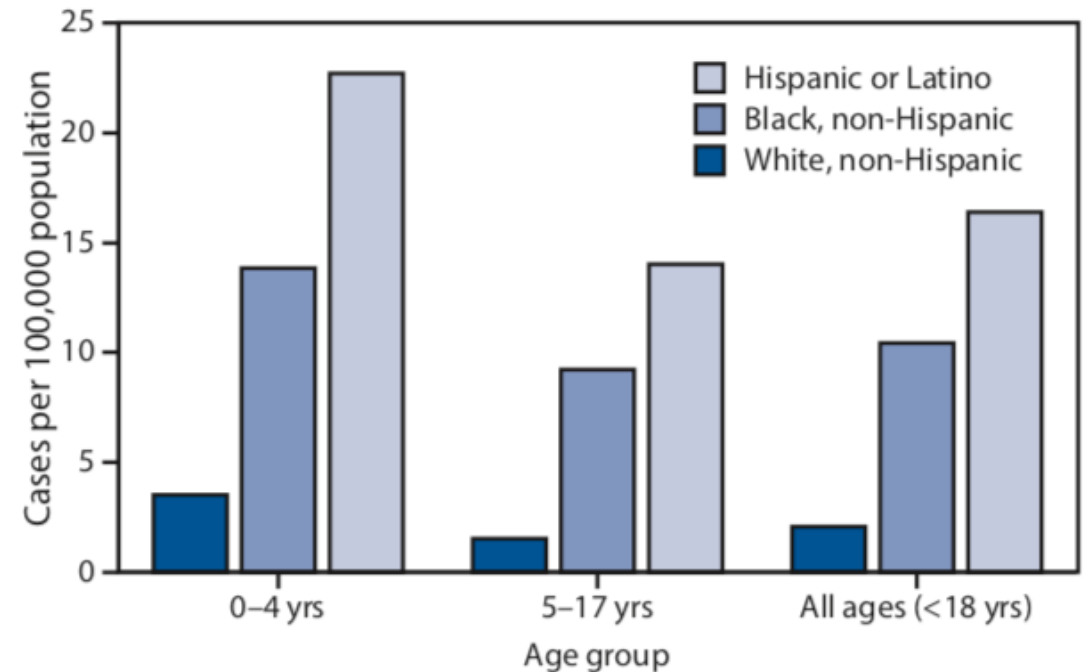
COVID-19 incidence in adolescents and children

What we know

- Children of all ages can get COVID-19 (10-13% of total cases)*
 - Preschoolers: 0 – 4 years: 17.4%
 - Elementary: 5 – 10 years: 25.7%
 - Middle School: 11 – 13: 18.6%
 - High School 14 – 17: 38.3%
- Children from racial and ethnic minorities are disproportionately affected

*As of 12/12/20 in the United States

FIGURE 2. Cumulative COVID-19-associated hospitalization rates* among children aged <18 years, by age group and race/ethnicity — COVID-NET, 14 states[†], March 1–July 25, 2020^{§,¶}



COVID-19 incidence in adolescents and children

What we don't know

- Why lower incidence than adults?
- Contrary to influenza and other respiratory viruses
- Lack of testing/recognition?
- Hidden or occult/asymptomatic infections?
- Different expression of angiotensin converting enzyme 2 (ACE-2) receptor of respiratory tract?

Table 2: Estimated rates of influenza-associated disease outcomes, per 100,000, by age group — United States, 2019–2020 influenza season

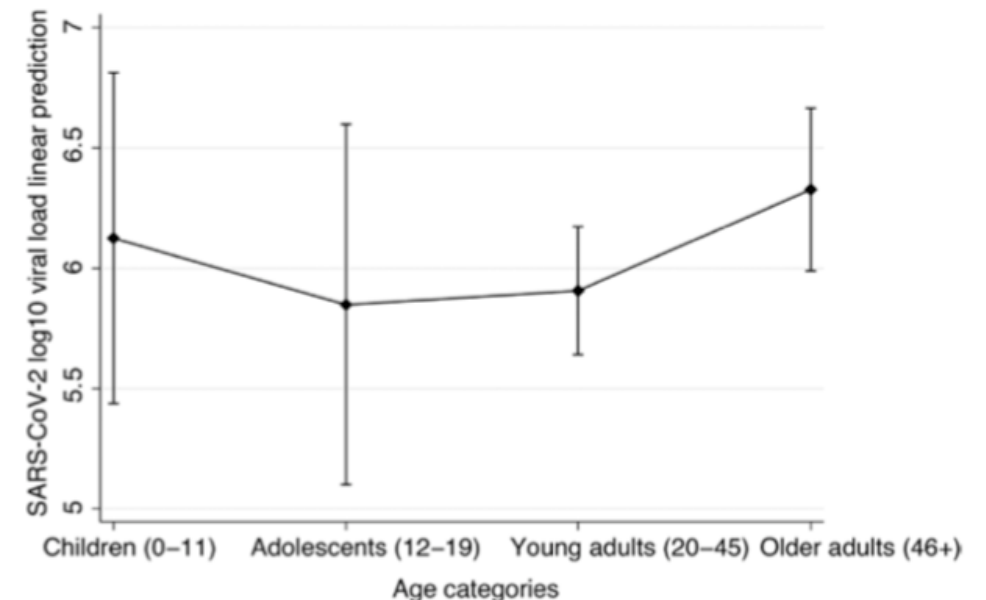
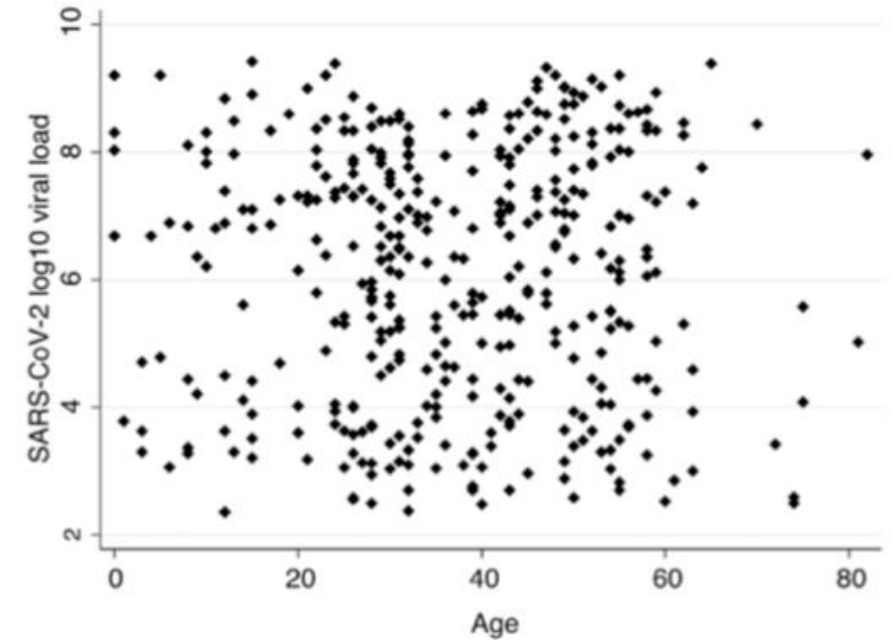
Age group	Illness rate		Medical visit rate		Hospitalization rate		Mortality rate	
	Estimate	95% UI	Estimate	95% UI	Estimate	95% UI	Estimate	95% UI
0-4 yrs	21,922.40	(15,658.6, 42,126.7)	14,688.00	(10,323.6, 28,323.6)	152.8	(109.2, 293.7)	1.3	(0.4, 2.8)
5-17 yrs	15,364.50	(12,253.9, 21,233.5)	7,989.60	(6,202.4, 11,244.7)	42.1	(33.6, 58.2)	0.3	(0.1, 0.8)
18-49 yrs	11,088.20	(8,536.0, 16,005.1)	4,102.60	(3,049.1, 6,065.5)	62.2	(47.9, 89.8)	1.9	(1.2, 3.3)
50-64 yrs	13,375.60	(10,994.6, 17,219.2)	5,751.50	(4,500.6, 7,596.4)	141.8	(116.6, 182.6)	8.2	(5.6, 13.9)
65+ yrs	3,600.10	(2,737.9, 5,334.4)	2,016.10	(1,476.1, 3,000.0)	327.3	(248.9, 484.9)	25.3	(19.1, 36.2)

†95% Uncertainty intervals

COVID-19 transmission in adolescents and children

What we know

- Children of all ages can transmit SARS-CoV-2 to others
- Rate of transmission at home > transmission at schools
 - Incidence in counties w/ in person K-12 education was similar to counties w/ virtual learning
- Transmission in presymptomatic children may be less common than adults
- Infected children shed SARS-CoV-2 virus with nasopharyngeal viral loads comparable to or higher than those in adults



COVID-19 transmission in adolescents and children

TABLE 2. Rates of secondary laboratory-confirmed SARS-CoV-2 infections among household members enrolled in a prospective study of SARS-CoV-2 household transmission — Tennessee and Wisconsin, April–September 2020

Characteristic	Laboratory-confirmed SARS-CoV-2 infections/ Household members at risk	Secondary infection rate % (95% CI)*
All household members	102/191	53 (46–60)
Nasal swab–positive tests only	89/191	47 (40–54)
RT-PCR–negative at enrollment	48/137	35 (28–43)
Index patient age group, yrs		
<12	9/17	53 (31–74)
12–17	11/29	38 (23–56)
18–49	64/116	55 (46–64)
≥50	18/29	62 (44–77)

What we think we know:

- Masks and physical distancing account for difference in school versus home transmission

What we don't know:

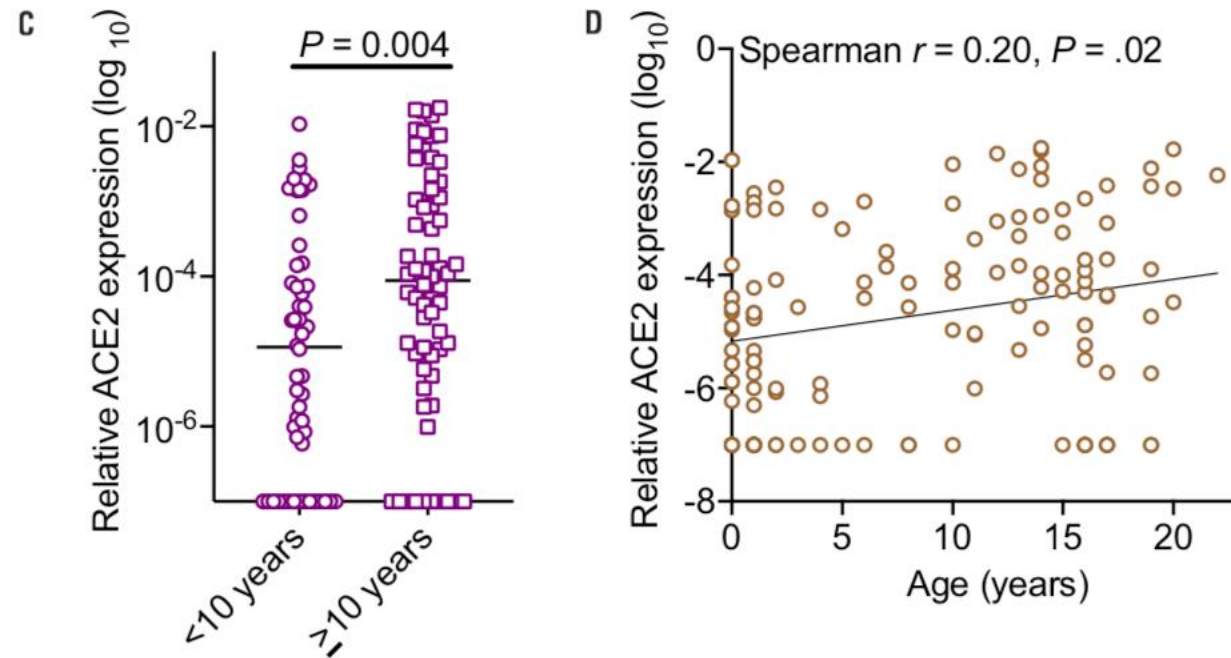
- Is transmission from children more dependent on symptomatic than asymptomatic infection?
- Lack expiratory force required to project viral droplets far distances?
 - (certainly not the case for influenza or other respiratory viral infections)

Acute COVID manifestations of adolescents and children

What we know

- Symptoms of COVID-19 are similar in children and adults but more mild
 - 0-9: fever 63%; loss of taste or smell <1%; GI: 31%
 - 10-19: fever 60%; loss of taste or smell < 10%; GI: 32%
 - Adults: fever 43%; loss of taste or smell < 10%; GI: 31%
- Dermatologic symptoms are likely more common in children
- A minority of children require hospitalization
 - < 3 months – 92% of infants hospitalized; 21% ICUs, 3% mechanical ventilation; no deaths were reported
- 0-17: 178 deaths* (<0.1% of total); most children have 1 or more underlying condition (chronic pulmonary disease, obesity, neurologic/developmental conditions, CV conditions)

Acute COVID manifestations of adolescents and children



What we don't know

- Why are there differences?
 - Contrary to influenza in which <5 are at high risk of complications
- Less intense immune response? Less initial cytokine release?
- Out-competed by other viral interference in the respiratory tract of young children?
- Pre-existing cross-reactive antibodies?
- Protective off-target effects of live vaccines?
- Healthier blood vessels in children than adults and less risk of thromboembolism?
- Different expression of ACE-2 receptor of respiratory tract?

Management of COVID-19 in adolescents and children

What we know

- Mainly supportive
- Remdesivir – unproven benefits but is used for severe disease
 - 3.5 kg and up
- Steroids: Trials in children are ongoing and benefits/risks are uncertain
- Bamlanivimab – other monoclonals >12 years and up

What we don't know

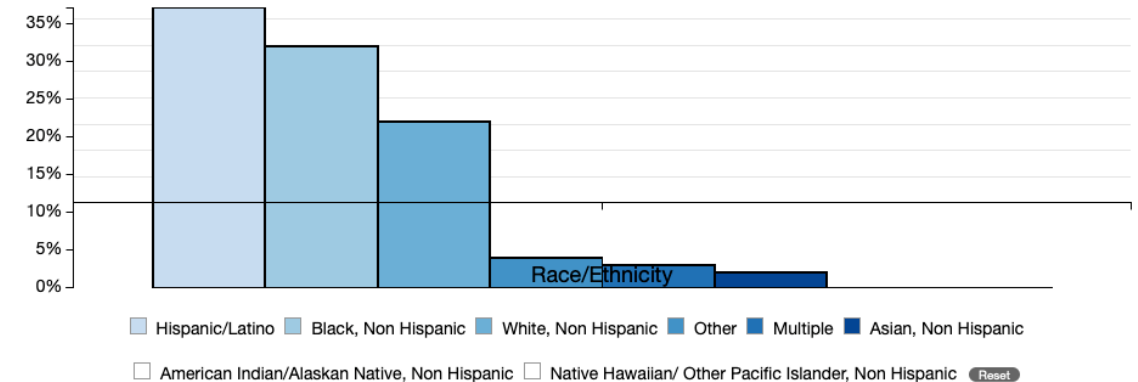
- Impact of remdesivir?
- Impact of steroids?
- Appropriate dosing and impact of monoclonal antibodies < 12 years?
- Vaccination?
 - Doses? Frequency? Risks? Benefits? Transmission?

Post-infectious: Multisystem inflammatory syndrome in children: MIS-C

What we know

- Rare but severe (2,060 US cases and 30 deaths*)
- Children from racial and ethnic minorities are disproportionately affected
- 4-8 weeks post infectious
- Name says it all
 - Age <21 presenting w/ fever and clinical/laboratory evidence of inflammation and multisystem (≥ 2 systems) involvement
 - Positive for current or recent SARS-CoV-2 infection
 - No alternative diagnosis

Cases by Race & Ethnicity



Daily MIS-C Cases (Seven-Day Moving Average)



Post-infectious: Multisystem inflammatory syndrome in children: MIS-C

What we know

- Spectrum of MIS-C
- End organ damage, cardiac compromise, coronary artery dilation/aneurysms, and death
- Treatment: Decrease amount of inflammation (intravenous immune globulin + steroids + aspirin)

Spectrum of MIS-C		
MIS-C w/o overlap	MIS-C w/ severe acute COVID overlap	MIS-C w/ KD overlap
More cardiac + GI involvement, +serology	More respiratory involvement; negative serology	Younger cohorts; more rash, less shock

Post-infectious: Multisystem inflammatory syndrome in children: MIS-C

What we don't know

- Why? What is the pathophysiology?
- Who? Defying higher risk characteristics
 - Pathogen specific? Host specific?
- How to distinguish?
 - MIS-C vs. Acute COVID vs. KD
 - MIS-C vs other
- Management: IVIG + steroids? Biologics?
- What happens next?
 - Long term complications of MIS-C?
 - Measles – subacute sclerosing panencephalitis (7-10 years later)

Spectrum of MIS-C		
MIS-C w/o overlap	MIS-C w/ severe acute COVID overlap	MIS-C w/ KD overlap
More cardiac + GI involvement, +serology	More respiratory involvement; negative serology	Younger cohorts; more rash, less shock

Different treatments for different groups?

Non-COVID impacts of Pediatric COVID

What we know

- Decreases in common childhood pathogens (Strep pharyngitis, influenza, EBV, pneumonia, sinus infections, upper respiratory tract infections)
- Disruption of immunizations and well child checks
- Adverse affect of children's physical and mental health
 - Prolonged home confinement
 - More time w/ devices
 - Poorer quality diet
 - Increased risk of injury at home
 - Self injury, suicidality, anxiety increasing
 - Increasing risk of violence, vulnerability, and decreased referrals to child protective services
 - Increasing substance abuse

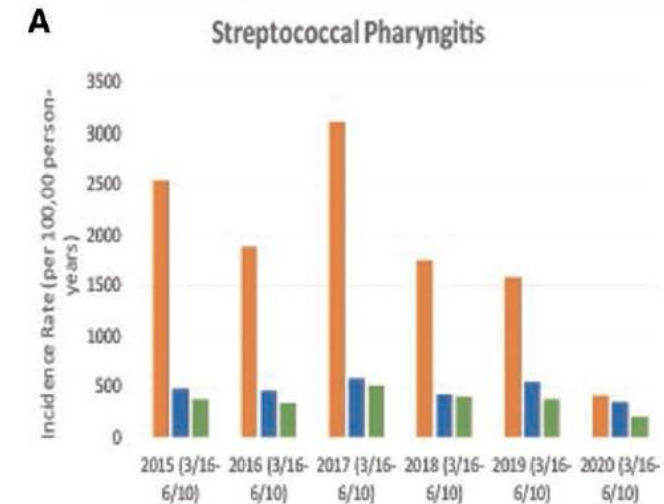
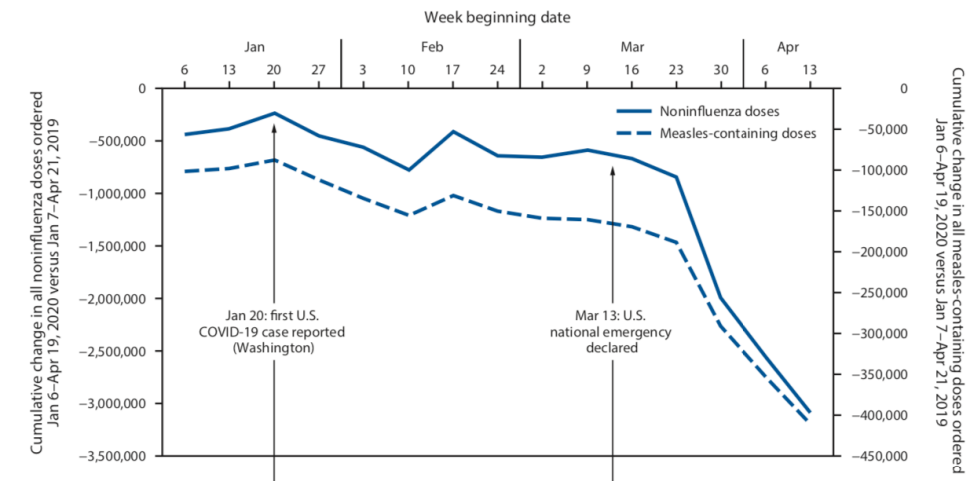


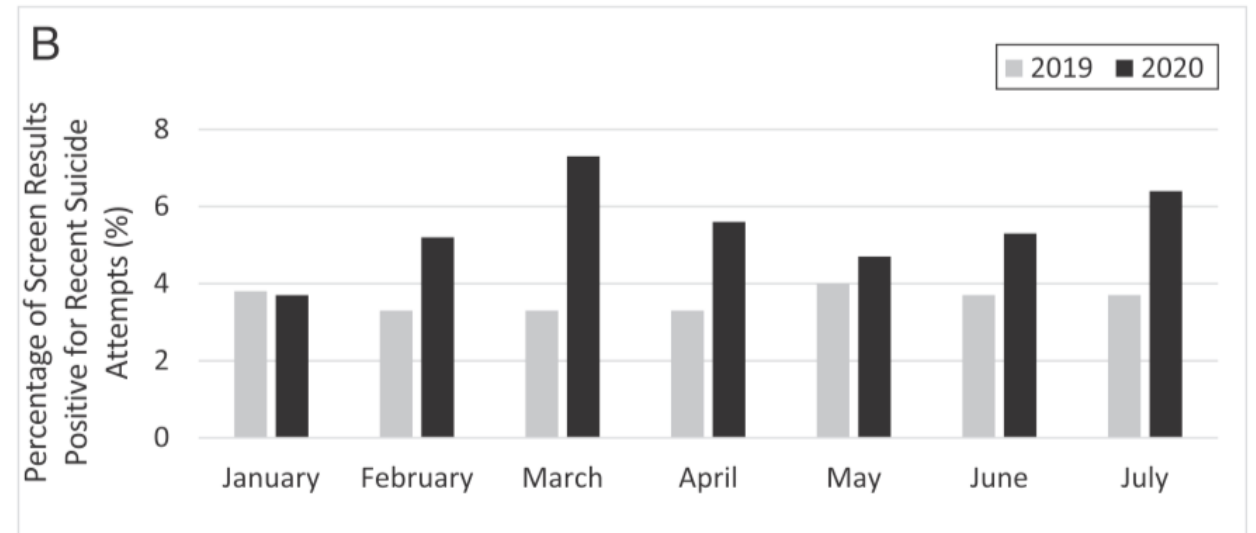
FIGURE. Weekly changes in Vaccines for Children Program (VFC) provider orders* and Vaccine Safety Datalink (VSD) doses administered† for routine pediatric vaccines — United States, January 6–April 19, 2020



Non-COVID impacts of Pediatric COVID

What we don't know

- Long term impact?
- Vaccine preventable illnesses
- Future viral infections
- Education
- Obesity
- Mental health



In summary

- There is a lot we have learned about COVID-19 this last year – but more questions remain
- This is especially true for pediatric and adolescent disease

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