



Contents include:

Brief summaries:

- The role of inflammation in the COVID-19 arrhythmic risk
- Adapting the training environment for fellows during COVID-19 era (article and commentary)

Articles reviewed:

- COVID-19 in Children in the United States: Intensive Care Admissions, Estimated Total Infected, and Projected Numbers of Severe Pediatric Cases in 2020
- The Role of Data Registries in the Time of COVID-19

The role of inflammation in the COVID-19 arrhythmic risk

- Palpitations are one of the most common presenting symptom (7.3%) with arrhythmia the second most common complication after ARDS (19.6% overall, 44.4% for those admitted to ICU) in patients with COVID-19
- Direct myocardial damage (direct cellular infection, hypoxia-induced cell death, cytokine-related cell damage) may be driving enhanced arrhythmia risk – those with higher troponin levels also have higher incidence of VT/VF
 - In vitro, high levels of IL-6 directly inhibit hERG-K⁺ channels leading to prolonged ventricular action potentials
- This underlying predisposition to arrhythmia may enhance the QT-prolonging effects of many of the current medications being trialed as therapies for COVID-19, further increasing the risk of malignant arrhythmias
 - IL-6 also affects cytochrome p450 esp CYP3A4 which leads to increased bioavailability of these medications and an exaggerated QT-prolonging response
- Additionally electrolyte imbalances and pro-arrhythmic vasoactive support increase arrhythmia risks
- Anti-inflammatory treatments, especially those targeting IL-6 (ie tocilizumab, which has been shown to acutely decrease QTc measurements), may reduce acute cardiovascular complications – specifically arrhythmia-related issues
- Perspective: Increased inflammation in cardiac myocytes likely exaggerates the QT-prolonging effect of many ICU drugs and COVID-19 therapies and may be the reason for the frequent complications seen with the chloroquine family of medications. It will be interesting to see if anti-inflammatory medications, especially those focusing on IL-6, are effective in reducing arrhythmia risk.
- Reference: Lazzerini PE, Boutjdir M, Capecchi PL. (2020). COVID-19, Arrhythmic Risk and Inflammation: Mind the Gap! *Circulation*. Epub ahead of print 14 Apr 2020 at www.ahajournals.org. DOI: <https://doi.org/10.1161/CIRCULATIONAHA.120.047293>

Adapting the training environment for fellows during COVID-19 era

- Workforce needs should be balanced with safety, education, and well-being of trainees
- Experiential learning – continued care for CVD patients while also learning about cardiac manifestations of COVID, exposure to leadership discussions about decision-making for staffing and patient-care planning
- Procedural learning – safety much be kept a priority which limits trainee involvement (ie echo guidelines) and lack of elective procedures will likely severely limit exposure; rebalancing of rotations after pandemic has calmed may be needed to allow graduating fellows to gain appropriate experience, with extension of training being a last resort
- Telemedicine – great opportunity for direct patient care with push to triage issues and deliver high-value care as well as potential opportunity for direct observation if three way calls are an option
- Virtual education – online conferences, both institutional and national, should help maintain continuity in didactic learning
- Fellows have a unique opportunity to design solutions to enhance learning while continuing to provide excellent patient care in whatever capacity they are able to
- Key question: How can overall curriculum be adapted to ensure fellows are not penalized for missing ACGME milestones?
- References:
 - DeFilippis EM, Stefanescu Schmidt AC, Reza N. (2020). Adapting the Educational Environment for Cardiovascular Fellows-in-Training During the COVID-19 Pandemic. *J Am Coll Cardiol*. Epub ahead of print 14 Apr 2020 at www.onlinejacc.org. DOI: <https://doi.org/10.1016/j.jacc.2020.04.013>
 - Sinha SS, Sharma G, Cullen MW. (2020). The Crucible of Crisis: Fellows' in Training and Early Career Cardiologists' Responses to the COVID-19 Pandemic. Epub ahead of print 14 Apr 2020 at www.onlinejacc.org. DOI: <https://doi.org/10.1016/j.jacc.2020.04.012>

Article Title:	COVID-19 in Children in the United States: Intensive Care Admissions, Estimated Total Infected, and Projected Numbers of Severe Pediatric Cases in 2020
Authors:	Pathak EB, Salemi JL, Sobers N, et al.
Full Citation:	Pathak EB, Salemi JL, Sobers N, et al. (2020). COVID-19 in Children in the United States: Intensive Care Admissions, Estimated Total Infected, and Projected Numbers of Severe Pediatric Cases in 2020. <i>J Pub Health Mgmt Prac.</i> Epub 15 Apr 2020. DOI: 10.1097/PHH.0000000000001190

Study objective:

“To provide evidence-based estimates of children infected with SARS-CoV-2 and projected cumulative numbers of severely ill pediatric COVID-19 cases requiring hospitalization during the US 2020 pandemic.”

Methods:

- Empirical case projection study using US PICU data through 4/6/20 in combination with clinical and spatiotemporal modelling studies from the COVID-19 pandemic in China
- Projected numbers of severe and critical illness in children were adjusted for US population data
- Models were repeated for several scenarios of cumulative proportions of pediatric infections
- Given different reported severity in different pediatric age groups, <1-1-5/6-15/16-17y age groups were separately analyzed and then combined
- Key assumptions: most infected children have not been tested AND infected children who have not been tested have no, mild, or moderate symptoms

Results:

- Overall estimate of 2,381 children infected in the community for each child admitted to the PICU
- As of 4/6/20, 74 children in 19 states had been admitted to a US PICU -> correlates with ~176K children having been infected with COVID-19
- In ‘best case’ scenario where cumulative infection proportion is 0.5% (1 in 200 of all children are infected with COVID-19), 991 would be severely ill (need hospitalization) and 109 would need PICU care
- In ‘worst case’ scenario where 60% of all children are infected (3 in 5), ~119K children would need hospitalization and ~13K would need PICU, overwhelming the US bed capacity (5100 PICU beds exist in the US currently – 94% in major metropolitan areas)
- Moderate cumulative infection proportion (between 0.5% and 60%) is most likely
- Most primary transmission to children occurs in family clusters – children where parents work outside the home, who have more siblings, or who live in high-density conditions (ie low-income housing) are at higher risk

Figure 1.
Cumulative Number of Confirmed COVID-19 Pediatric Intensive Care Patients United States, March 18, 2020 to April 6, 2020 (Source: myvps.org)

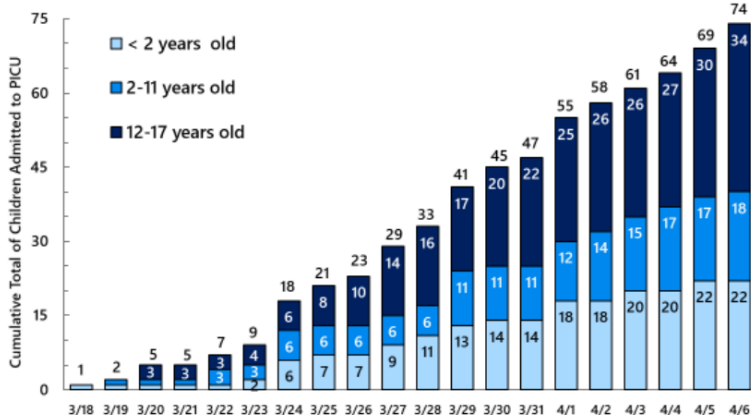


Figure 2.
Estimated Number of Children Infected with SARS-CoV-2 in the United States March 18, 2020 to April 6, 2020

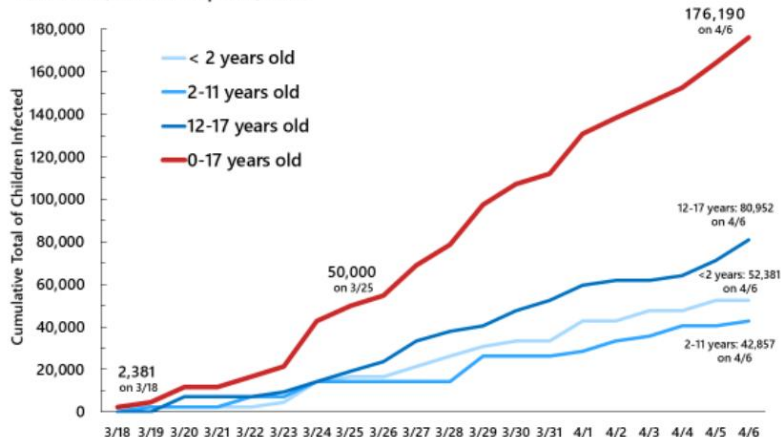


Table 1. Projected Numbers of Children (0 to 17 years) in the United States who will Require Hospitalization for COVID-19 During 2020, for Several Scenarios of Cumulative Pediatric Infection Proportion

SCENARIO: Percent of All Children Infected	Projected Number of Infected Children	Projected Number of Severely Ill Children	Projected Number of Critically Ill Children	Projected Number of Severely + Critically Ill Children
0.5	369,833	882	109	991
1.0	739,666	1,764	217	1,981
5.0	3,698,331	8,821	1,086	9,907
10.0	7,396,662	17,642	2,173	19,815
15.0	11,094,993	26,462	3,259	29,722
20.0	14,793,324	35,283	4,346	39,629
25.0	18,491,655	44,104	5,432	49,536
30.0	22,189,986	52,925	6,519	59,444
35.0	25,888,317	61,746	7,605	69,351
40.0	29,586,648	70,566	8,692	79,258
45.0	33,284,979	79,387	9,778	89,165
50.0	36,983,310	88,208	10,865	99,073
55.0	40,681,640	97,029	11,951	108,980
60.0	44,379,971	105,849	13,038	118,887

Conclusions:

- While the range of expected pediatric COVID-19 cases is wide, even moderate estimates suggest that existing PICU beds may be exhausted, especially when cases cluster away from large, metropolitan childrens' hospitals
- The social and geographic environments will play a significant role in which children are affected
- Current surveillance is inadequate – more granular data including more widespread testing to better estimate cumulative infection proportion (narrow down the 0.5% to 60% range) and geographic locations are keys to helping public health teams plan for the future
- Final recommendation: "Hospitals, PICUs, EMS systems, pediatricians, local health departments and other stakeholders should rush to completion county- and city-specific plans to care for severe pediatric cases of COVID-19, including transportation and regionalization plans."

Perspective:

A sobering model of what a worst-case scenario could be regarding severe and critical COVID-19 illness in children, even in the setting of their low chance of severe illness if they are infected. The effects of sociodemographic and geographic disparities are likely to be highlighted even more in the pediatric population than the adult population given limited PICU resources around the country, especially given the knowledge that these beds are not simply sitting open waiting to accept COVID patients. The model will be able to be narrowed as more US data is collected and the proportion of US children affected overall is better understood.

Summary written by: Katherine B. Saliccioli MD

Topic Areas: COVID-19, pediatrics, modeling, healthcare systems

Article Title:	The Role of Data Registries in the Time of COVID-19
Authors:	Alger HM, Williams JH, Walchok JG et al.
Full Citation:	Alger HM, Williams JH, Walchok JG et al. (2020). The Role of Data Registries in the Time of COVID-19. <i>Circulation: Cardiovascular Quality and Outcomes</i> . Epub ahead of print 16 Apr 2020 at www.ahajournals.org . DOI: https://doi.org/10.1161/CIRCOUTCOMES.120.006766

Key points to remember:

- “Clinical registry data can provide valuable insights into patient characteristics, treatment patterns, and clinical outcomes in patients hospitalized with CVD during [the COVID-19 pandemic]”
- AHA is adding COVID-19 specific data entry to existing ‘Get with the guidelines’ registries to help evaluate the effect of the pandemic specifically on those with cardiovascular disease
- Important to look at how patients with CVD are affected by COVID, but also how the COVID era affects routine care of CVD
- Important to study risk factors – for example, to definitively answer the questions about whether ACE-I/ARB affect susceptibility to severe complications with COVID
- Important to study long-term effects – how those with CVD are affected by COVID but also what long term CVD complications are seen by those who were healthy prior to COVID infection
- Moving forward, automation and ease of reporting will be critical as health care systems face financial challenges and will likely have limited time/money for registry work

Perspective:

This paper is a call to arms for expanding established research infrastructure to study COVID-19 and cardiovascular disease. What other types of registries can be adapted in real-time to facilitate COVID data-collection in already established ways? This will be key in producing high quality, multicenter research in a timely manner.

Summary written by: Katherine B. Saliccioli MD

Topic Areas: COVID-19, registries, clinical research