## Fundamentally changing pediatric respiratory illnesses... and less "bread and butter"

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As health systems which care for adult patients became overwhelmed with cases of SARS-CoV-2 during winter and early spring of 2020, pediatric units in general hospitals and pediatric hospitals and institutions did not. This decrease in pediatric healthcare encounters and admissions were reported in North America, South America, Great Britain, and Australia. (1-4) For 26 children's hospitals in the US, this resulted in a median decrease of \$276 million in charges per hospital. (5) Pediatric Intensive Care Units unsurprisingly demonstrated this decrease in the number of children admitted, as well. Admitting diagnoses and age of children were markedly different when compared to the same period in previous year(s). (2, 6-8)

Rather innovatively Maddux et al examined this period as a "natural experiment" for children's health. (9) Here they ask the question, is a substantial fraction of pediatric critical illness preventable?(9) They examine the volume and characteristics of admissions to six pediatric intensive care units as part of the "stay at home" orders, from 3/15/2020 to 5/14/2020, compared to the same period in years 2017, 2018, 2019 (baseline). They also examined the month immediately prior to the "stay at home order". The six pediatric intensive care units are in children's hospitals/institutions or larger health systems with pediatric units representing different regions of the US. Data was patient level (not just administrative data), and available through the Virtual Pediatric Systems, LLC (VPS) or the electronic health record (one unit only), with careful attention to differences of this unit compared to the other five. (Supplemental digital Content Table 6). Their analysis accounted for sources of variability, such as site effects. There were few repeated admissions, and a sensitivity analysis showed negligible differences, when accounted for in general linear mixed modeling. During the 'stay at home" period, daily admission volumes decreased by 42%, daily patient days decreased by 35% compared to the baseline, and these are reflected in lower admission volume of respiratory diagnoses and infectious diseases compared to baseline period. (Figure 1, ref 9) Admission volumes in 2020 during the period immediately preceding the "stay at home" order were similar in 2020 compared to 2017-2019, ruling out a "year effect". In multi-variant analysis, younger patients and patients of white race ethnicity compared to patients categorized as "other" were less likely to be admitted in 2020 vs baseline years (Figure 2, ref 9). Primary respiratory and infectious diagnoses were less likely in 2020 compared to baseline period, though poisoning/adverse effects and endocrinopathies were more common. Fewer patients in 2020 were supported with non-invasive ventilation (NIV) compared to baseline. There was no difference in duration of invasive mechanical ventilation (IMV), PICU, or hospital lengths of stay or mortality or, differences in distribution of subjects supported with CRRT, ECMO or IMV, or those with a

complicated PICU stay. It does not appear that patients delayed time-sensitive care. This last point is supported by other investigators. (2,4,8)

So to answer the primary question, a <u>substantial</u> fraction of pediatric critical illness <u>appears to</u> <u>be</u> preventable with public health measures. Other groups have suggested this as well. (1, 3, 8) It is important to highlight that public health measures were by no means uniform across all of the countries reported here. While many countries instituted a very strict "stay at home", others did not, yet the effect held. (3,4). It is unclear why this occurred. Therefore it requires a deeper understanding of which measures might be sustainable for primary prevention of seasonable respiratory diseases in children. (10)

The PICU community, and pediatric care providers writ large, recognize that we have made only a little progress in the last 20 years in substantially decreasing seasonal respiratory illnesses. Such cases heaavily populate our PICUS, and therefore become our "bread and butter" during certain seasons and years. Respiratory Syncytial Virus (RSV) was virtually non-existent from in the United States during the natural experiment, described by Maddux. This was equally true in other countries. (2,9, 1) RSV varies in different regions of the country and also by season, it affects the youngest children (< 2 years of age), and is the primary cause of bronchiolitis requiring hospitalization. (12) Other etiologies of respiratory illnesses (asthma, lower respiratory tract infection, respiratory failure, pneumonia ) were also affected by strict public health measures (1,2,9). While the effects of public health measures were greatest in < 2 year olds, it also was seen in those children with medical complexity, who are increasingly cared for in our PICUS in pediatric hospitals/institution. (9,13) Despite influenza vaccination recommendation for all children 6 months of age and older, there continues excessive, severe disease from influenza, whether it is acquired during a "pandemic" or during seasonal influenza periods. (14) Respiratory failure from any cause is never a benign or modest disease, even in children. It has long lasting consequences. (15) In this period of "stay at home", influenza deaths were already decreasing for children under 18, when COVID deaths began to appear. Influenza deaths remain rare events, which continues until the time of this writing. (16)

We can anticipate that the continued phases of the "natural experiment" will affect pediatric respiratory and infectious illness after June 2020. COVID 19 cases as of June 2021 are increasing dramatically for children throughout the United States, as are hospitalization for 12-17 year olds, though deaths remain relatively rare. (17,18) It is very possible that coronavirus (SARS-CoV2 and/or its successor variants) will contribute to seasonal childhood illnesses . (19) Note that while RSV activity

remained low from May 2020 to March 2021, since then, both antigen and PCR positive tests for south east United States and south central United States have increased dramatically.(11) This is marked interseasonal activity for RSV. We highlight that these regions of the country were some of the earliest to remove the public health measures for COVID 19.

We (as parents, caregivers, members of society) owe much to our pediatric critical care colleagues who asked a non-COVID question in the midst of a COVID-19 pandemic, about our acceptances of "childhood illnesses" as problematic but not addressable (except through immunizations ). (1,3,8,9) However given what we now know, can we as a community "stay silent" and inactive? To address this will require some public health measures. (10) We have shown throughout the COVID-19 Pandemic that we can limit infections in our own families, and in our institutions. It is unlikely that policy changes by governments and other public organizations (like school districts) will be reimposed, and we are not suggesting that they should. Nonetheless the public is becoming aware, that the measures used to decrease spread of COVID-19 , have also decreased those seasonal illnesses that even adults acquire. We may remain hopeful. (20)

Outside of the COVID-19 pandemic era, trends for hospitalization of children have changed markedly. Over the past decade or so, fewer children require hospitalization, those that do, are more likely to have medical complexity. At least for bronchiolitis, while the number of hospitalizations have decreased overall in both children's hospitals and general hospitals, the costs have risen dramatically, driven by costs in children's hospitals, though the majority of children with bronchiolitis do not have medical complexity. (21) Additional concerning trends have occurred in children's hospitals/ dedicated children's units in general hospitals: 1) ICU admissions increased for bronchiolitis by 200%, while overall ICU admissions for children less than 2 years increased by 30% 2) Non-invasive ventilation (NIV) increased seven fold, though IMV remained unchanged. (22) In this report, using an administrative database, it was not possible to determine whether NIV or high flow nasal cannula oxygen was in use.(22) Alverson and Ralston appropriately call into question practices of admissions to PICUs for children with bronchiolitis, and use of therapies that may not be needed. (23) Pediatric intensive care units (and pediatric institutions in general) may well be doubling up on our "bread and butter" unwittingly. Given the findings of Maddux and others regarding the "natural experiment", are we not obligated to strongly reconsider where we put our collective efforts? (3,1,8,9)

We applaud the work of our colleagues who have asked a critical question , and even as intensivists consider a public health approach to decrease, if not eliminate childhood respiratory illnesses. (9) We

reference our colleagues in the Pediatric Trauma Society who advocate for policies that minimize pediatric injuries, even as they care for children with injuries. (24) Might this be an example for public policy work, while we personally and institutionally work for change that will decrease pediatric respiratory illness overall?

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