In Reply Lin et al had the following comments regarding our article: “We suggest that the investigation of presleep time screen might strengthen the authors’ findings and clarify the possible mechanisms for evidence-based intervention.” We agree that future study is warranted to examine possible mechanisms, including the association between environmental factors and screen time, influence of interpersonal relationships, and interactions through screen time, for more evidence-based interventions. The hypothesis that melatonin may increase the risk of neurodevelopmental disorders, as described by Lin et al, may be a foundation for effective mechanism-based interventions. However, screen time prior to sleep (timing of screen time) was not observed in this study and should be considered in the future. In addition, further advanced research, including omics analyses and exposome studies, is needed to elucidate the mechanisms of disease onset and to clarify the extent to which inborn and environmental factors affect the onset and severity of disease as well as the conditions under which such effects are manifested. It is hoped that the mechanisms of onset and severity of autism spectrum disorders will be clarified through the consolidation of new findings in the future.

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Letters


Did We Forget That Masks, Lockdowns, and Other Nonpharmaceutical Interventions Also Play a Role in Respiratory Viral Disease?

To the Editor Encinosa et al compared outcomes in children with COVID-19 and children with influenza and respiratory syncytial virus (RSV) in a cross-sectional study. The study found that the hospitalization rate with COVID-19, including multisystem inflammatory syndrome, was 10.8 per 100 000 children, whereas the rates with influenza and RSV were 17 per 100 000 children and 6.2 per 100 000 children, respectively. The results indicated that COVID-19 infection among children might not be as severe as influenza. However, one limitation of this study must be emphasized.

Soon after the start of the COVID-19 pandemic, preventive measures such as wearing masks, social distancing, and lockdowns were quickly implemented. Previous studies found that wearing a mask can effectively reduce the risk of respiratory viral infection, including COVID-19. Other nonpharmaceutical interventions (NPIs), such as public gathering restrictions and school closures, also played important roles in controlling the pandemic, and the implementation of NPIs in the first wave of COVID-19 impacted people’s knowledge, perceptions, and behaviors. It was also noted that the positive rate of influenza testing decreased considerably and has remained at historically low levels following the adoption of community mitigation measures to control COVID-19. In this study, the COVID-19 hospitalization data were gathered during the first quarter of 2021, while the influenza and RSV hospitalization data were from the first quarter of 2017. However, Encinosa et al did not emphasize potential confounding factors, such as NPIs, that could have effectively reduced COVID-19 infection. Instead, the data of COVID-19 hospitalization when NPIs were widely enforced were compared with data of influenza and RSV when NPIs were not in place. Encinosa et al did mention that influenza and RSV were rare during the first quarter of 2021. When NPIs were widely used, hospitalization with COVID-19 was more prevalent than hospitalization with influenza and RSV. We recommend the authors address this limitation to avoid sending false information to the public that COVID-19 may be less severe than influenza among children.

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In Reply We thank Sun et al for their interest in our article comparing children aged 5 to 11 years with SARS-CoV-2 and its sequelae multisystem inflammation syndrome in children (MIS-C) vs those with influenza and respiratory syncytial virus infection (RSV). Our objective was to analyze the incidence and complication rates of SARS-CoV-2–infection hospitalizations in children, specifically MIS-C, compared with other common pediatric viruses with similar respiratory and gastrointestinal complication profiles. Thus, we compared COVID-19 data from 2021 with typical prepandemic data on influenza and RSV in 2017. We did not use 2021 influenza and RSV because there were virtually no cases (11 hospitalizations for RSV and 12 for influenza), likely owing to nonpharmaceutical interventions (NPIs), such as masks and lockdowns, and such data would not be representative of typical benchmark levels of influenza and RSV.

As Sun et al point out, we found that the rate of hospitalization with COVID-19 and MIS-C in 2021 was lower than that with influenza and RSV in 2017. However, Sun et al did not report our second finding, that hospitalizations with COVID-19 and MIS-C were more severe in terms of complications, to the extent that the total cumulative number of days in the hospital for all patients with COVID-19 and MIS-C was about the same as for those with influenza. In this sense, it would be wrong to conclude that COVID-19 and MIS-C are less severe than prepandemic influenza.

Sun et al make a good point that not accounting for NPIs may have confounded our COVID-19 hospitalization rates. We reported only average hospitalization rates across 11 states, not controlling for NPIs. To address the authors’ first concern, we stratified our data into low and high NPI states, using the Oxford COVID-19 Government Response Tracker’s Containment Index, a score from 1 to 100 that accounts for 14 possible pandemic interventions (NPIs) in place on January 1, 2021, such as school closures, lockdowns, and mask mandates. In the 11 states included in our study, the scores ranged from 48 to 69, with a higher score indicating more NPIs. Dividing our data at the median score of 62, we found that the 6 states with lower NPI scores were not much different in terms of outcomes than the 5 states with higher NPI scores. Both groups of states had a COVID-19 and MIS-C rate of 10.8 per 100 000 children, and both had an overall complication rate of 70% (cardiovascular, respiratory, neurologic, hematologic, kidney failure, gastrointestinal, and musculoskeletal). Thus, we found that our COVID-19 and MIS-C rates and outcomes did not vary with the magnitude of the states’ NPIs. These initial results should give the public confidence that our COVID-19 and MIS-C hospitalization rates and outcomes were not confounded by NPIs that we did not account for before. Future research should explore the impact of NPIs on COVID-19 and RSV in greater detail beyond these 11 states that represent 24% of the US pediatric population.

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Disclaimer: The views expressed in this reply are those of the authors, and no official endorsement by the US Department of Health and Human Services and the Agency for Healthcare Research and Quality is intended or should be inferred.

More Recent Literature Does Not Support Premise or Conclusions

To the Editor Frost and Hersh argue that nearly 75% of antibiotics used for the treatment of acute otitis media (AOM) may be unnecessary. Their position hinges on a review article that quotes a study conducted 50 years ago, which they claim shows that symptoms in children with AOM caused by Hemophilus influenzae or Moraxella catarrhalis are more likely to resolve spontaneously without treatment compared with symptoms in children with Streptococcus pneumoniae. However, as all children in the above study had tympanosentesis at entry, its data cannot be used to estimate spontaneous resolution rates. More recent data suggest that H influenzae, not S pneumoniae, is more likely to be recovered from middle ears of children experiencing treatment failure. In our recent placebo-controlled trial, failure rates were unrelated to the pathogen colonizing the nasopharynx at the time of diagnosis. However, in our 10 vs 5 trial, children with H influenzae in their nasopharynx at time of diagnosis were significantly more likely to have treatment failure than children with S pneumoniae. The