



COMMENT

The indirect effects of COVID-19 on pediatric research

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As members of the Research Committee of the Association of Medical School Pediatric Department Chairs, we write to comment on the review article by Fleming et al.¹ on the consequences of the COVID-19 pandemic on child and adolescent health and associated research. We agree with many of the observations that the authors have highlighted, specifically the important needs for involving children in trials of COVID-19 vaccines and treatments, for natural history studies of youth who acquire COVID-19, for highly coordinated and collaborative clinical trials and cohort studies among academic institutions, for streamlining approaches to effective research governance and protection of research subjects while guaranteeing high levels of patient privacy and safety, and for the study of the unfortunate immediate sequelae of acute COVID-19 in children, specifically the postinfectious disorder called multisystem inflammatory syndrome in children, also referred to as Pediatric Inflammatory Multisystem Syndrome Temporally Associated with COVID-19.

In addition, we stress that investigators worldwide should focus on the *indirect* sequelae of the pandemic. For more than a year, it has radically changed the way children and adolescents live and interact with each other, all with the potential for long-term impacts on their physical and mental health. For example, what are the intermediate and long-term physical and behavioral health consequences of reduced social interactions, increased screen time, decreased physical activity, canceled sports seasons, and missed or virtual school? Already, pediatric mental health providers and emergency departments are facing increasing numbers of youth suffering from anxiety, depression, and suicidal ideation, as well as suicide attempts.^{2,3} Concerns are rampant⁴ that the prevalence of childhood obesity and malnutrition will rise further due to sedentary lifestyles⁵ and lack of access to school-based meal programs.⁶

The COVID-19 pandemic has also increased health and healthcare disparities for children and adolescents.⁷ This stems in part from the relationships between limited family resources and (1) access to the technology required for remote learning and for telemedicine visits, (2) ability to navigate the greater complexity of healthcare systems with COVID-19 constraints in place, and (3) opportunity for consistent parental supervision of home schooling. It is difficult to know how long it might take for youth who have fallen behind their peers in school to regain lost ground and what resources that they might require. Similarly, it is difficult to know the full impact of delays in healthcare on the progression of chronic diseases. All these issues need to be tracked and studied.

While the Children's Hospital Association and the American Academy of Pediatrics have called for expanded funding for existing programs addressing mental health, social isolation, academic underachievement, and other disorders (<https://thehill.com/>

[business-a-lobbying/540148-childrens-hospitals-pediatricians-urge-biden-administration-to-prioritize](https://www.business-a-lobbying/540148-childrens-hospitals-pediatricians-urge-biden-administration-to-prioritize) and <https://www.aappublications.org/news/2021/02/22/townhall-02-22-21>), these health challenges also present opportunities for investigators to trial new and innovative solutions. The umbrella program entitled *Collaboration to Assess Risk and Identify Long-Term Outcomes for Children with COVID (CARING for Children with COVID)* (<https://www.nih.gov/news-events/news-releases/nih-effort-seeks-understand-mis-c-range-sars-cov-2-effects-children>), which is jointly sponsored by the Eunice Kennedy Shriver National Institute for Child Health and Human Development, the National Heart, Lung, and Blood Institute, and the National Institute for Allergy and Infectious Diseases and which encompasses a series of research networks, and the *PreVAiL kids* (<https://www.nichd.nih.gov/newsroom/news/122120-prevail-kids>) program focused on diagnostics for COVID-19 are encouraging starts. The *Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) Initiative* (<https://www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-launches-new-initiative-study-long-covid>), recently announced by the National Institutes of Health, is another exciting step forward. While these programs will provide funding for infectious and postinfectious direct sequelae of COVID-19, we must stress that funds supporting investigators studying the myriad noninfectious, indirect sequelae of the pandemic on children are equally important.

As we race to increase our understanding of COVID-19 and SARS-CoV2, we must also acknowledge the importance of maintaining and initiating programs in non-COVID-19-related pediatric research. Much of this research has been slowed by the long pauses in research activity at academic and nonacademic institutions around the world at the height of the pandemic and by the redirection of research programs to a focus on COVID-19. Studies based in labs, clinics, and the community have all been delayed. Social distancing has also altered the fundamental context for translational studies as key outcomes like the incidence of respiratory infections and behavioral changes in school have radically changed. In the meantime, children continue to experience morbidity due to the full spectrum of pediatric diseases, underscoring the need for improved understanding of the pathogenesis of many pediatric diseases and for improved approaches to their diagnosis and treatment.

The COVID-19-associated pauses in research have the gravest implications for those at the start of their academic careers. Of greatest concern are the futures of those young investigators on time-limited career development awards (R38, T32, K08, K23, and others) who have lost critical months. Many of these young scientists are not generating the data necessary to transition to independent R awards. We strongly urge funded extensions of their awards through bridge programs like the one recently announced by the NIH that provides 1-year extensions on a case-

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by-case basis to K awardees in the last year of their awards (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-052.html>). We also urge the NIH to extend early-stage investigator status from 10 to 12 years or more (<https://nexus.od.nih.gov/all/2020/04/09/can-esi-status-be-extended-due-to-disruptions-from-covid-19/>).

The COVID-19 pandemic has had an indelible impact on the health of children and adolescents and on the face of pediatric research. Nevertheless, with appropriate prioritization of resources by funding agencies and by academic and nonacademic institutions, we are optimistic that the broad consequences of COVID-19 will continue to wane, with an improved outlook on life for children and adolescents.

AUTHOR CONTRIBUTIONS

Both authors made substantial contributions to the conception and design of the manuscript and to drafting and revising it critically for important intellectual content. Both authors gave final approval of the version to be published.

ADDITIONAL INFORMATION

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