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EDITORIAL

Pediatric Research and COVID-19: the changed landscape

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INTRODUCTION

The COVID-19 pandemic has significantly impacted pediatric research globally. The inequity has been more striking for research dealing with vulnerable members of society, especially for children. Research funding has also been diverted to research involving adults who are disproportionately more seriously affected by SARS-CoV2. Children's health and well-being has been affected with loss of education, decreased physical activity, food insecurity, less well-child screening, increased mental health issues, and routine vaccination delays.[1] All of these have significantly affected minority and low-income children more than others.[2] However, during the pandemic there has been an exponential increase in the development and implementation of new technologies to improve communication and develop new clinical trials methodology. Scientific advances in the field of sepsis and immunology will also have direct benefits for children. Families and children have also had increased exposure to health care and scientific information potentially improving their medical literacy.[3,4]

CHILDREN AND FAMILIES

The COVID-19 pandemic has been a time of unprecedented stress for families especially with children with medical vulnerabilities. Although children appear to be mildly affected there is a small but significant number of children with serious issues such as the multisystem inflammatory syndrome (MISC) and long COVID.[5] In addition, there have been reports of pregnancy loss and issues related to placental inflammation.[6–8] Children, who are vulnerable members of our society, have suffered disproportionately during the pandemic from social isolation and discontinuation of routine recreation.

There has been major increase in research activity aiming to understand the immense changes to society, families, and healthcare. There is a risk that children would not be included in ongoing research due to their lower susceptibility to SARS-CoV2. Therefore, involving families and children in research is increasingly crucial. The RECOVERY (Randomised Evaluation of COVID-19 Therapy) trial in the UK involved all age-groups and used innovative methods to ensure rapid recruitment and results with 1000 patients recruited by day 16 of the study.[9,10] Van Driest et al. discussed techniques to improve engagement with families. Curtailed visiting and outpatient attendance by both parents has been very stressful for parents and impairs practitioner engagement with parents. However other benefits such as improved remote communication have been enhanced and have improved the ability to sustain more regular remote contact with the family. In addition, enhanced remote communications have broadened the reach of research projects which had previously been limited by geography. Other resources for research such as surveys and developmental checks have been improved. Van Driest et al.[11] noted a significant reduction in the consent rate for an observational research study in the early months of the COVID-19 pandemic and during implementation of a one-parent/visitor policy in our children's hospital especially for neonates and infants. The authors postulated that the increased stress of the pandemic may be responsible for this finding. However, as some parents cited a desire to discuss participation with the other parent prior to consenting, this may suggest that the policy is responsible in some way for the decrease in recruitment. Newer methods for research studies including direct-to-family study design, in which recruitment, intervention, and data collection all occur remotely (e.g., in participants' homes),[12] require additional technology.

SOCIAL DETERMINANTS OF HEALTH AND COVID-19

Sir Michael Marmot developed the concept of the Social Determinants of Health (SDH) finding that health outcomes are determined by "the conditions in which people are born, grow, live, work and age".[13] The importance of SDH has been particularly stark during the pandemic as those who suffer inequality or are socioeconomically disadvantaged have been disproportionately affected. Rates of infection are four to five times higher in people of Native American, Hispanic, or Black American origin with similar patterns in the UK. Although the causes for this disparity is not known, there is a higher prevalence of risk factors such as obesity, diabetes, and hypertension in these communities putting them at higher risk for infection.[13]

Other social determinants of health, including access to the internet, a computer and broadband (recently added as social determinants of health),[14] affect the impact of COVID-19 on schooling. Lack of access to the internet, a computer and broadband limit the ability to attend school remotely. This lack also reduces the availability of substitute education or additional learning on the internet.

Severity of infection in children may also be influenced by ethnicity and other comorbid conditions. Children with comorbidities including children with cerebral palsy and prematurity and those that are categorized as black, Asian, and minor ethnicities have more severe infection than those without.[15]

VACCINES

SARS-CoV-2 vaccination is progressing in adults at an unprecedented scale internationally but children younger than 12 years

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are only beginning to be enrolled in clinical trials. Vaccination programmes have now extended to younger children including infants and trials are ongoing. Cooper et al.[1] recently highlighted the key issues and knowledge gaps involved in pediatric vaccine development and implementation, including[1] rationale for childhood vaccination,[2] immune maturation in childhood,[3] ethical issues,[4] concerns specific to children with developmental disorders and chronic conditions,[5] health inequities socioeconomically and for children generally, and[6] vaccine hesitancy.[1] Recent developments in the understanding of children's immune systems have important implications for the development of immunotherapy.

POTENTIAL FOR RESEARCH INNOVATION

Since the pandemic began there has been great progress, better collaboration with improved communication and development of international consortia. Klingenberg et al.[16] reviewed guidelines and preparedness in middle- and low-income countries as a part of the International Neonatal COVID consortium. They found exacerbation of pre-existing resource challenges for neonatal care which provide opportunities for international collaboration.

Sharing pediatric COVID-19 data and resources across existing studies would strengthen our research capacity during the current pandemic, including long-term study of natural history and identification of rare complications. Instead of replacing individual or institutional studies, a practice of shared resources would provide a collaborative entity to complement local efforts.[17] Pediatric research fragmentation has been highlighted by the COVID-19 pandemic. Prospective formation of multi-institutional networks is essential so that standardized pediatric data can be collected for collaboration and re-use.[17] An example of an international collaborative data repository: the Repository of Aggregated Pediatric International Data on COVID-19 (RAPID-19) was recently described.[14] RAPID-19 aggregates de-identified clinical data on pediatric patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection (COVID-19), curated across existing research activities. The steering group ensures equity of access to the dataset and full transparency on site participation, data use, and collaborative research.

Alkhouri et al.[18] have shown a significant increase in publications in *Pediatric Research* since the onset of the COVID-19 pandemic and not exclusively related to papers related to COVID-19. Weiner et al.[19] in the Pediatric Policy council have highlighted the need for structured training for research and knowledge exchange in disaster medicine and epidemics.

FUTURE DIRECTIONS

Pediatric research has been significantly impacted by the pandemic. Decreased research funding, staff, and resources are key factors as well as difficulty communicating with parents due to restrictive visiting policies. Parents are also concerned about the risk of infection in a healthcare setting. However, innovative design of studies using the internet can enhance the participation and recruitment to clinical trials and dissemination. International collaboration has been facilitated by the increased use of the internet and remote meetings as well as allowing rapid research dissemination. These links are vital to develop the tools to combat future epidemics and ensure lessons from this pandemic are not lost.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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