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COVID-19 in Children Part I: Epidemiology, Prevention and Indirect Impacts

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Abstract

Children globally have been profoundly impacted by the COVID-19 pandemic. This review explores the direct and indirect public health impacts of COVID-19 on children. We discuss in detail the transmission dynamics, vaccination strategies and, importantly, the “shadow pandemic”, encompassing underappreciated indirect impacts of the pandemic on children. The indirect effects of COVID-19 will have a long-term impact beyond the immediate pandemic period. These include the mental health and wellbeing risks, disruption to family income and attendant stressors including increased family violence, delayed medical attention and the critical issue of prolonged loss of face-to-face learning in a normal school environment. Amplification of existing inequities and creation of new disadvantage are likely additional sequelae, with children from vulnerable families disproportionately affected. We emphasise the responsibility of paediatricians to advocate on behalf of this vulnerable group to ensure the longer-term effects of COVID-19 public health responses on the health and wellbeing of children are fully considered.

Introduction

The global impacts of the coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have been pervasive across societies.(1) Paediatricians and primary care providers are familiar with endemic seasonal coronaviruses causing mild upper respiratory tract infections.(2) By contrast, SARS-CoV-2 has manifested with an extraordinary rate of epidemic spread due to factors unique to the virus, host and environmental interactions.(3) COVID-19 vaccination programs have included children much later than adults due to an absence of early safety and effectiveness data and the relatively mild disease profile in paediatric populations. Children have made up a minority of infections worldwide, although this may be changing, and evidence to date suggests that children are not key drivers of transmission. However they have borne some of the highest indirect impacts of the pandemic through disrupted education and reduced social and developmental opportunities.(4) These negative effects have disproportionately affected disadvantaged children and will be a significant and ongoing concern amongst paediatricians and families for many years.

This review (Part 1 of 2) summarises current understanding of paediatric COVID-19 and future priorities for paediatricians and public health practitioners responsible for the wellbeing of children during and after the COVID-19 pandemic. The authorship group have together been active across research, clinical care, policy development and advocacy with respect to COVID-19 in children.

Epidemiology of COVID-19 in Children

General epidemiological features

Children account for a minority of SARS-CoV-2 infections at a population level (5) and typically acquire their infection from an adult contact.(6) Occasional transmission from symptomatic children to household contacts occurs with the ancestral (19A/19B) strain of SARS-CoV-2,(7, 8) however the contribution of these cases to the overall epidemic has been minimal.(6) Understanding on the applicability of this data to emerging and established

variants of concern such as Delta (B.1.617.2) is evolving.(9) Early Australian studies on the Delta variant suggest that transmission rates are higher, particularly within households, but transmission from adult source cases remains higher than from children.(10) Future variants of concern may present new challenges and it will be important to continue to critically appraise existing paradigms against new data pertaining to individual variants.

The virus is primarily spread between people in close contact, including via respiratory droplets. Increasing recognition of the potential for aerosol spread, especially with more infectious variants of concern, such as Delta (11) has resulted in modified World Health Organisation (WHO) and local infection control guidance.(12) The higher transmissibility of the Delta variant is reflected in a significantly greater household attack rate (13, 14) and basic reproduction number (R_0) (2, 15) (Table 1). Compared to the ancestral strain, the Delta variant also has a shorter average incubation period (Table 1),(16-18) presenting additional challenges to the test-trace-isolate approaches undertaken by public health services.

Though children were underrepresented in terms of disease burden in 2020,(5) high household attack rates with Delta (21) combined with higher vaccination rates in older adults appears to be shifting infection frequency towards younger age groups.(22, 23) Nonetheless, severity of disease remains mild in most children.(22, 24) Current epidemiology shows young adults rather than children predominating in Australia, the United States (US), and United Kingdom (UK),(25) likely representing a nexus of higher transmissibility in adults and lower vaccination rates in young people.

School-Based Transmission

One of the biggest impacts of COVID-19 on children has been the pattern of frequent and prolonged periods without face-to-face classroom activity. This shift to remote online learning is a key local issue for Australian children, while also affecting 1.5 billion children globally. Minimal attention to define a different policy approach that prioritises keeping children in the classroom while mitigating transmission has occurred in Australia despite strong advocacy from paediatricians. School closures have exacerbated societal inequities

globally and will have a significant impact on economic and social development in decades to come.(26)

Whilst school closures have been widely implemented, the degree to which this approach is warranted in the context of local SARS-CoV-2 patterns and circulating strains has varied across the world and has often escaped scrutiny. In 2020, large SARS-CoV-2 outbreaks in educational settings were reported, notably in a high school in Israel (27) and school camp in the US.(28) In contrast, a prospective study in New South Wales (NSW) schools and early childhood education centres (ECECs) in 2020 reported low transmission rates (0.9%).(29) Moreover, NSW schools were able to engage in face-to-face learning in the second half of 2020 (30, 31) in the context of low levels of community circulation of the ancestral SARS-CoV-2 strain. Elsewhere, studies from Israel and England in 2020 showed that school re-openings were not associated with a resurgence of infections in the community.(32, 33)

Numerous studies of SARS-CoV-2 in higher incidence settings have shown relatively lower rates of transmission in schools compared to households and the wider community.(34) Outbreaks, when they occurred, were predominantly among adult staff and in adolescents rather than younger children.

The Delta variant has added complexity in 2021, and future variants of concern will be expected to confer additional, potentially unforeseen challenges. In the UK, the frequency of school outbreaks increased just prior to the summer holidays (May-July 2021) (from 52 school outbreaks in epiweek 21 to 94 outbreaks in epiweek 22); 51% of those outbreaks were associated with the Delta variant.(35) In Australia, our understanding of the effects of the Delta variant on educational settings is still evolving. Symptom monitoring and testing among school students and staff have unmasked previously unknown community circulation of SARS-CoV-2, including within high schools in Queensland, the Australian Capital Territory and Victoria. Secondary and tertiary infections have been reported to result from school exposures but the relative contribution of schools to transmission needs to be carefully examined, especially when students and staff may have been exposed in the community or through para-educational social activities.

In NSW, schools returned to online learning for a majority of students in Greater Sydney from the 25 July 2021, but Early Childhood Education Centres (ECECs) remained fully open. As a consequence, introductions into ECECs were more commonly reported compared to schools. Preliminary evidence from NSW suggests that the secondary attack rate in ECECs is 7-fold higher in the current 2021 Delta outbreak compared to that observed in 2020 (6.4% versus 0.9%).⁽¹⁰⁾ Outbreaks have been associated with unvaccinated staff members in the context of limited access for young adults during the initial stages of vaccine roll-out in early 2021, though advocacy efforts have been strong to prioritise education professionals.

COVID-19 Vaccinations in Children

Several COVID-19 vaccines have been approved for use in children and/or adolescents in at least one country, including Comirnaty (Pfizer), Spikevax (Moderna) and CoronaVac (Sinovac Biotech). In Australia, Comirnaty's registration was recently extended to include adolescents aged 12-15 years, following results of an ongoing phase III trial in 2260 adolescents.⁽³⁶⁾ The trial reported vaccine efficacy against symptomatic COVID-19 from 7 days after the second dose of 100% (95% CI 78.1 – 100%). Neutralising antibody titres were higher in 12-15 year olds than in 16-25 year olds. Mild-to-moderate local and systemic adverse events were common, including injection site pain (80%), fatigue and headache (60%) and fever (20%). The safety and efficacy of Moderna's Spikevax has also been demonstrated in adolescents aged 12-17 years (n = 3700), and approval in Australia for this age group appears likely.⁽³⁷⁾ Trials of both vaccines in children aged ≥ 6 months are planned or underway. Early safety and efficacy data for the inactivated SARS-CoV-2 vaccine, CoronaVac are promising for children as young as 3 years.⁽³⁸⁾

Safety data in adolescents is mostly limited to clinical trials, which are under-powered to detect rare adverse events. Both Comirnaty and Spikevax are associated with a rare risk of myocarditis (2.7 per 100,000 persons), occurring more frequently in adolescents and young adults compared to people over 30 years.⁽³⁹⁾ Whilst concerning, the vaccine-associated cardiac events affecting predominantly young males after the second dose are short lived and occur with a 3.7-fold lower frequency than if caused by an acute SARS-CoV-2 infection

itself.(39) The paediatric trial of AstraZeneca's COVID-19 vaccine was halted following the identification of thrombosis with thrombocytopenia syndrome, a rare but serious adverse event which disproportionately affects younger adults (3.4 per 100,000 in persons aged < 50 years).(40)

Severe illness from acute COVID-19 is rare in healthy children, therefore the direct benefits of vaccination to the individual child may be lower relative to other age groups. In fact preliminary modelling suggests that population-wide health outcomes of SARS-CoV-2 will not be meaningfully affected by inclusion of 12-15 year olds in the broader vaccine roll-out programs.(41) There are also broader ethical issues at play, with the World Health Organization urging wealthy countries to consider donating vaccine doses intended for children to COVAX, where they could be distributed to adults in low and middle income countries.(42)

With recent Therapeutic Goods Administration (TGA) and Australian Technical Advisory Group on Immunisation (ATAGI) advice, vaccination of children from 12 years of age is now recommended in Australia,(43) and both Comirnaty and Spikevax have received TGA approval for this age group. The decision to expand vaccine use to younger children will be determined following assessment of safety from overseas vaccination programs, consideration of the indirect benefits of vaccinating younger children in reducing transmission to other age groups, and vaccine availability. Recent phase 2/3 data demonstrating high efficacy and safety for Comirnaty (given at a lower 10 microg dose) in 5 to 11 year old children (44) will inform these TGA recommendations.

Alongside the roll-out of vaccination programs for adolescents and children, high vaccination rates in adults working within childcare, school and health care settings must be encouraged to give indirect protection to children, minimise transmission events and ensure essential services for children continue uninterrupted.

Secondary Effects of the COVID-19 Pandemic on Children

Impact on other infectious diseases

The non-pharmaceutical interventions (NPIs) implemented in response to the COVID-19 pandemic in Australia have had a major impact on transmission of other infectious diseases, particularly respiratory viruses and travel-related infections.(45) Following the initial period of stay-at-home orders in April 2020, a marked reduction in respiratory syncytial virus (RSV) and influenza transmission was observed and this persisted through winter (June – August) 2020 in the context of ongoing border restrictions and despite the re-opening of schools.(46) Whilst influenza activity has remained absent to date, an inter-seasonal surge in RSV was observed across several states during late 2020-early 2021 with the number of cases and hospitalisations exceeding the usual winter peak.(47) An increased cohort of RSV-naïve infants and, possibly, waning immunity in older children due to the delayed 2020 season may have contributed to this unseasonal outbreak. It is expected that a similar impact may be seen when influenza re-emerges.

The dramatic alterations in respiratory virus seasonality in Australia during the COVID-19 pandemic highlight the potential impact of NPIs on RSV and influenza transmission particularly. Circulation of these respiratory viruses may not return to normal for a number of years,(47) necessitating close monitoring to facilitate preparedness for future unseasonal peaks in transmission. RSV has become nationally notifiable in Australia in July 2021 providing a lens to continue to monitor this in years to come. In future, exploration of effects of specific NPIs in reducing transmission of non-SARS-CoV-2 respiratory viruses amongst children, and the feasibility of implementing these measures, may add to the available strategies to mitigate impact of these important pathogens.

Incidence of other notifiable illnesses, such as invasive meningococcal disease, rotavirus and measles, has shown similar reductions in 2020.(45) Future surveillance will be important to monitor the impact of ongoing NPIs as well as the potential for re-introduction of travel-related infections when international borders are re-opened.

Impact on health systems including routine childhood immunisation programs

Internationally, health seeking behaviours were considerably altered by the COVID-19 pandemic.(48) In Australia, infection-related hospital admissions fell by over 50% and admission for non-infectious causes by 25% in early 2020.(49) Frequency of consultations

with general practitioners remained stable though 31% were conducted by telehealth.(50) Interestingly, a sustained reduction in antibiotic dispensing rates for respiratory infections was also observed in 2020, particularly in general practice.(50) Avoidance of health services due to fear of COVID-19 was a possible factor in parents not seeking prompt medical attention for their children,(49) leading to high levels of concern amongst paediatricians.

Immunisation programs have been disrupted, particularly in low and middle income countries, both as a result of reduced capacity of healthcare services and staff redeployment, reduced attendance by patients and in some cases temporary suspension of routine or mass immunisation campaigns.(51) Numerous high and low income countries are now experiencing a rapid decline in childhood immunisation rates as a result. In a survey across 19 countries in the South East Asia and Western Pacific regions, vaccination disruption was reported by respondents in 95% (18/19) of countries. This is likely to adversely impact the control of vaccine-preventable diseases and lead to the potential for outbreaks particularly when social distancing measures are relaxed. Once borders reopen, increased local incidence of vaccine-preventable illnesses, such as measles or diphtheria, via importation by returned travellers would not be unexpected.

In contrast to the experience in other countries, routine childhood immunisation coverage in Australia has fortunately remained high since the start of the pandemic,(52) and outbreaks of vaccine preventable disease have not been widely reported. Notably, influenza vaccine uptake was higher in 2020 than previous years with 44% of eligible children receiving a dose.(53) Given the potential for diverted immunisation services and the complexities of public messaging around receiving both influenza and SARS-CoV-2 vaccines, many clinicians are concerned that influenza vaccination rates may fall through 2021. With future expected re-emergence of influenza, adequate resourcing of influenza vaccine programs is crucial.

Educational and wellbeing impacts

Globally, early childhood centres, primary and secondary schools have experienced closures as part of COVID-19-related NPI measures. Risk communication around schools remaining

open could have been handled more effectively, as the evidence on closing schools to mitigate the pandemic remains uncertain.(54) Whilst there are direct health impacts for children that are mitigated by school closures for the individual (fewer infections) and possibly society (lower transmission), the expected indirect impacts are significant. These effects, including wellbeing and mental health repercussions, loss of crucial social interactions and developmental opportunities, a premature move to the online world, reduced educational attainment and loss of future productivity, will be felt for a lifetime.(55)

On a global scale, 463 million children have been unable to access remote learning in 2020, (26) with hunger, violence, poverty and declining educational attainment additional major consequences (Figure 1).(56) The Ebola epidemic in 2014 had already provided insights into some of the impacts now being felt by children worldwide from COVID-19 through non-attendance at school, including increases in child marriage, fewer females completing school and reduced educational attainment.(56)

In Australia, there are almost 4 million children currently enrolled in almost 10,000 schools. While Australian children have missed less school than their northern hemisphere peers, the impacts have still be profound.(57) In almost all Australian jurisdictions, periods of school closure in association with lockdowns have been implemented.(58)

Increased hospitalisation of young people with eating disorders and other mental health concerns has occurred.(59) Moderate to severe emotional distress has been reported in 40% of high school students, putting them at risk of future mental health challenges;(57) key contributors have been loneliness, disruption to routines and the stress of remote learning (Figure 1).(60) In a national parent survey of child health in 2021, online safety, mental health and loss of physical activity were leading health issues reported.(61) Whether this surge in emotional distress is directly linked to the pandemic, or part of a broader societal trend, has been difficult to tease out. Nonetheless, it is an important measure of wellbeing that will impact this generation of young people for decades to come.

The myriad of benefits to children from school attendance should not be underestimated,(62) and has historically been advocated strongly by both educators and

parents. Early on in the pandemic, the Australian Health Protection Principal Committee recommended that schools remain open and reinforced this at the start of 2021, with recommendations recently updated for the Delta variant.⁽⁶³⁾ Despite this, fragmented jurisdictional decision making has erred towards school closures in all states where a lockdown has been used, predominantly to reduce population movement.

All jurisdictions have a plan for schools to test, trace, isolate and clean when an index case is detected in a school. Traffic light systems – linking levels of community transmission with operational strategies for schools from full face-to-face learning with standard precautions (green) to 100% online delivery of learning (red) – have been developed in Victoria and NSW, to prioritise face-to-face learning wherever safe and feasible, but these have yet to be implemented nationwide. These approaches need to be part of a comprehensive mitigation plan around schools which includes vaccination of teachers, staff and children over 12 years at this stage.

Recognition of the disproportionate burden of school closures on the most vulnerable families and children is vital. With 13% of Australian households lacking internet access,⁽⁶²⁾ children from these households are disadvantaged in online learning programs, further compounding inequity.⁽⁵⁵⁾ Children with disabilities, low income families, full time working parents with very young children, and minority populations such as Aboriginal and Torres Strait Islander peoples must be explicitly prioritised in decision-making around COVID-19, including school-based decisions. Families from these sub-groups should be prioritised in vaccine roll-out programs and in accessing face-to-face learning opportunities, with targeted health education and support to ensure COVID-19 related messaging is appropriate, clear and accessible. As with many aspects of COVID-19 management, consideration of these important and vulnerable sub-populations is critical to ensure existing inequities are not accentuated.

Conclusions

The impacts of the COVID-19 pandemic have been far-reaching for children. Further research is critical to determine the unique features and consequences of this disease in children. Importantly, the indirect effects of COVID-19, including the impact on mental

health and wellbeing, delayed health-seeking behaviours, disrupted family income, increased household stress and school closures must not be underestimated. Children, particularly those from vulnerable families, bear the heaviest burden in this regard. Sadly, it is these children who are least empowered to advocate for more favourable consideration in the overall population risk-benefit assessment, yet they will feel the long-term impact of today's public health decisions. As we move into the next phase, it is time to acknowledge the "shadow pandemic" for children and their families, and listen to the voices of children, parents and paediatricians around the world to include them in the decision making.

Abbreviations

ATAGI, Australian Technical Advisory Group on Immunisation

COVID-19, coronavirus disease 2019

NPI, non-pharmaceutical interventions

R_0 , basic reproduction number

RSV, respiratory syncytial virus

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

TGA, Therapeutic Goods Administration

WHO, World Health Organisation

Figures and Tables.

Figure 1. Impact of the COVID-19 pandemic on the wellbeing of children.(26, 57, 60, 61)

Table 1. Comparison of epidemiological parameters between ancestral (19A/19B) and Delta (B.1.617.2) variants of SARS-CoV-2.

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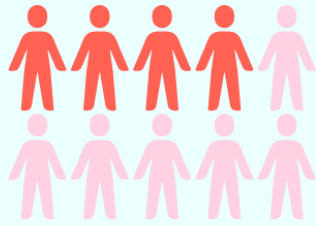
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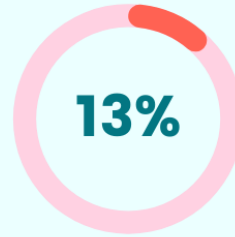
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Impacts of COVID-19 on the Wellbeing of Children



Four in ten Australian high school students have reported moderate to severe emotional distress due to the COVID-19 pandemic



Percentage of Australian households without internet access, leading to children being excessively disadvantaged by online learning



Key contributors to emotional distress:

- Loneliness
- Disruption to routine
- Stress of remote learning



Key Parental Concerns in 2021



Worldwide, 463 million children have been unable to access remote learning in 2020



370 million children may have missed nutritious school meals



An additional 6-7 million children under 5 years may have suffered from wasting or acute malnutrition



Table 1. Comparison of epidemiological parameters between ancestral (19A/19B) and Delta (B.1.617.2) variants of SARS-CoV-2.

	Ancestral variant	Delta variant
R_0	2.7 (19)	5.0-6.5 (15)
Household attack rate	12-17% (20)	80-100% (13)
Average incubation period	5-6 days (17, 18)	4 days (16)

R_0 , basic reproduction number