

Towards reopening schools: A narrative review of COVID-19 infection in children aged 1-10 years

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Abstract

In formulating a gradual "exit" strategy from the lockdown policies which many countries implemented to overcome the COVID-19 crisis, pressing questions include whether kindergartens and elementary schools should be reopened. In the earliest phase of the outbreak, some authorities claimed that children were potential "super-spreaders", justifying the closure of the education system and postponement of its reopening. This narrative review, performed by a multidisciplinary academic group in early April 2020, assessed the data then available on issues relating to COVID-19 in children aged 1-10 years, with a clear intention of advising policy-makers in Israel. Based on local and international data from published and unpublished sources, the information at that time demonstrated that even when schools remain open infection rates among children aged 1-10 years are low and the rate of severe COVID-19 illness is even lower. Direct assessment of transmissibility from children to other children or adults is inconclusive, yet indirect evidence suggested this may be lower than in adults. As for the contribution of school closure to the epidemic curve, this measure seems to be based primarily on a mistaken analogy with influenza. We concluded that SARS-CoV-2 poses a small risk to children in this age group. This low risk is far outweighed by the benefits of school attendance. The group recommended reopening of the lower school grades, cautiously and with continuous monitoring. Our findings were submitted to relevant stakeholders, spurring public debate eventually leading to gradual school reopening. This work demonstrates the potential contribution of academia in shaping policy, especially in times of crisis.

Introduction

In formulating a gradual "exit" strategy from the lockdown policies which many countries implemented to overcome the COVID-19 crisis, pressing questions include whether kindergartens and elementary schools should be reopened, how quickly this should be done, and what precautionary measures should be taken to protect children, parents and staff. Providing primary education is important not only for the children themselves, but also enables adults, and most often young mothers, to rejoin the workforce. Answers to these questions rest on the risk of infection among children, its severity, and the extent to which children transmit the disease to other children and adults. In the earliest phase of the crisis, various commentators in the news media claimed that children were potential "super-spreaders", justifying the closure of the educational system and postponement of its reopening. Indeed, the assumption that, like epidemic influenza, children and schools were a prime locus of transmission, was built into the most influential models predicting the course of the disease if measures were not taken to suppress it [1].

In view of the public need for clarification on this issue and in order to determine whether and how children could return to school, a multidisciplinary academic group was formed in mid-April 2020, comprised of epidemiologists, physicians with specialties in Infectious Diseases, Family Medicine, Public Health, Hematology and Pediatrics, as well as specialists in Demography, Statistics, and Health Policy. The group summarized and assessed the data available on the issues relating to COVID-19 in children, with the clear intention of influencing policy in Israel based on the best evidence available.

Sources for this narrative review included published and unpublished manuscripts identified through Pubmed, Google scholar, and medRxiv, articles published in leading newspapers and published and unpublished reports from countries and international organizations. Key words

used for searching included, COVID-19, children, school closures, SARS-COV2. We examined issues related to morbidity and disease severity among children, mortality, virus transmission by children, the role of school closures, the role of children in disease modelling and issues related to school re-opening.

The findings of this work were submitted to officials from the Israel Ministries of Health, Education and Finance. It spurred a public debate within these ministries as well as being extensively covered in the media. In part due to this report, a decision was taken to gradually open schools, beginning on May 3, 2020. This joint effort with the attendant results can serve as an example of how academia could and should contribute to shaping policy, especially in times of crisis. We were able to integrate fragmented pieces of information, from all over the world, into a unified picture contradicting the initial assumptions on the role of children in this pandemic.

1. Morbidity among children in general (focusing on ages 1-10 years).

a. Proportion of children among cases of confirmed SARS-Cov2 infection.

The morbidity of COVID-19 among children under 10 years of age is low in all countries where data on confirmed cases are publicly available [2-8]. A systematic review from March 18th found that children accounted for 1%-5% of diagnosed COVID-19 cases and that they often have milder disease than adults [7]. In most countries testing has been conducted mainly among specific risk groups (e.g., the symptomatic, contacts of confirmed cases, or returning travellers from an outbreak locus). As such, confirmed case rates probably underestimate true attack rate among children in the community, especially since there is evidence that the proportion of asymptomatic patients may be higher among children than adults [7]. In Israel, updated morbidity figures to May 2, 2020 indicate that while children

aged 0-9 comprise 20% of the total Israeli population, they make up only 6% of the country's 16,172 confirmed cases (Ministry of Health: May 2, 2020) [9].

In a study conducted in Shenzhen, China [10], among 391 confirmed cases of COVID-19, 20 (5%) were children between 0-9 years and 12 (3%) were 10-19 years. Close contacts of the 292 symptom-based cases were traced, totalling 1,286 individuals, of which approximately 13% were under 9 and 7% were 10-19 years. Among contacts, 11 of the 148 contacts aged 0-9 tested positive (7.4% attack rate), and 6 of 85 contacts aged 10-19 (7.1%). The observed rates were similar to the overall rate of 7.6% (98 of 1,286 contacts) and to the rates observed in most adult groups. These results demonstrated that children, most likely through household transmission, can be infected. However, the findings do not add any information on the transmission from children to others. Other reports from China, including Guangzhou [11], Wuhan and Shanghai [12], showed that children were much less likely to be infected than adults (odds ratios of 0.26 (95% CI: 0.13-0.54) versus older adults aged ≥ 60 and 0.34 (95% CI: 0.24-0.49) versus adults age 15-64, respectively).

b. Severity of disease in children with COVID-19.

In studies examining disease severity, critical illness was observed in a very small proportion of children aged 1-10. In Hubei Province (China), of the 306 confirmed cases aged 1-10 years, only 4 were severe and none has died. It should be noted that of the pediatric patients with severe disease presentations, five were under one year of age and seven over 15 [13]. In Italy, among 100 children under 18 years of age (median 3.3 years) in pediatric emergency departments with PCR-confirmed COVID-19 between March 3 and March 17, 2020, only one (with coexisting conditions) had low oxygen saturation levels. A further 19% were reported as having “moderate” disease and none had died [14]. The U.S. CDC issued a report [2], based on partial information until April 2, 2020 of 2,572 cases of children aged 0-17

(1.7% of all cases). Data on symptoms were available for only 11% of cases. The disease was found to be less acute in children, with PICU admission in only 15 cases (2%), 5 of whom were under one year of age. Reports from Switzerland [8] indicate that COVID-19 illness under the age of 20 is very rare. Data until April 29th show that 19 out of 3,634 hospitalised cases were under the age of 10 (0.5% of cases), a rate of 2.2 per 100,000 children in the Swiss population. In Israel, as of May 2nd, none of the 107 cases with severe disease is under the age of 10 (Ministry of Health: May 2, 2020).

Recently, concern was raised due to a series of reports of a COVID-19 associated systemic inflammatory disease with multi-organ involvement, resembling Kawasaki Disease in children. In the first report from California, a six-month old infant was diagnosed with Kawasaki Disease and had a concurrent positive nasopharyngeal PCR for SARS-CoV-2 [15]. An additional 19 cases were reported in the UK, leading the NHS to issue a warning to pediatricians regarding the possible link between Kawasaki disease and COVID-19 [16]. In the 6 out of 8 published cases, the work up was negative for the presence of SARS-CoV-2 [17]. In Israel, 4 cases of Kawasaki-like illness, all in adolescents, were described during the last week of April. All cases had myocardial involvement, and in some, a positive PCR result was obtained only after several negative ones (AGH, personal communication). To date, only one child with Kawasaki-like illness died; an adolescent with morbid obesity in the UK [17]. These data should be interpreted with caution. While it is possible that a previously undescribed clinical presentation has emerged in children with COVID-19, it should be kept in mind that the causative agent in Kawasaki disease is unknown, and there is a high proportion of concurrent positive respiratory virus PCR [15]. Furthermore, the spike in the report of Kawasaki-like illness may be related to an unrecognized seasonal or environmental agent, rather than to COVID [18].

c. Mortality among children.

Based on reports in different countries, the mortality rate among children is very low, approaching zero. For example, in Italy until April 27th, two deaths in the age group 0-19 were attributed to COVID-19 among 24,780 deaths reported [4]. In England and Wales until April 17, among 22,351 COVID-19 related deaths, there was one death aged 1-4, and one aged 10-14 [19]. In Spain, of the 15,956 deaths recorded until 29 April 2020, two were in children aged 0-9, but their exact ages are unknown [3]. In Switzerland of 1,408 deaths recorded until April 29th, none were of persons under the age of 30 [8], and in Sweden, of 2,462 deaths recorded until April 29th, none were of children under age 20 [5]. In Korea until March 3rd there were no deaths reported under age 30 [6]. In the USA there were ten reported deaths under age 14 up to May 6th, 4 of them under one year of age [20]. And in Israel, there have been no deaths under age 29.

d. COVID-19 prevalence among children in the general population.

Population-based surveys on COVID-19 morbidity in the community include studies from Iceland and the town of Vo in Italy. In the Icelandic study [21], 6.7% of children under 10 years who were considered high risk (symptomatic individuals, contacts with confirmed cases, or travellers from high-risk countries) tested positive for the virus, half the rate (13.7%) found for persons aged ≥ 10 . More importantly, among the 850 children under 10 years of age screened in the sample of 10,000 persons in the community, no cases were found, compared to 0.8% at age 10 and older. Another population-based study was conducted in Vo, the town where the first death from COVID-19 occurred in Italy. In this study, two surveys were carried out in the township at two-week intervals, the first when the lockdown began and the second when it was lifted. Of the 2,812 residents tested in the first survey (85.9% of the town's residents), 73 (2.6%) were positive for the SARS-Cov-2 virus by

PCR, and in the second survey, of 2,343 residents surveyed (71.5% of all residents), 29 positives (1.2%) were identified, eight of them new cases. Of the 234 children 0-10 years old tested, none were positive, even-though at least 13 of them shared a household with confirmed cases. In a preliminary report from the Netherlands [22], of the 2,096 persons examined until April 17 in a study designed to provide serological data over time, the percentage of persons under age 20 showing antibodies for COVID-19 was about 2%, whereas for adults it was 4.2%. These studies in Iceland and Italy support evidence for low infectivity in children, and suggest that the prevalence among asymptomatic children in the community is not substantial. This finding is consistent with the serological study in the Netherlands. Furthermore, some indirect support for low transmission rates between children is provided by the fact that in Iceland schools were never closed and that the first survey in Vo was conducted at the start of the lockdown.

More recently, a report of preliminary findings from a population based serological survey in Geneva showed a weekly increase in seroprevalence of SARS-CoV-2, with adults aged 20-49 showing similar rates of seroprevalence to children aged 5-19 (8.5%, 95%CI 4.99-11.7 versus 6.0%, 95% CI 2.3-10.2%, respectively) [23]. However, prevalence for the age group up to age 10 (the focus of this review) was not reported. The authors suggest that these findings may support similar attack rate for children and adults, yet other explanations exist, such as increased response rates among previously symptomatic households (given a low response rate of 30%) and household transmission from adults. Nevertheless this study is expected to provide important insights on COVID-19 infection in the population in the future, since it is based on a population-representative survey, and it plans to follow-up participants for at least one year.

2. Transmission by and to children

Currently, in contrast to flu, information on this topic is extremely limited. An unpublished report on viral load by age group found no significant statistical differences in viral load between children and adults [24]. However, only 1.3% (49/3712) patients in the study were children 1-10 years old, and the study failed to provide any information on clinical symptoms, or when in the course of disease these children were tested. Furthermore, while the study suggested that infectivity is considered above a threshold of 10^6 copies per ml, no analysis was done using this threshold, thus preventing any conclusion regarding children's relative infectivity.

Indirect information can be deduced from Sweden where kindergartens and elementary schools have continued to operate throughout the outbreak. Nevertheless, the distribution of cases in Sweden shows that the proportion of children under age 10 remains very low (103 out of 20,302 or 0.5%). Hence it may be possible to infer indirectly that the transmission rate from children is low [5]. It is noteworthy that on April 15th schools opened in Denmark, and although the R rate has increased simultaneously with school reopening and other relaxation measures, it is still under the epidemic value of 1 [25].

Some direct evidence for low transmission rates in children is provided by studies from different countries. In the aforementioned report from the Netherlands [22], among 709 contacts traced, 8% were infected, but none were infected by a source patient under age 19. Among 54 households surveyed, in which there were 116 children, no children under 12 were identified as first cases. In Norway there were 4 cases of transmission, all involving children above age 12 [26]. A joint report by the WHO and China from February concluded that morbidity among children up to age 18 was low (2.4% of all reported cases) and in Wuhan until mid-January, among the tests performed on symptomatic persons, no positive

results were obtained in children. Most children found to be positive for the virus were identified through contact investigations in households of older patients. The report states that the contact investigators interviewed by the report's authors did not recall a single case of transmission from children to adults [27]. A study on the role of children in the transmission chain summarised household transmission using published cases and reports from several countries [28]. The authors examined the proportion of household transmission clusters in which a child was the index case. Of the 31 such clusters they found in the literature, in only 3 cases (9.7%), was a child under 18 years of age identified as the index case. This is in sharp contrast to the transmission of other viruses, such as the H5N1 influenza virus, where children were the index case in 54% of clusters. Under a conservative scenario, the analysis showed that at most children were a source of infection in 21% (6/28) of clusters. In New South Wales, Australia five primary schools reported a total of six COVID-19 cases, among them one student and five staff members. Contact tracing among 168 of their contacts revealed one secondary case of transmission of the disease, presumably from a staff member to a student [29].

In a published case report, a child in a ski resort was found to have combined infection with three separate viruses: SARS-CoV-2 + picornavirus + influenza A (H1N1) pdm09 [30]. Epidemiological investigations of the affected child led to 172 contacts (including 112 ski school contacts). Despite the high number of contacts, there was no proven SARS-CoV-2 transmission, but there was a high rate transfer of picornavirus and influenza both in the ski schools he attended and in his family. The authors raise the possibility that the child's low SARS-2-CoV contagiousness may be linked to the combination of viruses.

The proportion of children in the Israeli population is large (36% under the age 19), and yet insofar as is known, to date no significant clusters of infection, as far as we know, were reported as stemming from educational settings in Israel prior to their closure. In contrast, in

China, Italy and in Europe in general the families are typically small, and therefore the pool of familial contacts is relatively low. Since the number of children in Israeli families is much larger (on average 4.9 persons per family [9]), there is ample opportunity for in-depth epidemiological investigations of intra-familial transmission, especially in families with multiple children and in areas with significant outbreaks. One such investigation has been reported in the popular press [31] and in personal communication (RCM). Among 14 families with large numbers of children, 110 family members were tested following the infection of the index cases. All but one index cases were adults and the only child index case was a youth of 14.5 years. An additional preliminary Israeli research report from the Gertner Institute which developed model-based estimates of infection by and transmission of SARS-Cov-2, by analysing household-level data of confirmed cases in the town of Bnei Brak, the locus of one of the most severe outbreaks in the country. The findings indicate that children under age 10 have a lower probability of infection than persons older than 10 (20%-50% lower), but the analysis did not have sufficient statistical power to determine how likely children in this age were less likely to transmit the virus [32].

3. Opening kindergartens and schools for lower grades.

A systematic review focused on school closures, surveying diverse studies that examined school closure as a means of controlling the epidemic [33]. The authors examined modelling studies as well as studies from other epidemics, since there was little direct empirical evidence regarding COVID-19. They found that the evidence for the effectiveness of school closures comes entirely from influenza outbreaks, where children tend to drive transmission, and policy relevant data on COVID-19 are entirely lacking. The authors conclude that the evidence supporting school closures as a measure to reduce COVID-19 outbreaks was particularly weak at the time of publication (April 6th). In particular, evidence of transmission from and to school-children was lacking, and the available data suggested that attack rates

and transmission rates were lower for children than for adults. Modelling studies showed that school closure alone would reduce mortality by no more than 2-4%, when not combined with other strong forms of social isolation [33]. Moreover, data from the SARS outbreak showed that school closures did not contribute to controlling the epidemic. The article also underscores the economic costs and the potential harms of school closure. In Taiwan, [Prof. Chang-Chuan Chan personal communication. OP], with a two-three week delay after the Chinese New Year's break, schools have been reopened continuously. So far, since January, not a single primary school has been closed due to infection, and only one high school was closed for two weeks after two confirmed cases were found.

4. Models predicting morbidity of COVID-19 and the contribution of children to these models.

The knowledge gathered over recent months makes it possible to conclude that the SARS-CoV-2 virus does not behave like influenza viruses. Nevertheless, models based on the propagation of both seasonal and pandemic flu have been used to predict the course of the epidemic, and to guide policy making. Significantly, children are a major source of transmission for all forms of influenza [34]. In the case of H1N1 ("swine flu") pandemic, infection and hospitalization rates were higher for children than in the case of seasonal flu, whereas rates for the elderly were lower [35, 36]. It is not surprising then, that models developed to evaluate measures that could have reduced the swine flu pandemic, school closure was an important component. The initial models for SARS-CoV-2 transmission relaxed the assumption slightly by assuming equal "attack rates" for all ages [37]. What is surprising is that these models were not varied to explore the possibility that children are a weaker link in transmission of SARS-CoV-2. This would have allowed exploration of alternatives as to how the disease would develop under such an assumption, and what policy options could suppress it.

These assumptions have now been partially tested, based on data from Wuhan and Shanghai [12]. The effect of school closure on epidemic spread was tested with a transmission model given age-specific contact and mixing patterns typical for these areas of China, and the findings of the authors that susceptibility to infection by SARS-Cov-2 increases with age. The authors found that school closures alone are not sufficient to interrupt transmission, but that they can reduce peak incidence by 40-60%. It should be noted that the model reduced susceptibility to infection for children, but did not reduce transmissibility, which was assumed to be equal by age. In addition, the question they addressed was whether strict lockdown was necessary, beyond school closure, in order to halt transmission. An alternative, where schools remained open while social distancing measures were adopted (with or without lower transmission by children), was not considered. Another model-based study explored the impact of differing national age-structures and age-specific social contact matrices on non-pharmaceutical methods such as school closure, workplace distancing and lockdown [38]. It found that the younger age profile of India and its three generation households would lead to higher initial R_0 than that of China or Italy, and a greater impact of school closure. In India the school was assumed to be the main channel of transmission within children. Unfortunately, whereas contacts in the model are structured by age, the probability of infection is not. Thus, like other models for this epidemic, the impact of age is explored in only one possible direction, that of increasing transmission of the disease. Indeed, if children are both less susceptible and weaker transmitters, models such as this might find that a younger age structure reduces R_0 and reduces the impact of school closures. This potential effect of age structure on R_0 may have a substantial beneficial effect in Israel given the large proportion of children in the population.

Conclusions

There are two potential justifications for school closure: protecting the health of children themselves and/or protecting the rest of the population. The information currently available from a variety of countries indicates that the threat to children themselves is very small. Data collected so far indicate that even when schools remain open, as in Sweden and Iceland, the infection rate in children aged 1-10 years is low and the rate for severe COVID-19 illness for these children is even lower. As for the contribution of schools' closure to the health of the rest of the population, this measure seems to be based primarily on an analogy with influenza. Fortunately, unlike flu, there is no evidence that children are the major source of infection for COVID-19, and most certainly not "super-spreaders" [39]. It is crucial that model-based policy exploration takes this into account.

A recent UN Policy Brief (15 April, 2020) on the impact of the Corona virus on children warns that the socio-economic implications of this pandemic on children and the measures taken to mitigate it may result, inadvertently, in poverty, heightened exposure to violence and abuse, and the denial of a proper education [40]. Needless to say, the damage will not be spread evenly across the population but will strike weaker groups first and foremost, and may enhance already existing inequalities, which the educational system strives to address [41]. The ethical question that needs to be addressed is the degree to which both the present and future welfare of children can be sacrificed to protect their more vulnerable elders from possible infection.

The findings of this work lead us to recommend to government ministries in Israel a gradual and well-monitored opening of schools in Israel. Precedents can be found in the Netherlands [42] and Denmark [43], which have developed well-thought out and detailed plans to reopen the schools while monitoring and maintaining safety. Our recommendations were circulated

among stake holders in Israel and initiated a public debate on the returning children to schools, which eventually lead to schools gradual opening beginning on May 3, 2020.

Initially, children grades 1-3 returned to schools, followed a week later by children in preschools. Several control measures were applied (e.g. classes were divided into smaller capsules of up to 15 children, hygiene, adults were prohibited from entering school grounds). These practices were maintained for 2 weeks without a reported increase in the number of cases.

However, on May 17, all levels of education – primary, middle and secondary – were reopened in full and all children returned to classrooms. This was done without limiting or reducing class sizes (which are among the highest of all OECD countries.[44]) at times reaching 40 students per class[45]. Measures such as the use of masks, and other hygiene and physical distancing measures were recommended[46] but were relaxed in the heat wave which prevailed in the country in early May, and generally were not enforced. All these blended in with a general attitude that the danger of infection was over. Additionally, no focused measures for monitoring new cases in the school system were implemented. This imprudent return lead to a new outbreak in Israel, with an acute locus in high schools in Jerusalem, approximately 10 days after the return of the older children to school[47] .

It should be noted that no such outbreak was registered in the early primary grades, which reinforced our earlier conclusions. The unequivocal lesson from the reopening of schools in Israel is that measures taken to reopen the school system must conform to practical knowledge which had accumulated on this disease: relaxing restrictions where the dangers are minimal and the costs great, and implementing sometimes burdensome measures to limit the spread of SARS-Cov-2 infection. These include both enforcing hygiene and physical distancing measures for students and staff, as well as implementing efficient monitoring and

tracing measures focused on the school system itself. We have communicated our concerns and recommendation to the Ministry of Health, Education and Finance, have had further discussions with senior representatives, and have maintained the activities of our group in pooling policy-relevant information on children and COVID-19 so that these can be assessed and made available to decision makers.

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