COVID-19: lessons to date from China

Xiaoxia Lu,[1] Yuhan Xing,[2] Gary Wing-Kin Wong [2]

[1]Department of Respiratory Medicine, Wuhan Children's Hospital, Wuhan, Hubei, China
[2]Department of Paediatrics, Faculty of Medicine, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China

Correspondence to
Dr Gary Wing-Kin Wong, Department of Paediatrics, Faculty of Medicine, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin HK23, Hong Kong, China; wingkinwong@cuhk.edu.hk

Received 21 April 2020
Revised 26 April 2020
Accepted 29 April 2020
Published Online First 12 May 2020

To cite: Lu X, Xing Y, Wong GW-K. *Arch Dis Child* 2020;**105**:1146–1150.

ABSTRACT

The pandemic due to a novel coronavirus has been sweeping across different regions of the globe since January 2020. Early reports of this infection due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) consisted of mostly adult patients. As the outbreak spreads rapidly beyond the epicentre of Wuhan, it becomes clear that infants and children of all ages are susceptible to this infection. In China, there have been more than 1200 paediatric cases. Most paediatric patients acquire the infection through household contact with infected adults. The disease in children is usually self-limiting and most infected children will recover uneventfully within 7–10 days. Other than symptoms of the respiratory tract, many children may present with gastrointestinal symptoms. Older children are more likely to have asymptomatic infection. Although deaths related to SARS-CoV-2 are rarely reported in the paediatric age group, young children and those with underlying medical conditions are more likely to develop severe illness. Only a small fraction of neonates born to infected mother would acquire the virus by vertical transmission. Because a large proportion of children and adolescents may have asymptomatic or mildly symptomatic infection, children are likely to play an important role in community transmission of this infection. Screening of children who have a definitive contact history will facilitate early diagnosis and isolation of all infected children. This review summarises the lessons learned in China with regard to the current understanding of SARS-CoV-2 infection in the paediatric population.

INTRODUCTION

In late December of 2019, a cluster of cases of severe pneumonia in adults of unknown aetiology was reported in Wuhan, China.[1] The causative agent was identified as a novel coronavirus, later named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the infection mainly spreads through respiratory droplets and close contacts.[1 2] The disease is called novel coronavirus disease 2019 (COVID-19). As of 16 April 2020, more than two million cases of COVID-19 have been reported in 210 countries and regions, causing more than 150 000 deaths.[3]

During the early stages of the COVID-19 outbreak, children were thought to be less affected as the initial reports consisted of almost exclusively adult patients.[4 5] The first paediatric case of COVID-19 was reported in Shenzhen and this family cluster confirmed human to human transmission of COVID-19.[5] According to the data reported by the China Centers for Disease Control and Prevention (CDC), only 0.9% of COVID-19 cases were children under 10 years of age.[1] Low number of infected paediatric patients in the early stage may be attributable to the nationwide school suspension in China, as children were at home reducing their chance of exposure to other infected individuals. As the infection spreads rapidly outside of the epicentre of Wuhan, COVID-19 has been reported to occur from preterm infants to school-aged children and adolescents.[1 6 7] However, their disease manifestations and the clinical course of the illness are mild when compared with those in adults. Here, we aim to summarise the early lessons learned about this novel infection in children and provide insights into the development of possible measures to control this ongoing pandemic.

Coronaviruses and human diseases

Prior to the emergence of SARS-CoV-2, there were six species of coronavirus (CoVs) known to infect humans. Four common strains of CoVs, namely, 229E, OC43, NL63 and HKU1, are known to cause common cold symptoms in immunocompetent hosts. Two other viruses, severe acute respiratory syndrome CoV (SARS-CoV) and Middle East respiratory syndrome CoV (MERS-CoV), are highly pathogenic and may cause life-threatening infections especially in adults. Although the number of children infected with these two viruses were small, severe or fatal disease in children rarely occurred.[8]

Outbreak of COVID-19

In December 2019, a cluster of severe pneumonia cases of unknown aetiology was reported in Wuhan, Hubei Province, China. Initial epidemiological investigations suggested the possible origin from a local seafood wholesale market.[4] The causative agent was isolated from human airway epithelial cells and the genome of the virus indicated it is a member of beta-CoV genus distinct from SARS-CoV and MERS-CoV.[2] This novel virus was later named SARS-CoV-2. Subsequent full-genome sequencing analysis illustrated that SARS-CoV-2 is 89% similar to bat SARS-like CoVZXC21 and 82% identical to that of human SARS-CoV.[9]

Similar to SARS-CoV and MERS-CoV, SARS-CoV-2 is likely a zoonotic disease that the virus had jumped the species barrier. Although bats are the most likely natural reservoir, the exact intermediate hosts for SARS-CoV-2 are still unclear.[10] The infection is primarily transmitted by respiratory droplets. At the onset of the outbreak in Wuhan, nosocomial transmission to healthcare workers was common because appropriate personal protection equipment (PPE) was not used.[4 11] Based on data during the early stage of the outbreak in China, reproductive number has been estimated to be between 2 and 3, with a median incubation period of 3–7 days (range 0–24 days).[12] Although

Table 1 Epidemiological characteristics of SARS-CoV, MERS-CoV and SARS-CoV-2

	SARS-CoV	MERS-CoV	SARS-CoV-2
Emerged year	2002	2012	2019
Intermediate host	Palm civet and raccoon dogs	Dromedary camels	To be determined
Incubation period	2–10 days	2–14 days	1–14 days
Number of confirmed cases	8096	2519 (as of 31 January 2020)	2 072 114 (as of 15 April 2020)
Associated deaths	774	886 (as of 31 January 2020)	138 475 (as of 15 April 2020)
Mortality	10%	25%–50%	2%–5%
Number of affected countries	29	27	210

MERS-CoV, Middle East respiratory syndrome coronavirus ; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SARS-CoV, severe acute respiratory syndrome coronavirus .

the case fatality rate for COVID-19 is lower than those of SARS and MERS, the total number of deaths attributable to COVID-19 has already far exceeded than those caused by SARS or MERS.[8 12] A comparison of the epidemiological features of SARS-CoV, MERS-CoV and SARS-CoV-2 is shown in table 1.

Epidemiological and clinical features

In spite of early studies suggesting that children might be less susceptible to this infection,[4 5] subsequent data revealed that children of all age groups can be infected. One salient feature of paediatric patients with COVID-19 is that most children acquired the virus via household contact with family members whose symptoms developed earlier.[6 7 13–15] In the initial paediatric cohort from Wuhan Children's Hospital, there were four families that the children presented with symptoms prior to the onset of symptoms in the infected adults within the same household.[6] Although the child and the adult in the same household could have been exposed to the same source of infection, we could not rule out the possibility that the child was the index case who passed the infection to the adult. Table 2 summarised the clinical and radiological features of paediatric patients. Clinical manifestations of COVID-19 greatly resemble those of SARS and MERS, ranging from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome.[4 5 12] However, the clinical presentations and course of illness are milder in children with a shorter time to resolution when compared with adult patients.[6 8 13–15] Fever was only present in less than half of infected children and it only lasted for a few days.[6 13–15] Screening of cases by detection of fever will miss a large proportion of infected children. Other common symptoms include dry cough, sore throat and dyspnoea, and the symptoms usually resolve within 7 to 10 days.[6 13 14] Unlike many viral respiratory infections in children, wheeze is not a common presenting feature of COVID-19. Approximately 10% of infected children present initially with gastrointestinal symptoms such as diarrhoea, abdominal pain and vomiting, making it difficult to distinguish COVID-19 from other common childhood diseases.[6 15]

Younger children are over-represented in the infected paediatric population. In the patients treated at Wuhan Children's Hospital, 18% of them were infants under 1 year of age.[6] Furthermore, neonates and infants constituted the majority of critically ill cases.[6 13] The exact reasons for more severe diseases in this age group remain to be explored.

Table 2 Epidemiological, clinical and radiological features in Paediatric Series of 2019 novel coronavirus disease (COVID-19)

	Qiu *et al*[14]	Lu *et al*[6]	CDC COVID-19 Response Team[15]
Number of patients	36	171	2572
Place of recruitment	Zhejiang Province, China	Wuhan, Hubei Province, China	USA
Median age (range)	3.5 years (0–15 years)	6.7 years (0–15 years)	11 years (0–17 years)
Female (%)	13 (36.1)	67 (39.2)	1,082/2,490 (43.5)
Epidemiological features, n (%)			
Household contact with confirmed or suspected cases	32 (89)	154 (90.1)	168/184 (91.3)
Contact with other confirmed or suspected cases	0	2 (1.2)	–
Travel exposure	12 (33)	All from Wuhan	16/184 (8.7)
Unidentified source of infection	0	15 (8.8)	–
Clinical classifications, n (%)			
Asymptomatic infection	10 (27.7)	27 (15.8)	NA
Upper respiratory infection	7 (19.4)	33 (19.3)	NA
Pneumonia	19 (52.8)	111 (64.9)	NA
Intensive care	0	3 (1.8)	15/745 (estimated range 0.58–2.0)
Signs and symptoms, n (%)			
Fever	13 (36.1)	71 (41.5)	163/291 (56)
Cough	7 (19.4)	83 (48.5)	158/291 (54)
Pharyngeal congestion or sore throat	2 (5.6)	79 (46.2)	71/291 (24)
Rhinorrhoea	0	13 (7.6)	21/291 (7.2)
Diarrhoea	2 (5.6)	15 (8.8)	37/291 (13)
Vomiting	2 (5.6)	11 (6.4)	31/291 (11)
Laboratory findings, n (%)			
Leucopenia	7 (19.4)	45 (26.3)	NA
Lymphopenia	11 (30.5)	6 (3.5)	NA
Elevated procalcitonin	6 (16.7)	105 (64.0)	NA
Elevated C reactive protein	1 (2.8)	33 (19.7)	NA
Elevated D-dimer	3 (8.3)	21 (14.1)	NA
Chest CT, n (%)			
Ground-glass opacity	19 (52.8)	56 (32.7)	NA

CDC, Centers for Disease Control and Prevention; NA, not available.

Many pregnant mothers in Wuhan have also been infected, however, only a small percentage of neonates (9%) born to infected mothers would get infected by vertical transmission.[7] Perinatal infection may contribute to adverse events in neonates such as fetal distress, preterm labour and neonatal respiratory distress.[7] In contrast with the disease in adults, severe diseases requiring intensive care support and death are rare.[6 15] Children with underlying comorbid conditions were more likely to develop severe disease.[6 16] In the cohort of infected children from Wuhan Children's Hospital, only 3 out of 171 patients (1.8%) required invasive mechanical ventilation and all three children had underlying comorbidities.[6] The paediatric data from US CDC are largely consistent with data from Wuhan Children's Hospital.[15] There have only been two deaths in children among over 1200 reported paediatric cases in China. One had leukaemia and the other was a 10-month old infant who presented with intussusception and was complicated with bowel necrosis.[6 13] Large proportions of children with few or no symptoms have been reported in the older age group.[6 15] Up to 20% of infected children from

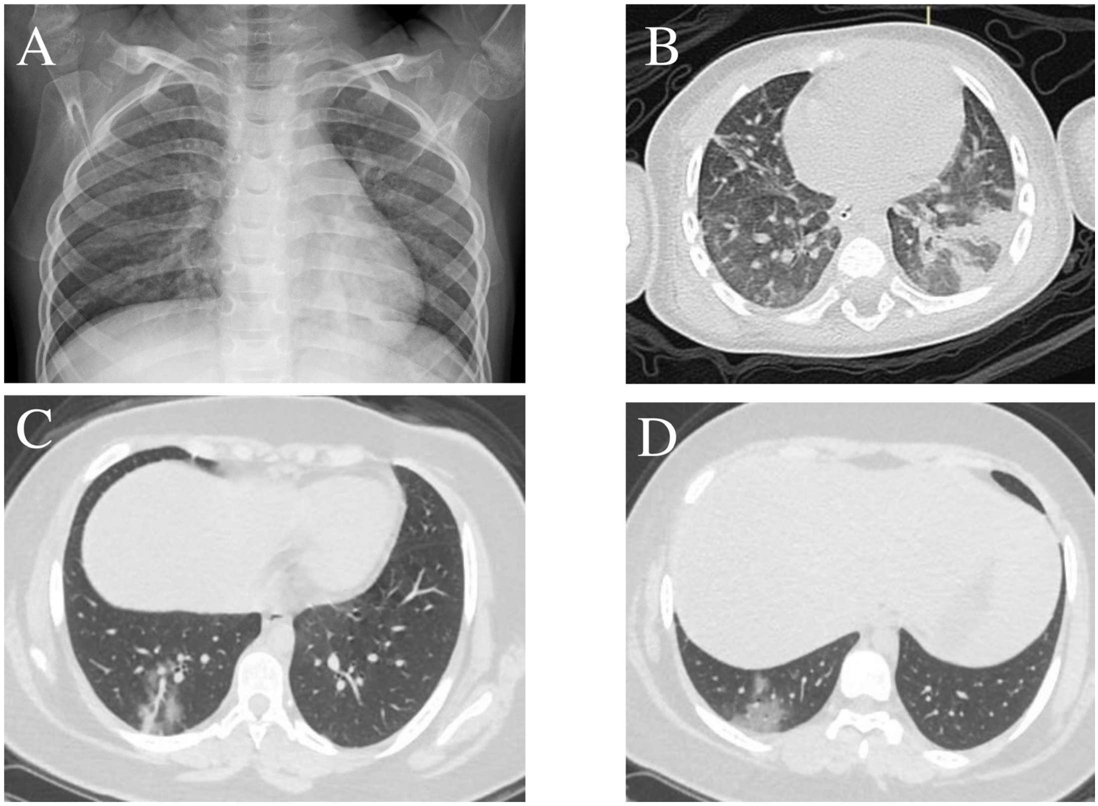

Figure 1 Chest radiograph and CT images of representative patients. Typical changes include ground glass opacities especially in the peripheral lung fields (panels B, C, D). Radiograph showing interstitial infiltrates (A).

Wuhan were asymptomatic.[6] Studies of adult patients have shown that asymptomatic patients or minimally symptomatic patients shed as many viruses as symptomatic ones, suggesting the transmission possibility of SARS-CoV-2 by these asymptomatic carriers.[17 18]

The mechanisms explaining the milder nature of disease in children are yet to be determined. It has been speculated that children are less likely to mount an excessive immune responses and cytokine storm as seen in adult patients.[14] SARS-CoV-2 shares the same host cell receptor, ACE2, with SARS-CoV, although the pathogenic mechanisms induced by the two viruses may be different. On binding to ACE2 with its surface spike (S) glycoprotein, SARS-CoV-2 enters the host cells leading to the subsequent steps of infection in the lungs and other organs, and the milder nature of COVID-19 in children can be partly explained by fewer and immature ACE2 proteins which are highly expressed on the alveolar type 2 cells.[9] Besides, children are often exposed in daycare and school environments where other viral or bacterial infections constantly circulate. It has also been postulated that prior exposure to milder respiratory pathogens may train the host immune system to defend against similar coronavirus. However, early data suggested that there was no cross protection against SARS-CoV-2 from antibodies of other common coronavirus.[19] Codetection with other respiratory pathogens such as influenza virus and *Mycoplasma pneumoniae* was not uncommon among paediatric patients.[15] Studies have shown that other respiratory viruses could be detected in up to two-thirds of children infected with coronaviruses.[20] Whether such coinfection may lead to altered immune response to SARS-CoV-2 remains unanswered.

Laboratory and radiological features of COVID-19

The laboratory features in paediatric patients with COVID-19 are non-specific. Lymphopenia was one of the most common haematological abnormalities. In adult patients, a significant or progressive decrease in the absolute number of peripheral blood lymphocytes was observed in the acute phase of SARS-CoV-2 infection.[4] Such finding suggested that SARS-CoV-2 might consume lymphocytes, providing a possible explanation for the feature of lymphopenia in the early stage of the disease. In paediatric patients, however, the absolute number of lymphocytes in most patients is within the normal range,[6 15] suggesting less immune dysfunction induced by SARS-CoV-2 in children. Other laboratory abnormalities include elevation of procalcitonin, C reactive protein and D-dimer.[6 14 15] Chest CT findings are similar to those seen in adult patients, but the changes in children are usually milder.[4 6] Characteristic unilateral or bilateral ground-glass opacities occur in about two-thirds of paediatric patients. Chest CT images and radiograph from representative patients are shown in figure 1. Other radiological changes include patchy shadows and lung consolations.[5 6 14]

Although chest CT is more sensitive than chest X-ray in detecting parenchymal changes in asymptomatic patients, the role of chest CT in the diagnosis and management of the infection in children will need to be determined.[6 14] Throat swabs or nasopharyngeal aspirations for RT-PCR testing is the accepted standard for diagnosis. As there are limits of the sensitivity and specificity of RT-PCR testing, studies are ongoing to determine the role of antibody assay for the diagnosis and management of COVID-19.[19] Longitudinal studies of infected adults and children revealed that they would shed viral particles via the respiratory tract for at least 2 weeks and viral particles could be detected in stool samples for prolonged period of time even after the respiratory samples became negative. Determination of the infectious potential of stool from patients with COVID-19 is needed to inform proper infection control precautions.[21] In the meantime, proper hygiene and disposal of soiled diapers from infected infants are warranted.

Treatment and control measures

The management of paediatric patients with COVID-19 is largely supportive.[4–6] There is no proven effective antiviral therapies for COVID-19. Inhibition of viral dissemination and replication, and dampening of the inflammatory cascades such as reducing the production of proinflammatory cytokines and chemokines including interleukin 6 (IL-6) and IL-1β, may have their roles in minimising the immunopathology related to COVID-19. Although a small open-labelled study suggested that hydroxychloroquine and azithromycin might reduce the viral load, the results should be interpreted with caution and appropriately powered randomised controlled trials assessing important clinical outcomes are needed to evaluate such treatment properly.[22] Animal studies and early clinical experience of using remdesivir in adults are promising, and large randomised trials are underway to evaluate the efficacy of such treatment.[23] Given the small number of paediatric patients with severe disease, it will be difficult to obtain solid evidence of benefits of these experimental treatments in the paediatric population.

By early April 2020, the outbreak within China is largely under control and the majority of new cases are imported from overseas. Although it may be difficult to determine clearly what measures were important in controlling the outbreak in China, several strategies were probably pivotal and might provide lessons for other countries. In 2002–2003, the outbreak of SARS was contained primarily by identification and isolation of infected cases so as to stop the chain of transmission.[8] Unlike SARS, the major problem in controlling COVID-19 is that infected individuals are already shedding large number of viral particles before they become symptomatic and many patients are asymptomatic. Therefore, massive upscale in testing capability is important for identification of all potentially infected patients. Testing of children and young adults is of particular importance as many of those infected in such age group do not manifest a lot of symptoms. However, they are likely to play an important role in spreading the infection in the community. Social distancing was strictly enforced throughout China during the outbreak and this may contribute to the reduction of transmission. The value of universal masking by the general public is controversial. Until recently, the WHO and US CDC did not recommend the general public to wear mask in public places.[24] Strict adherences to the use of appropriate personal protective equipment for healthcare workers cannot be overemphasised as infection control in the healthcare settings is of paramount importance to safeguard the human resources in fighting the pandemic. Public health researchers will likely debate for years to come regarding what community measures may be feasible and effective for controlling future outbreaks. Many countries across the world are using various forms of social distancing and some types of lockdown in trying minimise community transmission of the disease. The drastic measures used in the lockdown of Wuhan, including the use of highly restrictive form of social distancing, strict traffic control, universal use of mask, home confinement and universal symptoms survey of all households, were associated with dramatic decrease in community spread and eventually led to the cessation of community transmission.[16] However, such restrictive public health measures would be difficult to implement elsewhere as there are major social, legal and constitutional differences among different countries. One will need to strike a balance between infringement of personal rights or freedom, and the potential destruction and casualty of a pandemic. Haffajee and Mello had summarised in a recent editorial regarding an important lesson of the COVID-19 pandemic as follows: "when epidemiologists warn that a pathogen has pandemic potential, the time to fly the flag of local freedom is over".[25] Table 3 summarises the important novel viral infections that have emerged over the past two decades and most of them are zoonotic diseases. With the ever-increasing global population and the constant human intrusion into the habitat of different wildlife, it is a matter of time that we will encounter another novel zoonotic infection with pandemic potential. We need to learn from our past lessons and to be better prepared for the next one to come.

Table 3 Novel respiratory viruses emerged in the past two decades

Infectious agent	Year of emergence	Location of emergence
Influenza H5N1 (avian)	1997	Hong Kong
SARS coronavirus	2002	China
Human coronavirus NL63	2004	The Netherlands
Bocavirus	2005	Sweden
Pandemic H1N1 2009	2009	USA/Mexico
MERS coronavirus	2012	Saudi Arabia
Influenza H7N9 (avian)	2013	China
Influenza H5N6 (avian)	2014	China
SARS-CoV-2	2019	China

MERS, Middle East respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

CONCLUSIONS

The clinical course of COVID-19 in paediatric patients is mild compared with that of infected adults. A large proportion of infected patients is asymptomatic or mildly symptomatic. Although infants and children with underlying diseases were more likely to develop severe disease, the rare fatal infections in previously healthy children do occur. As early detection of infected patients and timely isolation of cases who have a definitive contact history is of vital importance to control the outbreak, a low threshold of testing and upscale of testing capability are likely to be some of the keys for the success in controlling the outbreak. Fully elucidating why children are less severely affected by SARS-CoV-2 infection could provide new insights into the development of preventive and treatment strategies. Clear understanding of the pathogenesis and underlying immunological responses to the virus in different age groups will enable us to develop novel treatments to reduce the possible immune-related injuries in patients with severe disease.

Contributors XL and YX have contributed equally to the review of literature and manuscript preparation. All authors prepared the first draft and revised the subsequent version of the draft.

Funding This work has been partly supported by the TS Lo Foundation.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed.

ORCID iD
Gary Wing-Kin Wong http://orcid.org/0000-0001-5939-812X

REFERENCES

1 Wu Z, McGoogan JM, Wu Z, *et al*. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA* 2020. doi: 10.1001/jama.2020.2648
2 Zhu N, Zhang D, Wang W, *et al*. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382:727–33.
3 WHO. Novel coronavirus (COVID-19) situation. World Health organization, 2020. Available: https://who.sprinklr.com/ [Accessed 16 Apr 2020].
4 Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
5 Chan JF-W, Yuan S, Kok K-H, *et al*. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514–23.
6 Lu X, Zhang L, Du H, *et al*. SARS-CoV-2 infection in children. *N Engl J Med* 2020;382:1663–5.
7 Zeng L, Xia S, Yuan W, *et al*. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr* 2020. doi:10.1001/jamapediatrics.2020.0878. [Epub ahead of print: 26 Mar 2020].
8 de Wit E, van Doremalen N, Falzarano D, *et al*. Sars and MERS: recent insights into emerging coronaviruses. *Nat Rev Microbiol* 2016;14:523–34.
9 Zhou P, Yang X-L, Wang X-G, *et al*. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579:270–3.
10 Lam TT-Y, Shum MH-H, Zhu H-C, *et al*. Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins. *Nature* 2020. doi:10.1038/s41586-020-2169-0. [Epub ahead of print: 26 Mar 2020].
11 Zhan M, Qin Y, Xue X, *et al*. Death from Covid-19 of 23 health care workers in China. *N Engl J Med* 2020. doi:10.1056/NEJMc2005696. [Epub ahead of print: 15 Apr 2020].
12 Guan WJ, ZY N, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020. doi: 10.1056/NEJMoa2002032
13 Dong Y, Mo X, Hu Y, *et al*. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020:e20200702.
14 Qiu H, Wu J, Hong L, *et al*. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis* 2020.
15 CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children–United States, February 12–April 2, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:422–6.
16 Pan A, Liu L, Wang C, *et al*. Association of public health interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. *JAMA* 2020. doi:10.1001/jama.2020.6130. [Epub ahead of print: 10 Apr 2020].
17 Zou L, Ruan F, Huang M, *et al*. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 2020;382:1177–9.
18 Bai Y, Yao L, Wei T, *et al*. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020. doi:10.1001/jama.2020.2565. [Epub ahead of print: 21 Feb 2020].
19 Guo L, Ren L, Yang S, *et al*. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin Infect Dis* 2020:ciaa310.
20 Heimdal I, Moe N, Krokstad S, *et al*. Human coronavirus in hospitalized children with respiratory tract infections: a 9-year population-based study from Norway. *J Infect Dis* 2019;219:1198–206.
21 Cheung KS, Hung IF, Chan PP, *et al*. Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from the Hong Kong cohort and systematic review and meta-analysis. *Gastroenterology* 2020. doi:10.1053/j.gastro.2020.03.065. [Epub ahead of print: 03 Apr 2020].
22 Gautret P, Lagier J-C, Parola P, *et al*. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* 2020:105949.
23 Holshue ML, DeBolt C, Lindquist S, *et al*. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020;382:929–36.
24 United States centers of disease control and prevention. Available: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/diy-cloth-face-coverings.html
25 Haffajee RL, Mello MM, Globally T. Thinking globally, acting locally–the U.S. response to Covid-19. *N Engl J Med Overseas Ed* 2020.