Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Presenting symptoms of COVID-19 in children: a meta-analysis of published studies

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Editor—The coronavirus disease 2019 (COVID-19) pandemic has led to drastic changes in the structure of clinical care worldwide.[1] During the rising phase of the epidemic spread, health systems are being overwhelmed by critically ill COVID-19 patients.[2] Once the peak of COVID-19 cases has passed, delayed medical and surgical care will become a priority. The high transmission rate of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection mandated two major organisational priorities: (i) avoid nosocomial spread of COVID-19 and (ii) minimise COVID-19 disease in healthcare staff.[3] Most guidelines recommend confirming the diagnosis of COVID-19 (using real-time quantitative polymerase chain reaction [RT–qPCR]) in suspected cases based on clinical symptoms and signs or previous contact with confirmed cases.[3] Given these and the importance of better understanding SARS-CoV-2 infection in paediatric populations, we performed a meta-analysis of COVID-19 symptoms in children with positive RT–qPCR tests.

The primary objective was to describe the proportion of paediatric patients diagnosed with SARS-CoV-2 (using RT–qPCR) presenting with general, respiratory, smell and taste (anosmia and ageusia),[3] gastrointestinal,[3] or dermatological symptoms (vesicles or pustules, other vesicular

Table 1 Analysis of primary and secondary outcomes of the meta-analysis. Results are expressed as mean percentages (95% confidence interval [CI]). I^2, heterogeneity of the result; P, level of significance of the heterogeneity. *Classification of severity was based on Dong and colleagues.[5]

Outcome	Number of patients included for the outcome	Number of studies included for the outcome	Percentage (95% CI)	I^2 statistics (%); P for I^2	Egger test (level of significance)	Begg-Mazumdar test (level of significance)
Asymptomatic	1600	26	16 (10; 23)	88.5; <0.0001	0.001	0.006
Fever	887	27	48 (42; 54)	51.2; 0.001	0.7	0.7
Headache	482	6	13 (4; 25)	88; <0.0001	—	—
Myalgia	312	3	14 (4; 29)	58.4; 0.09	—	—
Fatigue	372	9	8 (5; 11)	0; 0.7	—	—
Sneezing	19	2	23 (8; 44)	0; 0.9	—	—
Rhinorrhoea	741	14	16 (11; 22)	68.3; <0.0001	0.02	0.05
Sore throat	548	14	14 (7; 22)	76.6; <0.0001	0.7	0.06
Cough	837	25	40 (33; 47)	67.2; <0.0001	0.2	0.8
Nausea or vomiting	800	16	9 (6; 13)	50.5; 0.02	0.6	0.2
Diarrhoea or constipation	824	19	10 (7; 14)	40.9; 0.03	0.6	0.05
Abdominal pain	478	8	6 (4; 8)	0; 0.7	—	—
Mild infection*	1543	23	37 (26–48)	92.7; <0.0001	0.02	0.4
Moderate infection*	1543	23	45 (35–54)	88; <0.0001	0.04	0.7
Severe infection*	1543	23	3 (1–5)	63.2; <0.0001	0.2	0.006
Critical infection*	1543	23	0.6 (0.3–1)	0; 0.9	0.5	0.004
CT scan	401	17	55 (45; 64)	64.5; 0.0001	0.02	1

eruptions, urticarial lesions, maculopapular eruptions, and livedo or necrosis).[4] Secondary outcomes included COVID-19 disease severity categorised as mild, moderate, severe, or critical as defined by Dong and colleagues,[5] and the presence of specific radiological signs (characteristic ground glass appearance on chest CT).[3]

This meta-analysis was registered (https://osf.io/3u8nh) and performed according to the *Cochrane Handbook for Systematic Reviews of Interventions* guidelines.[6] Literature searches included PubMed and Embase. The following keyword associations were entered ['COVID-19' or 'Sars-Cov2' or 'Sars-Cov-2'] and 'Children'. The most recent search was performed on May 3, 2020. Articles with the following criteria were selected: studies describing paediatric patients suffering from COVID-19, and confirmatory diagnosis using RT–qPCR, including a description of the country in which the study was performed, details about COVID-19 suspicion criteria (symptoms or contact with a sick person), and details of clinical signs and symptoms and CT scan results. Articles describing patient clusters or case reports of less than two patients were excluded from the analysis.

Bias analysis was performed using the Risk of Bias in Longitudinal Symptom Research studies tool edited by The Joanna Briggs Institute Critical Appraisal tools for use in JBI Systematic Reviews: Checklist for Case Series.[7] Analyses used the inverse of the Freeman–Tukey double arcsine transformation. Result heterogeneity was assessed using Cochran's heterogeneity statistic (Q) and the I^2 statistic; I^2 >40% was considered meaningful heterogeneity and indicated use of a random-effects model. Publication bias was assessed (when aggregating at least 10 studies) using the Begg–Mazumdar and Egger tests.

Overall, 737 articles were identified, and 28 (including 1614 patients) were relevant for analyses (see Supplementary file for references). All studies but one were retrospective and included patients from China with the exception of four studies (from Malaysia, Spain, Italy, and the USA). Despite the retrospective nature of most studies, studies exhibited a low risk of bias in most of items. However, the representativeness of studies was probably biased given the absence of information about the consecutiveness of recruitment in most studies. The proportion of patients exhibiting each clinical sign, the severity of COVID-19, and CT imaging signs are displayed in Table 1. Most results exhibited high heterogeneity. Publication bias was not observed apart for asymptomatic patient outcome (Table 1).

Fever and cough were the most common signs of COVID-19 after SARS-CoV-2 infection in children. Our study conclusively confirmed the clinical impression that COVID-19 in children typically presents as a mild (37%) or moderate (45%) upper respiratory tract infection and is rarely severe or critical. This result is of great significance with respect to the planning of healthcare resource use over the coming months worldwide. Given that the pandemic will continue across seasons and overlap with peak influenza periods, it will be difficult to distinguish symptomatic paediatric COVID-19 patients from patients with influenza.

In our analysis, 16% of SARS-CoV-2-infected paediatric patients were asymptomatic. This proportion of asymptomatic patients is very likely a representation of RT–qPCR testing after contact. Asymptomatic patients have been estimated to represent 85% of infected patients in the general population,[8] and a recent study in pregnant women found 13.5% of asymptomatic patients with a positive RT–qPCR test.[9] Consequently, in the context of community SARS-CoV-2 spread, generalised population-based screening using RT–qPCR appears the most effective strategy for detecting SARS-CoV-2-infected paediatric patients with no clinical signs or known contacts.

Our results are of particular interest when considering the future management of hospitalised patients. There is a good case to be made for screening all hospital inpatients, or

at least considering a strategy relying on a careful screening of patients for clinical signs or a recent contact with an infected person followed by an RT–qPCR confirmation. However, one must also keep in mind that a negative result is no guarantee of the absence of infection. Studies have shown that RT–qPCR test sensitivity averages 70% when samples were taken from the nasopharynx.[10] Therefore, any patient with a high index of suspicion of COVID-19 should be treated as such in terms of protective measures, even where the RT–qPCR is negative. Radiological findings have shown promise as diagnostic tests for COVID-19 in adult patients.[3] In children, according to our results, typical CT changes were present in just 55% of patients, which indicates that CT scanning is of lesser value in children compared with adults.

In conclusion, our meta-analysis sheds light on (i) the absence of specificity regarding COVID-19 symptoms in children and (ii) the relatively high proportion of asymptomatic patients. Our results should be considered when policy is determined for detecting SARS-CoV-2 infection in children in the context of medical and surgical management.

Declarations of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.05.026.

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Anaesthesia preparedness for COVID-19 pandemic readiness: a medication preservation strategy

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Editor—The rapidly evolving global coronavirus disease 2019 (COVID-19) pandemic has highlighted the growing imbalance between supply and demand for medical resources as a result of limited global production capacity and changing demands. Information on pandemic-related pharmaceutical preparedness is particularly limited, and no Australian or international guidance is available thus far. Strategies to reduce, conserve, refine, replace, or substitute medications for sustainability during the current pandemic, and for the future, are a critical component to pandemic or disaster preparedness. A critical shortage of essential medications could severely limit access to best patient care and impact