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A systematic review and meta-analysis of otorhinolaryngological manifestations of coronavirus disease 2019 in paediatric patients

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Review Article

Dr A Singh takes responsibility for the integrity of the content of the paper

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Abstract

Background. This meta-analysis provides a quantitative measure of the otorhinolaryngological manifestations of coronavirus disease 2019 in children.

Methods. A structured literature review was carried out using PubMed, Embase and Cochrane Central, employing pertinent search terms. The statistical analysis was performed using Stata version 14.2 software, and the analysed data were expressed as the pooled prevalence of the symptoms with 95 per cent confidence intervals.

Results. The commonest symptoms noted were cough (38 per cent (95 per cent confidence interval = 33–42; $I^2 = 97.5$ per cent)), sore throat (12 per cent (95 per cent confidence interval = 10–14; $I^2 = 93.7$ per cent)), and nasal discharge (15 per cent (95 per cent confidence interval = 12–19; $I^2 = 96.9$ per cent)). Anosmia and taste disturbances showed a pooled prevalence of 8 per cent each. Hearing loss, vertigo and hoarseness were rarely reported.

Conclusion. Cough, sore throat and nasal discharge were the commonest otorhinolaryngological symptoms in paediatric patients with coronavirus disease 2019. Compared with adults, anosmia and taste disturbances were infrequently reported in children.

Introduction

The coronavirus disease 2019 (Covid-19) pandemic, which started in Wuhan, China, has affected 242 348 657 people worldwide to date and has claimed 4 927 723 lives as of 22 October 2021.[1] The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus classically homes to the upper respiratory system, which acts as a gateway to the lower respiratory system, and spreads predominantly by aerosol transmission. Though the lower respiratory system involvement is associated with much of the morbidity and mortality, the upper respiratory symptoms are often present in isolation or precede the onset of lower respiratory system symptoms. Therefore, quantitative documentation of upper respiratory tract manifestations is vital to help identify the disease symptoms early within the community, and possibly undertake testing and containment steps at an early stage in order to curb the community transmission.

There are well-documented differences in the disease characteristics and disease course between paediatric and adult patients. The disease in children usually behaves mildly with lower mortality (0.17 out of 100 000) compared with adult patients.[2] Severe illness has been reported to occur in almost 7 per cent of children compared with 26 per cent of adults.[3] Nevertheless, this lower disease severity may still be associated with sustained transmission to those susceptible to more severe disease.

Because the upper aerodigestive tract serves as the sentinel to the entry of SARS-CoV-2, Covid-19 symptoms often begin with or are concomitantly present in the upper respiratory tract. The information on clinical aspects of the disease in children is still evolving and is quite limited compared with that in adults. The lower respiratory manifestations and systemic symptoms are well documented in the literature, but focused quantitative documentation regarding upper respiratory symptomatology is still lacking. Though ENT symptoms encountered in Covid-19 patients are unlikely to be life-threatening (as opposed to, for example, shortness of breath, pneumonia and acute respiratory distress syndrome), a close familiarity with the symptoms is vital to identify and isolate the affected individuals in a timely fashion. We conducted this meta-analysis to summarise the upper respiratory tract and otorhinolaryngological manifestations of Covid-19 in children.

Methods

We aimed to evaluate the pooled prevalence of 10 otorhinolaryngological symptoms: loss of smell, loss or alteration of taste, cough, nasal discharge, nasal blockage, hearing loss, vertigo, sore throat, throat pain and hoarseness.

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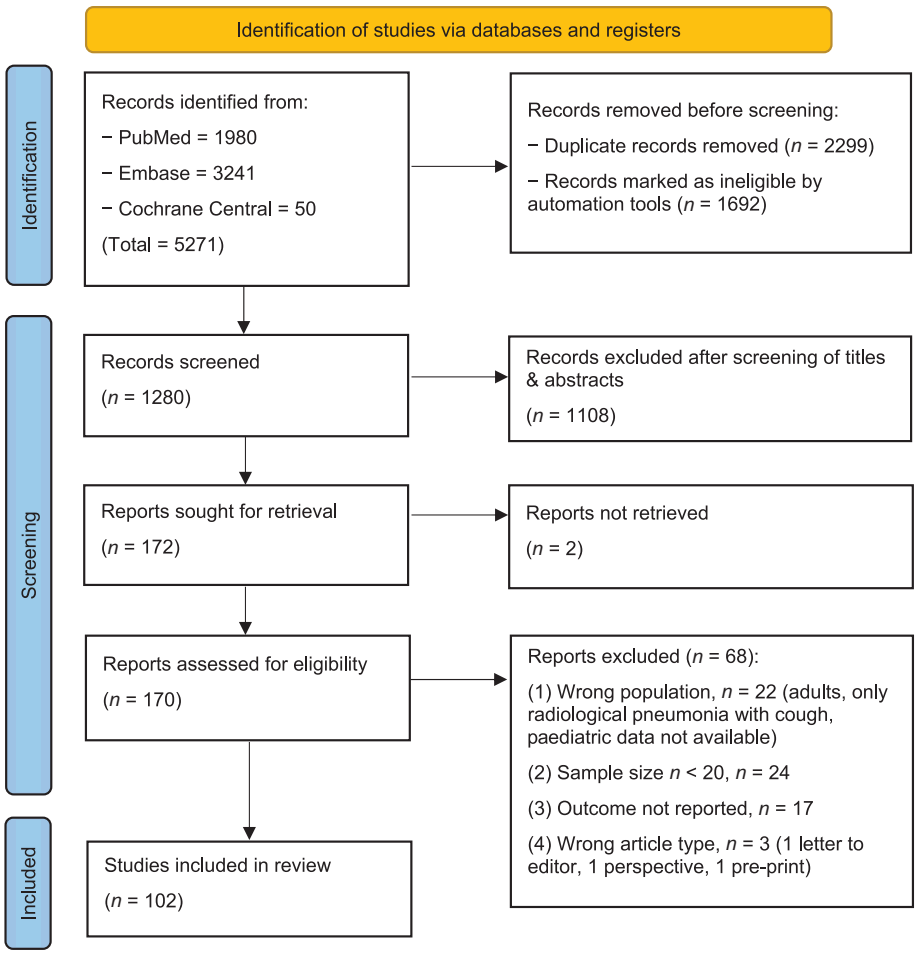

Fig. 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') flowchart.

Two authors (AS and MY) independently searched three databases (PubMed, Embase and Cochrane Central Register of Controlled Trials) for the relevant information published between December 2019 and June 2021. The search was conducted using three basic groups of terminologies or key words; the search terms related to: the infection being studied (Covid-19), the patient population (child*/pediatr*) and the otorhinolaryngological manifestations (ear/ oto* /cough/ hearing/ vertigo/ dizziness/ pharynx/ pharyng*/ throat/ larynx/ laryng*/ hoarse*/ taste/ smell/ olfact*/ nasal/ nose/ naso*/ rhino*/ sinus/ ageusia/ dysgeusia). The bibliographic information obtained from selected articles was also searched manually to include further relevant articles. The protocol was registered in the 'Prospero' International Prospective Register of Systematic Reviews (code: CRD42021230455), and we followed the Meta-analyses of Observational Studies in Epidemiology ('MOOSE') guidelines when reporting the findings.[4]

Study selection

The complete search strategy (including Medical Subject Headings (MeSH) terms) can be found in Supplementary Table 1.

The inclusion criteria were: prospective or retrospective studies, or clinical trials, reporting otorhinolaryngological symptoms in the paediatric population (aged 18 years or younger). We excluded: (1) case reports or series reporting fewer than 20 patients; (2) review articles; (3) editorials, opinions, technical reports, and conference abstracts with insufficient information; and (4) studies involving all age groups where no separate paediatric data were available. Non-English-language articles and studies reporting solely on multisystem inflammatory syndrome in children were also excluded. Any discrepancies relating to study inclusion were resolved through discussion with a third reviewer (JMS). The Preferred Reporting Items for Systematic Reviews and Meta-analyses ('PRISMA') flowchart (Figure 1) depicts the process of study selection and inclusion.

Data extraction and quality or bias assessment

Data were extracted using a well-structured, standardised proforma. Specifically, we documented the following: first author's name; year of publication; journal title; study setting and design; methods; study population; baseline demographic characteristics; details of intervention and control groups (in the case of clinical trials); case definition of Covid-19; prevalence of smell loss, taste loss or alteration, cough, nasal discharge, nasal blockage, hearing loss, vertigo, sore throat, throat pain, and hoarseness; and information for assessment of risk of bias. The risk of bias was evaluated using the scale by Hoy *et al.*[5] Two investigators performed the risk of bias assessment independently (AS, MY), and any discrepancies encountered were resolved by discussion with a third reviewer (JMS). Wherever provided, the data on asymptomatic patients were also recorded.

Data synthesis and statistical analysis

We undertook a quantitative synthesis of the prevalence of various otolaryngological symptoms of Covid-19 in children from the included studies. The categorical data were expressed in

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Table 1. Characteristics of included studies

Study (year)	Country	Patients (*n*)	Population characteristics	Study design	Risk of bias
Prata-Barbosa *et al.*[7] (2020)	Brazil	79	Median age = 4 y; 41% had co-morbidities; intensive care setting	Multicentric, prospective	Low
Hurst *et al.*[8] (2021)	USA	293	<21 y eligible, median age = 10.4 y; 36% had co-morbidities	Multicentric, prospective	Low
Hijazi *et al.*[9] (2021)	Saudi Arabia	660	3–15 y; mean age = 8.42 y; 43.6% asymptomatic; 4.4% hospitalised; 0.3% died	Unicentric, retrospective	High
Bernaola Abraira *et al.*[10] (2021)	Spain	30	Asymptomatic patients & <6 y excluded; mean age = 11.1 y; 63.3% hospitalised; 40% had severe disease	Unicentric, retrospective	High
Adedeji *et al.*[11] (2020)	Nigeria	53	Mean age = 12.6 y, majority (60%) asymptomatic; no severe or critical disease	Unicentric, retrospective	High
Alnajjar *et al.*[12] (2021)	Saudi Arabia	62	<14 y; median age = 6 y; 12.9% hospitalised; 6.4% required intensive care; 14.5% had co-morbidities	Unicentric, retrospective	High
Arslan *et al.*[13] (2021)	Turkey	176	Median age = 79 months; 13% had moderate–severe illness; 1.7% had underlying disease	Unicentric, retrospective	High
Bai *et al.*[14] (2020)	China	25	<18 y; median age = 11 y; none severe or critical; only 1 child had underlying disease; all were hospitalised	Multicentric, retrospective	High
Bardellini *et al.*[15] (2021)	Italy	27	0–14 y; mean age = 4.2 y; none required oxygen supplementation	Unicentric, retrospective	High
Bayesheva *et al.*[16] (2020)	Kazakhstan	650	<19 y eligible; mean age = 7.1 y; 18.8% were neonates or infants; 74% were city dwellers	Multicentric, retrospective	Moderate
Natera-de Benito *et al.*[17] (2021)	Spain	29	Children with neuromuscular disorders; mean age = 8.4 y; 38% asymptomatic; 90% did not require hospitalisation	Multicentric, retrospective	High
Böncüoğlu *et al.*[18] (2021)	Turkey	101	Mean age = 14.1 y; 77.2% were ≥13 y; compared findings with abnormality on lung imaging	Unicentric, retrospective	High
Bustos-Cordova *et al.*[19] (2020)	Mexico	50	<18 y eligible; median age = 56.6 months; 50% were hospitalised; 22% were asymptomatic; 52% had pre-existing chronic medical condition	Unicentric, prospective	Moderate
Cairoli *et al.*[20] (2020)	Argentina	191	Hospitalised population, median age = 7.7 y; 27.7% had co-morbidities	Unicentric, unclear	Moderate
Calitri *et al.*[21] (2021)	Italy	46	<14 y; median age = 8 y; 23.9% were asymptomatic; 8.7% were hospitalised; 13% had mild chronic disease	Unicentric, unclear	Moderate
Caro-Dominguez *et al.*[22] (2020)	Multiple	91	Median = 6.1 y, majority (93%) were symptomatic	Multicentric, retrospective	High
CDC COVID-19 Response Team[23] (2020)	USA	291	<18 y eligible; median age = 11 y; 23% had underlying conditions	Multicentric, retrospective	High
Chen *et al.*[24] (2020)	China	32	Mean age = 9.5 y; all were previously healthy; 14 had lung involvement; none with severe illness	Multicentric, retrospective	High
Chua *et al.*[25] (2020)	China, Korea, Hong Kong	423	<19 y eligible; all had mild disease; 26% were asymptomatic; mean age = 6.6 y in patients from Wuhan	Multicentric, retrospective	High
Chua *et al.*[26] (2021)	Hong Kong	265	≤18 y; mean age = 9.95 y; none had pneumonia or oxygen requirement; 58.1% were asymptomatic; compared data of 3 waves	Multicentric, retrospective	Moderate
Cleto-Yamane *et al.*[27] (2021)	Brazil	35	0–18 y eligible if serology findings were positive; median age = 11 y; immunosuppressed children (cancer or solid organ transplant patients); 77.1% were asymptomatic; all received out-patient care	Unicentric, prospective	High
Concheiro-Guisan *et al.*[28] (2021)	Spain	33	≤15 y; mean age = 8.4 y; otherwise well children; >6 y olds completed olfactory test	Unicentric, unclear	Moderate
Costa *et al.*[29] (2022)	Portugal	94	Median age = 11 y; all symptomatic; none hospitalised; 21% had underlying conditions	Unicentric, retrospective	High
De Jacobis *et al.*[30] (2021)	Italy	66	All were hospitalised; median age = 5.98 y; 13.6% had co-infections; 21.2% asymptomatic	Unicentric, retrospective	High
Du *et al.*[31] (2020)	China	182	Hospitalised children <16 y were eligible; median age = 6 y; 83.5% were ≤10 y; 30.2% were asymptomatic; 43 had history of allergy	Unicentric, retrospective	Moderate

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Table 1. (*Continued.*)

Study (year)	Country	Patients (*n*)	Population characteristics	Study design	Risk of bias
Duramaz *et al.*[32] (2021)	Turkey	43	28 days to 18 y; median age = 10.5 y in PCR-positive patients; emergency department setting; all were symptomatic; RT-PCR negative patients were also included; 79.1% were previously healthy	Multicentric, retrospective	High
Elghoudi *et al.*[33] (2021)	UAE	288	Mean age = 7.3 y; 67% were hospitalised; 19.4% had underlying health conditions; none required invasive ventilation	Unicentric, retrospective	Moderate
Erat & Güler[34] (2021)	Turkey	69	Median age = 11 y; hospitalised patients; 50.7% were ≥10 y; 1 with co-morbidities; none required intensive care	Unicentric, retrospective	High
Fakiri *et al.*[35] (2020)	Morocco	74	<18 y (excluding newborns) were enrolled; median age = 7 y; 73% were asymptomatic & the rest had mild symptoms	Unicentric, retrospective	High
Foster *et al.*[36] (2021)	USA	1215	≤21 y; median age = 7.1 y; 6.5% were 18–21 y; 8% were hospitalised, of which 35% required intensive care; 63.9% of admitted patients had underlying medical conditions; 15.9% were asymptomatic	Multicentric, retrospective	Moderate
Gaborieau *et al.*[37] (2020)	France	192	Confirmed or highly suspicious cases; median age = 1 y; 29% with underlying condition; hospitalised children, of which 12.5% required intensive care	Multicentric, prospective	Moderate
Garazzino *et al.*[38] (2021)	Italy	759	Mean age = 7.3 y; 21.1% were infants; 17.9% had underlying chronic disease; 48.9% were out-patients; 12% were asymptomatic; 28.3% had co-infections; 4% required intensive care; 3.9% had multisystem inflammatory syndrome	Multicentric, unclear	Moderate
Geis *et al.*[39] (2021)	Germany	148	All diagnosed by serology; patients with previous chronic disease were excluded; mean age = 7.5 y; 25.7% were asymptomatic; 1.3% were hospitalised	Multicentric, unclear	High
Goss *et al.*[40] (2021)	USA	26	Solid organ transplant recipient; ≤18 y at time of transplant; median age = 8 y (5 months to 18 y)	Multicentric, retrospective	High
Guo *et al.*[41] (2020)	China	136	<14 y olds were eligible; median age = 7 y; 5.9% were asymptomatic; 99.3% had mild–moderate illness	Multicentric, retrospective	High
Han *et al.*[42] (2021)	Korea	91	<19 y; median age = 11 y; hospital & non-hospital isolation facilities; 22% were asymptomatic; 7% had underlying diseases; 3% required oxygen supplementation; none required ventilation	Multicentric, retrospective	High
Hassan *et al.*[43] (2021)	Qatar	41	Neonates & young infants (<8 weeks); 3% required intensive care	Unicentric, retrospective	High
Jamjoom[44] (2021)	Saudi Arabia	52	0–14 y were eligible; emergency department setting; median age = 6 y; 8% had chronic illness; 85% had mild disease	Unicentric, retrospective	High
Li *et al.*[45] (2020)	Singapore	39	Mean age = 7.8 y; 37.5% had co-morbidities; 38.5% asymptomatic; compared features between symptomatic & asymptomatic patients	Unicentric, unclear	Moderate
Kainth *et al.*[46] (2020)	USA	65	<22 y were eligible; median age = 10.3 y; 48% were ≥12 y; 55% had underlying medical condition	Unicentric, retrospective	High
Kanburoglu *et al.*[47] (2020)	Turkey	37	Neonatal intensive care setting (73% admitted); all were symptomatic; 2 had congenital anomalies; 41% required oxygen	Multicentric, prospective	Moderate
Kanthimathinathan *et al.*[48] (2020)	UK	45	All were in-patients; median age = 3.5 y; 33% were infants; 205 received supplemental oxygen; 64% had some pre-existing condition	Unicentric, retrospective	High
Karbuz *et al.*[49] (2021)	Turkey	1156	Median age = 10.75 y; 1.5% had severe disease; 7.8% were <1 y; 12.9% had underlying conditions	Multicentric, retrospective	Moderate
Kilani *et al.*[50] (2020)	Jordan	61	≤18 y; median age = 6 y; 44.2% were asymptomatic; 3.3% had underlying condition	Unicentric, retrospective	Moderate
Kim *et al.*[51] (2020)	Uzbekistan	46	Adult patients were included; information provided as per age bands; none received oxygen; 14.3% children were asymptomatic	Multicentric, retrospective	High
King *et al.*[52] (2021)	Canada	1987	<18 y; 0.4% were admitted; mean age = 9.3 y; 35.9% were asymptomatic	Multicentric, unclear	Moderate

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Table 1. (*Continued.*)

Study (year)	Country	Patients (*n*)	Population characteristics	Study design	Risk of bias
Korkmaz *et al.*[53] (2020)	Turkey	81	Median age = 9.5 y; 54% were hospitalised; included 2 newborns (both asymptomatic)	Unicentric, retrospective	High
Krajcar *et al.*[54] (2020)	Croatia	230	≤19 y eligible; median age = 10 y; 16.1% had pre-existing illness; 41.3% had no symptoms	Multicentric, retrospective	High
Li *et al.*[55] (2020)	China	72	Median age = 2 y; comparative analysis with adenovirus; 22 were asymptomatic	Multicentric, retrospective	High
Kumar *et al.*[56] (2021)	India	141	10–19 y olds with mild–moderate Covid-19; mean age = 15.2 y; severe disease excluded	Unicentric, prospective	High
Lavaine *et al.*[57] (2021)	France	33	Median age = 1 y & 9 months; 21.2% were asymptomatic; 78.8% were hospitalised; 27.2% had co-existing conditions	Unicentric, retrospective	High
Lazzerini *et al.*[58] (2021)	Italy	159	54% were ≥10 y; 17.6% had co-morbidities; 78% cases were mild; 28.3% were hospitalised; 5.0% were asymptomatic	Multicentric, retrospective	Moderate
Leung[59] (2020)	Brazil	3213	≤2 y, 23% neonates, 49.6% males	Multicentric, retrospective	Moderate
Liang *et al.*[60] (2021)	China	71	Median age = 2.6 y; compared features with influenza A	Multicentric, retrospective	High
Liu *et al.*[61] (2020)	China	46	<1 y enrolled; 84.8% were ≥28 days old; 87% had moderate disease; 21.7% had co-morbidities	Unicentric, retrospective	Moderate
Luo *et al.*[62] (2020)	China	37	625 patients; 37 (5.9%) were ≤18 y; no severe or critical cases	Multicentric, retrospective	Moderate
Madhusoodhan *et al.*[63] (2020)	USA	98	Paediatric oncology patients ≤21 y receiving anti-cancer therapy; median age = 12.8 y; 37.8% were ≥15 y; 22% were obese; 67.3% were symptomatic; 17.3% had severe disease; 7.1% required ventilation	Multicentric, retrospective	High
Mahmoudi *et al.*[64] (2020)	Iran	35	All were in-patients; median age = 7.5 y; 40% had severe pneumonia; 51% had pre-existing medical condition	Unicentric, unclear	High
Mania *et al.*[65] (2021)	Poland	106	1 month to 17 y; mean age = 9.27 y; 88.7% were out-patients; 3.8% had underlying disorders; none ventilated	Unicentric, unclear	High
Mamishi *et al.*[66] (2020)	Iran	24	All in-patients; median age = 6 y; 71% cases were severe	Unicentric, retrospective	High
Mannheim *et al.*[67] (2020)	USA	64	<18 y; median age = 11 y; 45% were ≥14 y; 26% had pre-existing conditions; 16% were hospitalised; 5% had no symptoms	Multicentric, retrospective	High
He *et al.*[68] (2020)	China	35	<16 y were eligible; mean age = 7.1 y; 4 had co-infections & only 2 had co-morbidities; 20% were asymptomatic	Unicentric, retrospective	High
Mizrahi *et al.*[69] (2020)	Israel	862	Mixed age group; separate paediatric data; mild Covid-19; mean age of children group = 10.7 y; 14% had chronic medical condition	Multicentric, retrospective	Moderate
Nallasamy *et al.*[70] (2021)	India	31	≤14 y; median age = 33 months; 19% had co-morbidities; 58% were asymptomatic; 10% required intensive care	Unicentric, retrospective	High
Ma *et al.*[71] (2020)	China	216	Median age = 7.25 y; 47% were mild cases; 25% had associated medical history	Unicentric, retrospective	Moderate
Nanavati *et al.*[72] (2021)	India	21	Neonates; 33.3% were symptomatic; 28.6% required intensive care	Unicentric, retrospective	High
Nathan *et al.*[73] (2020)	France	23	Hospitalised, median age = 4.9 y, 56.5% had co-morbidities	Unicentric, retrospective	High
Ozkan & Erdeniz[74] (2021)	Turkey	30	Median age = 10 y; 11.5% had co-morbidities; 56.6% were ≥10 y; 16.6% were asymptomatic; all except 1 had mild course	Unicentric, retrospective	High
Parri *et al.*[75] (2020)	Italy	170	0–18 y eligible; emergency department setting; median age = 45 months; 22% had co-morbidities; 17% were asymptomatic; 63% were mild cases; 43% were hospitalised	Multicentric, retrospective	High

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Table 1. (*Continued.*)

Study (year)	Country	Patients (*n*)	Population characteristics	Study design	Risk of bias
Peng *et al.*[76] (2021)	China	211	Median age = 6 y; 70% were symptomatic	Unicentric, retrospective	Moderate
Pérez-Gaxiola *et al.*[77] (2021)	Mexico	51	Median age = 10 y; 39% were ≥12 y; 62.2% had mild disease; 8.1% cases were fatal	Unicentric, retrospective	High
Pourakbari *et al.*[78] (2021)	Iran	96	Median age = 7.5 y; 6% had RNAemia; 57% had underlying disease; 39.6% had severe disease; 10.4% died	Unicentric, unclear	Moderate
Qiu *et al.*[79] (2020)	China	36	≤16 y; mean age = 8.3 y; 47% had mild disease; 28% were asymptomatic	Multicentric, retrospective	Moderate
Otto *et al.*[80] (2020)	USA	424	Median age = 10 y; 11% were 18–21 y; 18% of positive patients were hospitalised; 57% had medical co-morbidity	Multicentric, retrospective	High
Rabha *et al.*[81] (2020)	Brazil	115	<18 y eligible; median age = 2 y; 26.1% had co-morbidities; 14% had severe pneumonia; 50.4% were <3 y; oxygen required in 7 cases; none ventilated	Multicentric, retrospective	High
Ramteke *et al.*[82] (2021)	India	30	Median age = 10.5 y; 8 months to 14 y; hospitalised children; only 30% were symptomatic	Unicentric, unclear	Moderate
Ranabothu *et al.*[83] (2020)	USA	1353	≤18 y; 19% were in-patients; 1.9% were in intensive care	Multicentric, retrospective	Moderate
Rouger-Gaudichon *et al.*[84] (2020)	France	37	Mean age = 11.2 y; 6 patients were >18 y; had undergone cancer therapy in previous 6 months; 5 patients admitted to intensive care	Multicentric, unclear	High
Rusetsky *et al.*[85] (2021)	Russia	79	≥5 y; severe cases excluded; median age = 12.9 y; all were hospitalised	Unicentric, prospective	Moderate
Sarangi *et al.*[86] (2020)	India	50	Median age = 6 y; 58% were asymptomatic; 40% had mild disease; none had hypoxemia; only 2 had co-morbidities	Unicentric, unclear	High
Sena *et al.*[87] (2021)	Brazil	682	<20 y; mean age = 9 y; 10.9% had co-morbidities; 46.2% were hospitalised; 5.6% cases were fatal	Unicentric, retrospective	Moderate
Shahbaznejad *et al.*[88] (2021)	Iran	100	Mean age = 8.7 y; 62% required oxygen supplementation; 6% required invasive ventilation; 4% cases were fatal; 13% had multisystem inflammatory syndrome	Multicentric, retrospective	High
Sharma *et al.*[89] (2020)	Nepal	121	Mean age = 8.8 y; 40.5% were adolescents; 71.9% were asymptomatic; only 1.8% required oxygen support	Multicentric, unclear	Moderate
Siddiqui *et al.*[90] (2021)	Turkey	206	Median age = 7.55 y; compared features with influenza A or B; 9.2% had underlying chronic disease; 3.4% were hospitalised; 2.4% were intensive care admissions	Unicentric, retrospective	Moderate
Somekh *et al.*[91] (2020)	Israel	31	Both children & adults studied in 20 families; 31 were aged 5–17 y; out-patient setting	Unicentric, unclear	High
Song *et al.*[92] (2020)	USA	315	Median age = 9.7 y; compared clinical features to seasonal influenza; 17.1% were hospitalised & 5.7% required intensive care	Unicentric, retrospective	High
Sousa *et al.*[93] (2020)	Brazil	2570	<20 y; all were admitted; 38% had pre-existing co-morbidities; 25% had intensive care support	Multicentric, unclear	High
Soysal *et al.*[94] (2020)	Turkey	237	0–17 y; median age = 87 months; 30% were asymptomatic; 28% were hospitalised; 1.2% required intensive care; no severe or critical cases; 5 had underlying chronic disease	Multicentric, retrospective	High
Sun *et al.*[95] (2020)	China	74	Median age = 5.8 y; 48.7% were >6 y; 18.9% had pre-existing illnesses; 1 patient received oxygen; 29.7% were asymptomatic	Unicentric, retrospective	High
Szépfalusi *et al.*[96] (2021)	Austria	28	5–21 y; median age = 13 y; chiefly serology-based data; 46.2% were asymptomatic; 23.1% had chronic disease	Unicentric, prospective	Moderate
Temel *et al.*[97] (2021)	Turkey	81	Mean age = 9.3 y; 26% were asymptomatic; 60% were mild cases; only 3 hospitalised	Unicentric, unclear	High

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Table 1. (*Continued.*)

Study (year)	Country	Patients (*n*)	Population characteristics	Study design	Risk of bias
Tripathi *et al.*[98] (2021)	USA	233	<18 y eligible; median age = 10.8 y; non-multisystem inflammatory patients (56.5%) compared with multisystem inflammatory syndrome patients; 61.9% had co-morbidities; critical illness in 30.9%; only 33.6% without oxygen therapy; 20.2% were ventilated	Multicentric, retrospective	High
Wu *et al.*[99] (2020)	China	74	Hospitalised children; median age = 6 y; 20 were asymptomatic; 1 had severe pneumonia	Multicentric, retrospective	High
Xia *et al.*[100] (2020)	China	114	<16 y eligible; Wuhan residents; 10% were aged <6 months; 72% had abnormal lung imaging	Multicentric, retrospective	High
Xiong *et al.*[101] (2020)	China	244	≤18 y; median age = 82 months, 34.8% were asymptomatic; 1.6% required ventilation; compared features with SARS 2003	Unicentric, retrospective	Moderate
Xu *et al.*[102] (2020)	China	32	<18 y; mean age = 8.7 y; 9% had co-morbidities; 34% were asymptomatic	Multicentric, retrospective	High
Yilmaz *et al.*[103] (2020)	Turkey	105	Mean age = 9 y; co-morbidities in 3.8%; 56% were asymptomatic	Unicentric, retrospective	High
Zhamankulov *et al.*[104] (2021)	Kazakhstan	94	3–17 y with recurrent respiratory infections; excluded those with co-morbidities; mean age = 5.9 y; evaluated as atopic phenotype & vitamin D deficiency phenotype groups	Unicentric, retrospective	High
Zhang *et al.*[105] (2020)	China	34	Median age = 2.7 y; 47% had mixed infections; 82% had moderate disease; 17.6% had co-morbidities	Multicentric, retrospective	High
Zhang *et al.*[106] (2020)	China	41	≤14 y; mean age = 5.9 y; 73.2% were mild cases; none were severe	Unicentric, retrospective	Moderate
Zhang & Huang[107] (2020)	China	33	<19 y eligible; mean age = 9.6 y; all were admitted but none was critical	Multicentric, retrospective	High
Zheng *et al.*[108] (2020)	China	52	0–18 y (excluding newborns); median age = 9 y; 21.1% were ≤3 y; 23.1% were asymptomatic; none with co-morbidities; none required ventilation	Multicentric, retrospective	Moderate

y = years; CDC = Centers for Disease Control and Prevention; UAE = United Arab Emirates; PCR = polymerase chain reaction; RT-PCR = reverse transcriptase transcription polymerase chain reaction; Covid-19 = coronavirus disease 2019; SARS = severe acute respiratory syndrome or median with interquartile range

percentages, while the continuous data were expressed as means and standard deviations. The statistical analysis was performed using Stata® version 14.2 software, and the analysed data were expressed as the numerical value of the pooled prevalence of the symptoms with 95 per cent confidence intervals (CIs).

The studies that did not report an outcome were excluded from the denominator for the pooled prevalence. Wherever explicitly stated as absent from the cohort, we considered zero prevalence towards the final pooled estimate.

Heterogeneity between studies was explored using I^2 statistics, and the data were pooled using a random-effects model. A subgroup analysis was performed to explain any heterogeneity detected in the most prevalent symptoms (i.e. those with a pooled prevalence of more than 10 per cent).

A sensitivity analysis was performed to assess the effect of studies with a high risk of bias on final prevalence estimates. The funnel plot asymmetry and Egger's test were used to determine the publication bias.

Results

Study selection and characteristics

The search strategy produced 5271 results; 2299 duplicates were manually removed and 1692 were deemed ineligible by automation tools. The title and abstracts of 1280 records were screened manually and using Rayyan® software; the latter is an application designed to expedite the initial screening of abstracts and titles.[6] Of the subsequent 170 retrieved reports, 68 were excluded after full-text review (Figure 1). Eventually, 102 publications, comprising 24 335 children with Covid-19, were included in the meta-analysis.[7–108] The number of children enrolled in the individual studies ranged from 21 to 3213.

Table 1 provides the key characteristics of the included studies.[7–108] Of the included studies, 22 (21.6 per cent) were from China, while 12 were from Turkey and 11 were from the USA. Most studies ($n = 96$) had provided clinical information for children only; the remaining six studies investigated both adult and paediatric populations but had provided the paediatric data separately.

Retrospective reports ($n = 76$, 74.5 per cent) constituted the majority of studies, and nearly half ($n = 48$, 47 per cent) were multicentric studies. The diagnosis of Covid-19 was based on: reverse transcription polymerase chain reaction ($n = 76$, 74.5 per cent), a combination of clinical and laboratory parameters ($n = 16$, 15.7 per cent), or serology alone ($n = 2$). Eight studies lacked clear information on the method employed to confirm the Covid-19 diagnosis. The median age of participants was 7.8 years (interquartile range = 6, 10), and they ranged from newborns to 15.2 years. Both sexes were equally represented across the studies.

The risk of bias was moderate ($n = 35$) to high ($n = 65$) in almost all the eligible studies; only two studies were considered to have a low risk of bias. The lack of random selection of the sample and data collection from hospital records (not directly from study subjects) were the most commonly observed biases noted in the eligible studies.

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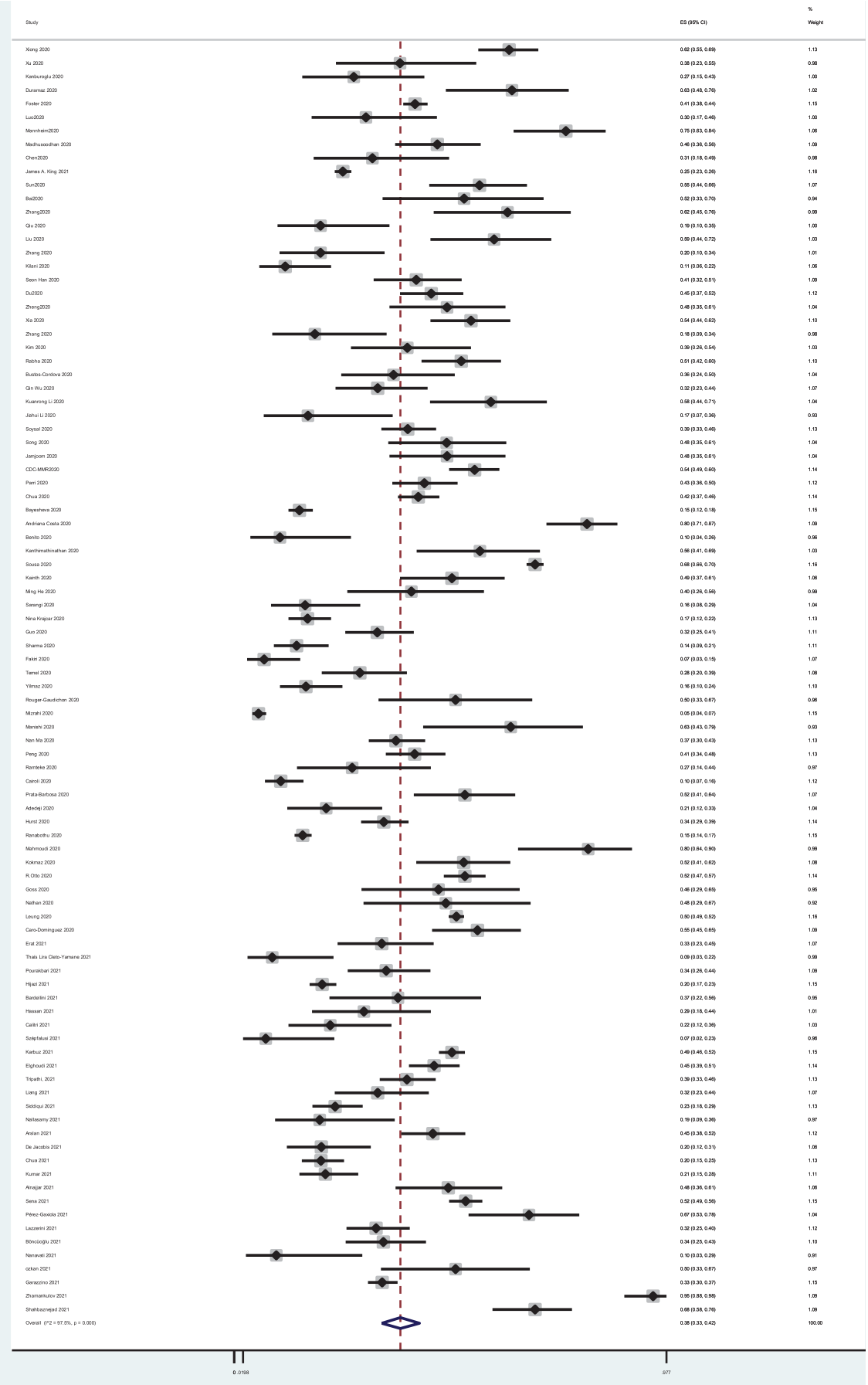

Fig. 2. Forest plot showing the pooled prevalence of cough. ES = effect size; CI = confidence interval; CDC = Centers for Disease Control and Prevention; Covid-19 = coronavirus disease 2019

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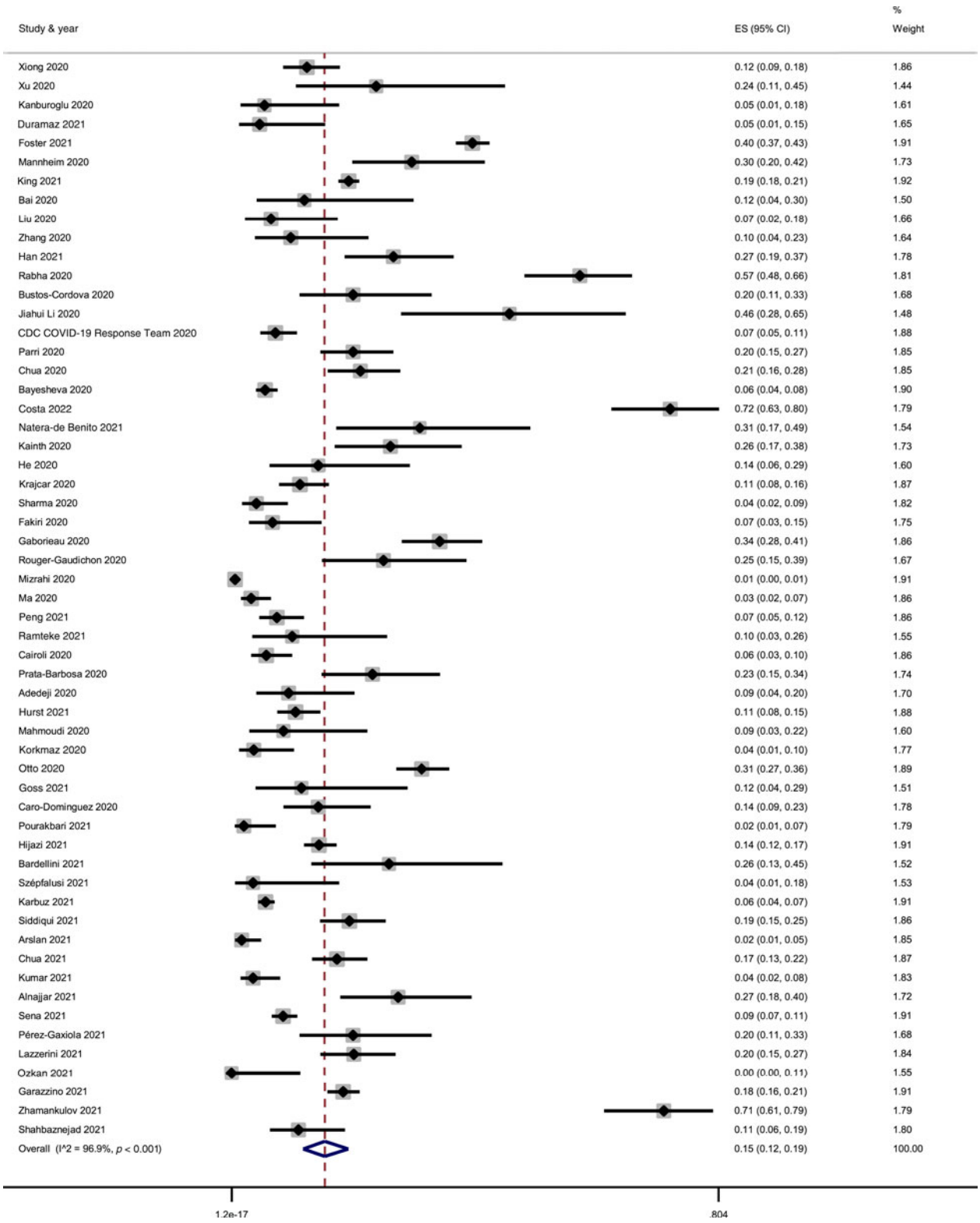

Fig. 3. Forest plot showing the pooled prevalence of nasal discharge. ES = effect size; CI = confidence interval; CDC = Centers for Disease Control and Prevention; Covid-19 = coronavirus disease 2019

Clinical symptoms

The commonest symptoms were cough, nasal discharge and sore throat (Figures 2–4, and Supplementary Figure 1). The pooled prevalence of cough was 38 per cent (95 per cent CI = 33–42; $I^2 = 97.5$ per cent), while that of sore throat was 12 per cent (95 per cent CI = 10–14; $I^2 = 93.7$ per cent). The prevalence of nasal discharge was 15 per cent (95 per cent CI = 12–19; $I^2 = 96.9$ per cent; Table 2). The least commonly reported symptoms were hearing loss, throat pain and hoarseness, with fewer than five contributory studies for each symptom. Loss of taste or smell was less commonly reported, with an expectedly similar pooled prevalence of 8 per cent (95 per cent CI = 6–10 for smell and 5–10 for taste). Vertigo and hoarseness of voice had a much lower pooled prevalence of 1 per cent each. Table 2 shows the pooled prevalence of these 10 symptoms and the proportion of asymptomatic patients in the eligible studies.

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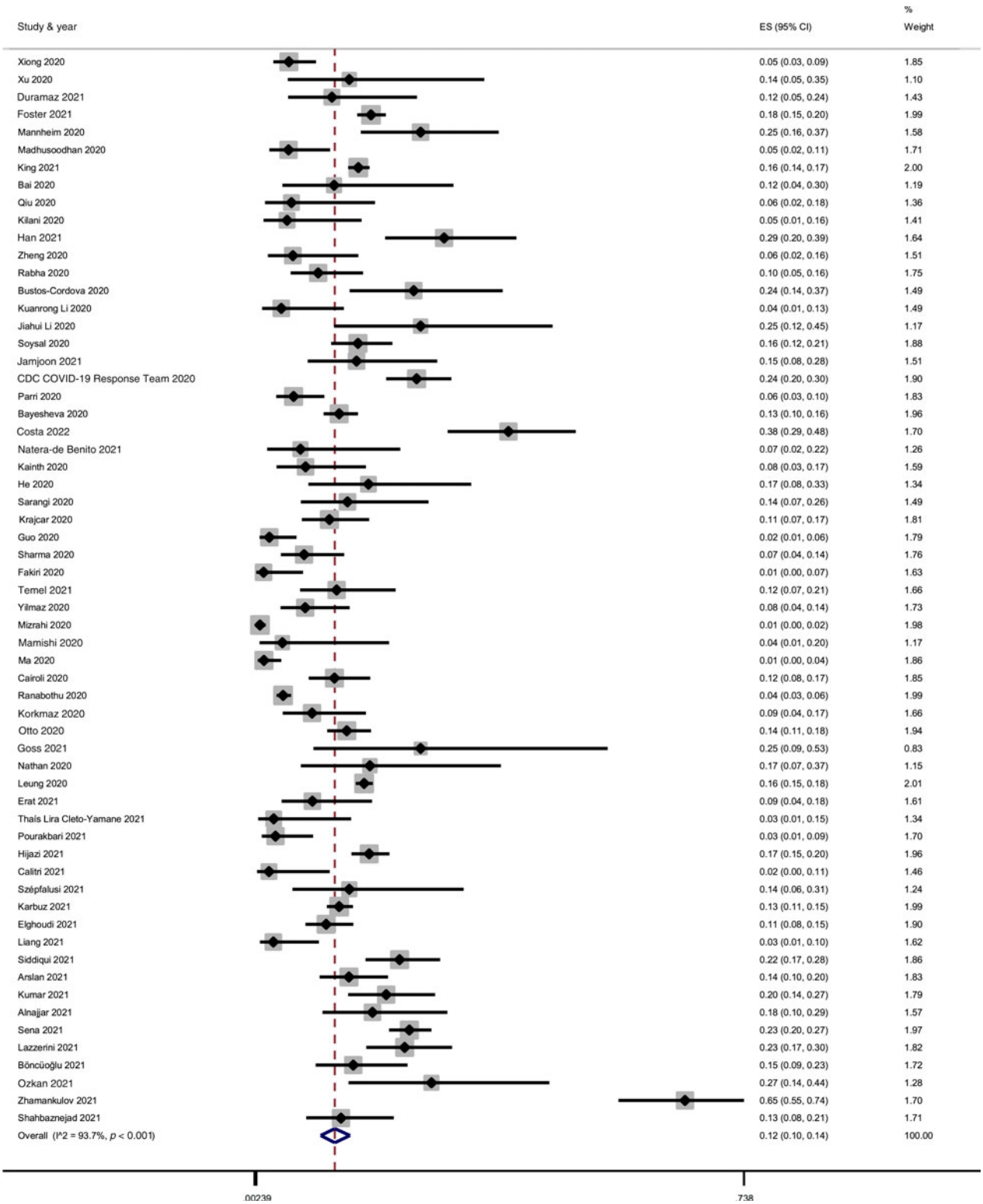

Fig. 4. Forest plot showing the pooled prevalence of sore throat. ES = effect size; CI = confidence interval; CDC = Centers for Disease Control and Prevention; Covid-19 = coronavirus disease 2019

Only 66 studies had information regarding the proportion of asymptomatic children, and the resultant estimate of 27 per cent (95 per cent CI = 23–32) was derived from information across 12 687 children.

Publication bias

The funnel plot suggested a reporting bias for anosmia but appeared symmetrical for cough (Figure 5). We also used Egger's test to assess the publication bias. While Egger's test for anosmia showed significant small study effects ($p < 0.001$), this was not the case for studies reporting cough ($p = 0.14$).

Subgroup and sensitivity analysis

We performed subgroup analyses based on study design, case definition, and risk of bias for the three most prevalent symptoms: sore throat, cough and nasal discharge (Supplementary

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Table 2. Pooled prevalence of various otorhinolaryngological manifestations

Outcome	Studies (patients) (*n*)	Pooled prevalence (%)	95% CI	I^2 (%)	*P**
Loss of smell	54 (11 804)	8	6–10	93.7	0.07
Loss of taste	42 (10 895)	8	5–10	93.6	0.06
Cough	94 (22 938)	38	33–42	97.5	0.17
Nasal discharge	57 (13 361)	15	12–19	96.9	0.14
Nasal block	23 (6748)	8	5–12	93.9	0.06
Hearing loss	01 (862)	0.2	–	–	–
Vertigo	09 (3270)	1	0–2	65.3	<0.001
Sore throat	61 (16 998)	12	10–14	93.7	0.06
Throat pain	02 (120)	7	3–12	–	–
Hoarseness	04 (1173)	1	0–5	84.7	0.03
Asymptomatic	66 (12 687)	27	23–32	96.9	0.17

**P* for heterogeneity. CI = confidence interval

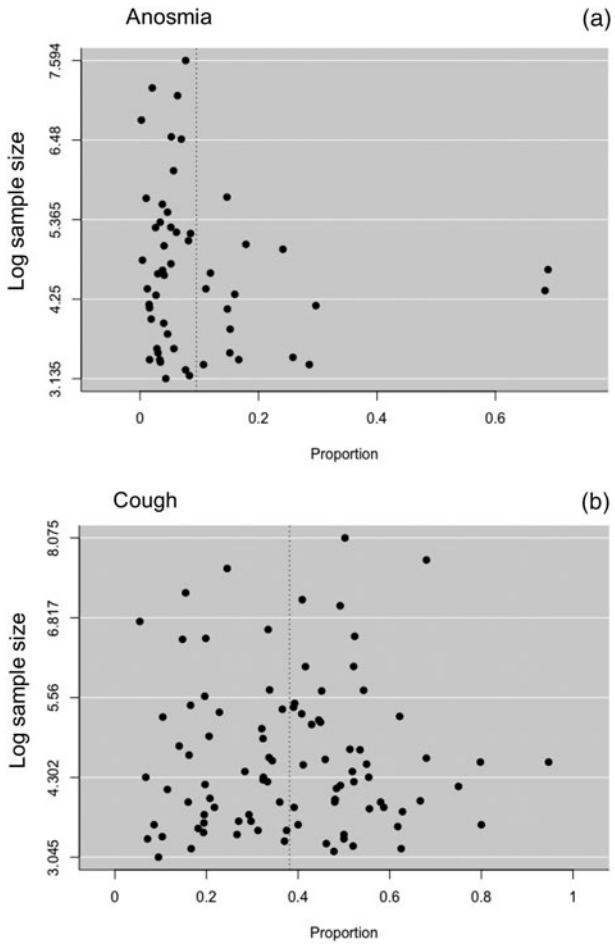

Fig. 5. Funnel plot for studies reporting (a) anosmia and (b) cough.

Figures 2–4 and Table 3). Only two studies had a low risk of bias, and pooled prevalence of cough and nasal discharge was 37 per cent (95 per cent CI = 32–42) and 13 per cent (95 per cent CI = 9–16), respectively, in these two studies.[7,8] Data on sore throat were limited to studies with moderate to high risk of bias. Sensitivity analysis, after the exclusion of studies with a high risk of bias, did not show a significant change in the pooled prevalence of sore throat (10 per cent (95 per cent CI = 7–14)) or nasal discharge (12 per cent (95 per cent CI = 8–17)). However, heterogeneity was significant for the pooled prevalence of cough, and the pooled prevalence was 30 per cent (95 per cent CI = 24–36) after the exclusion of studies with a high risk of bias.

The subgroup analyses based on study design and case definition also demonstrated significant heterogeneity (Table 3). The studies with mixed definitions of Covid-19, rather than based on reverse transcription polymerase chain reaction or serology alone, demonstrated more homogeneous results for the prevalence of sore throat (15 per cent (95 per cent CI = 14–17); $I^2 = 0$ per cent, $p = 0.01$).

We also performed meta-regression analyses to assess the effect of the four different covariates (multicentric, sample size, risk of bias and study design) on the pooled estimates for cough, sore throat and nasal discharge. We did not observe any significant effect on the pooled estimates of these symptoms with meta-regression analyses (Supplementary Tables 2–4).

Discussion

The current meta-analysis summarises the pooled Covid-19 symptoms frequency and distribution values related to the otorhinolaryngological domain in 24 000 paediatric patients. The commonest otorhinolaryngological symptom was cough, followed by sore throat and nasal discharge. Previous reviews[109] have revealed the commonest presenting symptoms in children to be fever (pooled prevalence of 51 per cent; 95 per cent CI = 45–57) and cough (pooled prevalence of 41 per cent; 95 per cent CI = 35–47). By comparison, the commonest otorhinolaryngological symptoms noted in adult patients, by Qiu *et al.*,[110] were olfactory dysfunction (47 per cent), sneezing (27 per cent) and nasal congestion (19 per cent). These findings highlight the differences between the otolaryngological symptom profiles of children and adults.

Cough is a common symptom of Covid-19 infection that may arise with both upper and lower respiratory involvement. We found cough to be the commonest symptom, with a pooled prevalence of 38 per cent, as reported from 94 studies. This is similar to the findings of previous reports. Though severe lower respiratory involvement often manifests with accompanying symptoms, it may be difficult to localise the focus to the

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Table 3. Subgroup and sensitivity analysis for cough, sore throat and nasal discharge

Outcome	Subgroup	Pooled prevalence (%)	95% CI	I^2 (%); *P*-value
Cough	*Risk of bias*			
	– High	42	36–48	95.78; <0.001
	– Moderate	29	23–36	98.32; <0.001
	– Low	37	32–42	–
	Study design			
	– Retrospective	40	35–44	97.04; <0.001
	– Prospective	26	17–37	85.95; <0.001
	– Unclear	32	18–46	98.96; <0.001
	Case definition			
	– RT-PCR	36	31–42	97.63; <0.001
	– Serology alone	9	3–22	–
	– Mixed	43	36–51	92.46; <0.001
	– Unclear	44	26–62	97.68; <0.001
Sore throat	*Risk of bias*			
	– High	13	10–17	87.62; <0.001
	– Moderate	10	7–14	96.52; <0.001
	– Low	–		
	Study design			
	– Retrospective	12	10–15	94.63; <0.001
	– Prospective	15	7–25	68.88; 0.02
	– Unclear	10	6–15	93.66; <0.001
	Case definition			
	– RT-PCR	12	9–15	93.82; <0.001
	– Serology alone	3	1–15	–
	– Mixed	15	14–17	0.00; 0.81
	– Unclear	14	5–25	95.71; <0.001
Nasal discharge	*Risk of bias*			
	– High	19	13–25	94.92; <0.001
	– Moderate	12	7–17	97.98; <0.001
	– Low	13	9–16	–
	Study design			
	– Retrospective	16	11–22	97.49; <0.001
	– Prospective	13	5–24	92.38; <0.001
	– Unclear	12	8–18	91.63; <0.001
	Case definition			
	– RT-PCR	15	11–20	97.50; <0.001
	– Serology alone	–		
	– Mixed	14	8–23	91.94; <0.001
	– Unclear	18	9–29	87.18; <0.001

CI = confidence interval; RT-PCR = reverse transcription polymerase chain reaction

upper versus the lower respiratory tract in milder cases presenting with cough. Regardless, given the potential for significant aerosol generation, cough remains an important symptom for disease transmission. In addition, the high prevalence of cough in children suggests the potential for transmissibility to other vulnerable age groups and caregivers.

Given the frequent occurrence of common cold symptoms in children irrespective of Covid-19 infection, it is possible to mistake Covid-19 infection for common cold symptoms in this age group, leading to a higher propensity of community transmission. Compared with the common cold and allergic rhinitis, nasal symptoms are less frequent in Covid-19 patients.[111] Rhinorrhoea and nasal congestion are reported in fewer than one-fifth of Covid-19 cases.[109] The present analysis showed the pooled prevalence of rhinorrhoea and congestion to be 15 per cent and 8 per cent, respectively.

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Olfactory and taste dysfunction is one of the most familiar manifestations of Covid-19 encountered in adults. The high rate of olfactory symptoms correlates with the neurotropism exhibited by SARS-CoV-2 towards the neuroepithelium present in the olfactory cleft. These symptoms can occur in isolation without other nasal symptoms, they typically signal a milder disease course, and they are reversible in the majority of patients.[112,113] The meta-analysis by Qiu *et al.*,[110] involving 54 studies and 16 478 adult patients, revealed the pooled prevalence of olfactory symptoms to be 47 per cent (95 per cent CI = 29–65). However, in the paediatric age group, the olfactory and taste symptoms are relatively infrequent. A higher prevalence is noted in older children.[9] This may be attributed to an age-related biological difference, or may be secondary to the inability of the children to identify or communicate these symptoms effectively. Regarding the pooled incidence, these symptoms affected less than a tenth of infected children. A recent meta-analysis by Yan *et al.*[114] showed the prevalence of smell and taste disturbances in children to be 15 per cent and 9 per cent, respectively. Older age and female gender were associated with a higher prevalence of smell disturbances.

Laryngeal and otological symptoms have been infrequent in adult and paediatric populations, and were described as case reports or case series. The current report showed fewer than 10 per cent of the studies reporting on the presence or absence of these symptoms.[115–119]

The current analysis showed asymptomatic infections in almost a fourth of affected children. Previous reviews reported the proportion of asymptomatic infections as 40–45 per cent,[120] while the pooled prevalence of asymptomatic cases was calculated to be 48 per cent by Syangtan *et al.* using a random effect model.[121] The same meta-analysis revealed the largest proportion of asymptomatic cases in children (49.6 per cent), followed by the adult (30.3 per cent) and elderly (16.9 per cent) populations. The prevalence of asymptomatic infections apparent from our data is lower (27 per cent). However, given that many asymptomatic infected individuals possibly never visited the hospital, we assume this percentage is larger than that reflected in the current data. Asymptomatic, equally infectious individuals are likely to continue spreading the infection in the community if not detected and isolated. The lower exposure rate for children compared with adults, secondary to the lack of workplace and travel-related exposures, may contribute to the lower predisposition of children to the viral infection. Once exposed, the children are equally likely as adults to acquire the infection.[122] However, the more favourable immunity profile, a different pattern of *de novo* angiotensin-converting enzyme 2 (ACE-2) receptor expression in the airway, or a different pattern of induction of the lower airway ACE-2 receptor after homing of the virus to the upper airways in children may underlie the higher rate of 'asymptomatic' infections.[123,124] The usual lack of associated co-morbidities in children is also protective.

Strength and limitations

This meta-analysis has certain limitations. The inclusion of English-only articles limited the results obtained. The prognostic importance of otorhinolaryngological manifestations could not be assessed because of the paucity of such studies in children. In addition, heterogeneity was significant, limiting the interpretation of pooled estimates. Despite these limitations, the current meta-analysis may serve as a helpful reference database for the pooled prevalence of otorhinolaryngological symptoms, with data obtained from over 100 studies enrolling over 24 000 children with Covid-19.

Conclusion

The commonest otorhinolaryngological manifestation of Covid-19 in paediatric patients was cough, followed by sore throat and nasal discharge. Anosmia and taste disturbances were less prevalent in children compared with adults based on the data available in the literature. Hearing loss, vertigo, throat pain and hoarseness were infrequently reported. Almost a fourth of the paediatric patients infected with Covid-19 were found to be asymptomatic.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0022215122000536

Competing interests. None declared

References

1 WHO Coronavirus (COVID-19) Dashboard. In: https://covid19.who.int [23 October 2021]
2 Bhopal SS, Bagaria J, Olabi B, Bhopal R. Children and young people remain at low risk of COVID-19 mortality. *Lancet Child Adolesc Health* 2021;**5**:e12–13
3 Fu L, Wang B, Yuan T, Chen X, Ao Y, Fitzpatrick T *et al.* Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and meta-analysis. *J Infect* 2020;**80**:656–65
4 Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;**283**:2008–12
5 Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C *et al.* Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012;**65**:934–9
6 Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan--a web and mobile app for systematic reviews. *Syst Rev* 2016;**5**:210
7 Prata-Barbosa A, Lima-Setta F, Santos GRD, Lanziotti VS, de Castro REV, de Souza DC *et al.* Pediatric patients with COVID-19 admitted to intensive care units in Brazil: a prospective multicenter study. *J Pediatr (Rio J)* 2020;**96**:582–92
8 Hurst JH, Heston SM, Chambers HN, Cunningham HM, Price MJ, Suarez L *et al.* SARS-CoV-2 infections among children in the Biospecimens from Respiratory Virus-Exposed Kids (BRAVE Kids) study. *Clin Infect Dis* 2021;**73**:e2875–82
9 Hijazi LO, Alaraifi AK, Alsaab F. Otolaryngology manifestations of COVID-19 in pediatric patients. *Int J Pediatr Otorhinolaryngol* 2021;**144**:110701
10 Bernaola Abraira M, Bartha De Las Peñas I, López-Araujo GA, Escudero Diez C, Rodríguez Del Río P, Morales-Cabeza C *et al.* Olfactory and gustatory dysfunction in pediatric patients with coronavirus disease (COVID-19). *J Investig Allergol Clin Immunol* 2021;**31**:277–9
11 Adedeji IA, Abdu YM, Bashir MF, Adamu AS, Gwarzo GD, Yaro BS *et al.* Profile of children with COVID-19 infection: a cross sectional study from North-East Nigeria. *Pan Afr Med J* 2020;**35**(suppl 2):145
12 Alnajjar AA, Dohain AM, Abdelmohsen GA, Alahmadi TS, Zaher ZF, Abdelgalil AA. Clinical characteristics and outcomes of children with COVID-19 in Saudi Arabia. *Saudi Med J* 2021;**42**:391–8
13 Arslan G, Aktürk H, Duman M. Clinical characteristics of pediatric COVID-19 and predictors of PCR positivity. *Pediatr Int* 2021;**63**:1055–61
14 Bai K, Liu W, Liu C, Fu Y, Hu J, Qin Y *et al.* Clinical analysis of 25 COVID-19 infections in children. *Pediatr Infect Dis J* 2020;**39**:e100–3
15 Bardellini E, Bondioni MP, Amadori F, Veneri F, Lougaris V, Meini A *et al.* Non-specific oral and cutaneous manifestations of coronavirus disease 2019 in children. *Med Oral Patol Oral Cir Bucal* 2021;**26**:e549–53
16 Bayesheva D, Boranbayeva R, Turdalina B, Fakhradiyev I, Saliev T, Tanabayeva S *et al.* COVID-19 in the paediatric population of Kazakhstan. *Paediatr Int Child Health* 2020;**41**:76–8
17 Natera-de Benito D, Aguilera-Albesa S, Costa-Comellas L, García-Romero M, Miranda-Herrero MC, Rúbies Olives J *et al.*

COVID-19 in children with neuromuscular disorders. *J Neurol* 2021;**268**:3081–5
18 Böncüoğlu E, Coşkun M, Kıymet E, Öztürk Atasoy T, Şahinkaya Ş, Cem E *et al*. Can laboratory findings predict pulmonary involvement in children with COVID-19 infection? *Pediatr Pulmonol* 2021;**56**:2489–94
19 Bustos-Cordova E, Castillo-García D, Cerón-Rodríguez M, Soler-Quiñones N. Clinical spectrum of COVID-19 in a Mexican pediatric population. *Indian Pediatr* 2020;**58**:126–8
20 Cairoli H, Raiden S, Chiolo MJ, Di Lalla S, Ferrero F. Patients assisted at the department of medicine of a pediatric hospital at the beginning of the COVID-19 pandemic in Buenos Aires, Argentina. *Arch Argent Pediatr* 2020;**118**:418–26
21 Calitri C, Fantone F, Benetti S, Lupica MM, Ignaccolo MG, Banino E *et al*. Long-term clinical and serological follow-up of paediatric patients infected by SARS-CoV-2. *Infez Med* 2021;**29**:216–23
22 Caro-Dominguez P, Shelmerdine SC, Toso S, Secinaro A, Toma P, Damasio MB *et al*. Thoracic imaging of coronavirus disease 2019 (COVID-19) in children: a series of 91 cases. *Pediatr Radiol* 2020;**50**:1354–68
23 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
24 Chen Z, Tong L, Zhou Y, Hua C, Wang W, Fu J *et al*. Childhood COVID-19: a multicentre retrospective study. *Clin Microbiol Infect* 2020;**26**:1260.e1–4
25 Chua GT, Xiong X, Choi EH, Han MS, Chang SH, Jin BL *et al*. COVID-19 in children across three Asian cosmopolitan regions. *Emerg Microbes Infect* 2020;**9**:2588–96
26 Chua GT, Wong JSC, Lam I, Ho PPK, Chan WH, Yau FYS *et al*. Clinical characteristics and transmission of COVID-19 in children and youths during 3 waves of outbreaks in Hong Kong. *JAMA Netw Open* 2021;**4**:e218824
27 Cleto-Yamane TL, Rodrigues-Santos G, de Magalhães-Barbosa MC, Moura PG, Vasconcelos RD, Gouveia JLS *et al*. Screening of COVID-19 in outpatient children with cancer or solid organ transplantation: preliminary report. *Eur J Pediatr* 2021;**180**:3237–41
28 Concheiro-Guisan A, Fiel-Ozores A, Novoa-Carballal R, González-Duran ML, Portugués de la Red M, Martínez-Reglero C *et al*. Subtle olfactory dysfunction after SARS-CoV-2 virus infection in children. *Int J Pediatr Otorhinolaryngol* 2021;**140**:110539
29 Costa A, Almeida H, Moniz M, Alves C. COVID-19 screening in a Portuguese pediatric population. *Enferm Infecc Microbiol Clin* (*Engl Ed*) 2022;**40**:28–31
30 De Jacobis IT, Vona R, Cittadini C, Marchesi A, Cursi L, Gambardella L *et al*. Clinical characteristics of children infected with SARS-CoV-2 in Italy. *Ital J Pediatr* 2021;**47**:90
31 Du H, Dong X, Zhang J-J, Cao Y-Y, Akdis M, Huang P-Q *et al*. Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status. *Allergy* 2020;**76**:510–32
32 Duramaz BB, Turel O, Korkmaz C, Karadogan MT, Yozgat CY, Iscan A *et al*. A snapshot of pediatric patients with COVID-19 in a pandemic hospital. *Klin Padiatr* 2021;**233**:24–30
33 Elghoudi A, Aldhanhani H, Ghatasheh G, Sharif E, Narchi H. Covid-19 in children and young adolescents in Al Ain, United Arab Emirates - a retrospective cross-sectional study. *Front Pediatr* 2021;**8**:603741
34 Erat T, Güler Ş. Use of radiological tests in COVID-19 positive child cases: is chest computed tomography necessary? *Int J Clin Pract* 2021;**75**:e14259
35 Fakiri KE, Nassih H, Sab IA, Draiss G, Bouskraoui M. Epidemiology and clinical features of coronavirus disease 2019 in Moroccan children. *Indian Pediatr* 2020;**57**:808–10
36 Foster CE, Marquez L, Davis AL, Tocco E, Koy TH, Dunn J *et al*. A surge in pediatric coronavirus disease 2019 cases: the experience of Texas Children's Hospital from March to June 2020. *J Pediatric Infect Dis Soc* 2021;**10**:593–8
37 Gaborieau L, Delestrain C, Bensaid P, Vizeneux A, Blanc P, Garraffo A *et al*. Epidemiology and clinical presentation of children hospitalized with SARS-CoV-2 infection in suburbs of Paris. *J Clin Med* 2020;**9**:2227
38 Garazzino S, Lo Vecchio A, Pierantoni L, Calò Carducci FI, Marchetti F, Meini A *et al*. Epidemiology, clinical features and prognostic factors of pediatric SARS-CoV-2 infection: results from an Italian multicenter study. *Front Pediatr* 2021;**9**:649358
39 Geis T, Brandstetter S, Toncheva AA, Laub O, Leipold G, Wagner R *et al*. Serum neurofilament light chain (sNfL) values in a large cross-sectional population of children with asymptomatic to moderate COVID-19. *J Neurol* 2021;**268**:3969–74
40 Goss MB, Galván NTN, Ruan W, Munoz FM, Brewer ED, O'Mahony CA *et al*. The pediatric solid organ transplant experience with COVID-19: an initial multi-center, multi-organ case series. *Pediatr Transplant* 2021;**25**:e13868
41 Guo CX, He L, Yin JY, Meng XG, Tan W, Yang GP *et al*. Epidemiological and clinical features of pediatric COVID-19. *BMC Med* 2020;**18**:250
42 Han MS, Choi EH, Chang SH, Jin B-L, Lee EJ, Kim BN *et al*. Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the Republic of Korea. *JAMA Pediatr* 2021;**175**:73–80
43 Hassan M, Khalil A, Magboul S, Alomari O, Abdalla T, Alsliman H *et al*. Neonates and young infants with Covid-19 presented with sepsis-like syndrome: a retrospective case controlled study. *Front Pediatr* 2021;**9**:634844
44 Jamjoom RS. Coronavirus disease 2019 (COVID-19) in pediatric emergency. Presentation and disposition. *Saudi Med J* 2021;**42**:105–9
45 Li J, Thoon KC, Chong CY, Maiwald M, Kam KQ, Nadua K *et al*. Comparative analysis of symptomatic and asymptomatic SARS-CoV-2 infection in children. *Ann Acad Med Singap* 2020;**49**:530–7
46 Kainth MK, Goenka PK, Williamson KA, Fishbein JS, Subramony A, Barone S *et al*. Early experience of COVID-19 in a US children's hospital. *Pediatrics* 2020;**146**:e2020003186
47 Kanburoglu MK, Tayman C, Oncel MY, Akin IM, Can E, Demir N *et al*. A multicentered study on epidemiologic and clinical characteristics of 37 neonates with community-acquired COVID-19. *Pediatr Infect Dis J* 2020;**39**:e297–302
48 Kanthimathinathan HK, Dhesi A, Hartshorn S, Ali SH, Kirk J, Nagakumar P *et al*. COVID-19: a UK children's hospital experience. *Hosp Pediatr* 2020;**10**:802–5
49 Karbuz A, Akkoc G, Bedir Demirdag T, Yilmaz Ciftdogan D, Ozer A, Cakir D *et al*. Epidemiological, clinical, and laboratory features of children with COVID-19 in Turkey. *Front Pediatr* 2021;**9**:631547
50 Kilani MM, Odeh MM, Shalabi M, Al Qassieh R, Al-Tamimi M. Clinical and laboratory characteristics of SARS-CoV2-infected paediatric patients in Jordan: serial RT-PCR testing until discharge. *Paediatr Int Child Health* 2020;**41**:83–92
51 Kim K, Choi JW, Moon J, Akilov H, Tuychiev L, Rakhimov B *et al*. Clinical features of COVID-19 in Uzbekistan. *J Korean Med Sci* 2020;**35**:e404
52 King JA, Whitten TA, Bakal JA, McAlister FA. Symptoms associated with a positive result for a swab for SARS-CoV-2 infection among children in Alberta. *CMAJ* 2021;**193**:E1–9
53 Korkmaz MF, Türe E, Dorum BA, Kılıç ZB. The epidemiological and clinical characteristics of 81 children with COVID-19 in a pandemic hospital in Turkey: an observational cohort study. *J Korean Med Sci* 2020;**35**:e236
54 Krajcar N, Stemberger Marić L, Šurina A, Kurečić Filipović S, Trkulja V, Roglić S *et al*. Epidemiological and clinical features of Croatian children and adolescents with a PCR-confirmed coronavirus disease 2019: differences between the first and second epidemic wave. *Croat Med J* 2020;**61**:491–500
55 Li K, Li L, Wang X, Li H, Chen J, Liu L *et al*. Comparative analysis of clinical features of SARS-CoV-2 and adenovirus infection among children. *Virol J* 2020;**17**:193
56 Kumar L, Kahlon N, Jain A, Kaur J, Singh M, Pandey AK. Loss of smell and taste in COVID-19 infection in adolescents. *Int J Pediatr Otorhinolaryngol* 2021;**142**:110626
57 Lavaine O, Spizzo J, Arbitre C, Muller J, Kuhn P, Laugel V *et al*. COVID-19 in children at Strasbourg University Hospital: a retrospective study of the first 2 months of the epidemic. *Arch Pediatr* 2021;**28**:405–10
58 Lazzerini M, Sforzi I, Trapani S, Biban P, Silvagni D, Villa G *et al*. Characteristics and risk factors for SARS-CoV-2 in children tested in the early phase of the pandemic: a cross-sectional study, Italy, 23 February to 24 May 2020. *Euro Surveill* 2021;**26**:2001248
59 Leung C. The younger the milder clinical course of COVID-19: even in newborns? *Pediatr Allergy Immunol* 2020;**32**:358–62
60 Liang F, Wang X, Shao J, Chen J, Liu L, Li H *et al*. Comparison of clinical features on admission between coronavirus disease 2019 and influenza A among children: a retrospective study in China. *BMC Infect Dis* 2021;**21**:365
61 Liu X, Tang J, Xie R, Li W, Chen J, Guo Y *et al*. Clinical and epidemiological features of 46 children <1 year old with coronavirus disease 2019 in Wuhan, China: a descriptive study. *J Infect Dis* 2020;**222**:1293–7

https://doi.org/10.1017/S0022215122000536 Published online by Cambridge University Press

62 Luo H, Liu S, Wang Y, Phillips-Howard PA, Ju S, Yang Y *et al.* Age differences in clinical features and outcomes in patients with COVID-19, Jiangsu, China: a retrospective, multicentre cohort study. *BMJ Open* 2020;**10**:e039887

63 Madhusoodhan PP, Pierro J, Musante J, Kothari P, Gampel B, Appel B *et al.* Characterization of COVID-19 disease in pediatric oncology patients: the New York-New Jersey regional experience. *Pediatr Blood Cancer* 2020;**68**:e28843

64 Mahmoudi S, Mehdizadeh M, Shervin Badv R, Navaeian A, Pourakbari B, Rostamyan M *et al.* The coronavirus disease 2019 (COVID-19) in children: a study in an Iranian children's referral hospital. *Infect Drug Resist* 2020;**13**:2649–55

65 Mania A, Mazur-Melewska K, Lubarski K, Kuczma-Napierała J, Mazurek J, Jończyk-Potoczna K *et al.* Wide spectrum of clinical picture of COVID-19 in children - from mild to severe disease. *J Infect Public Health* 2021;**14**:374–9

66 Mamishi S, Heydari H, Aziz-Ahari A, Shokrollahi MR, Pourakbari B, Mahmoudi S *et al.* Novel coronavirus disease 2019 (COVID-19) outbreak in children in Iran: atypical CT manifestations and mortality risk of severe COVID-19 infection. *J Microbiol Immunol Infect* 2020;**54**:839–44

67 Mannheim J, Gretsch S, Layden JE, Fricchione MJ. Characteristics of hospitalized pediatric coronavirus disease 2019 cases in Chicago, Illinois, March-April 2020. *J Pediatr Infect Dis Soc* 2020;**9**:519–22

68 He M, Wang C, Xu L, Zhang H, Liu Y, Zhao Y *et al.* Epidemiological and clinical characteristics of 35 children with COVID-19 in Beijing, China. *Pediatr Investig* 2020;**4**:230–5

69 Mizrahi B, Shilo S, Rossman H, Kalkstein N, Marcus K, Barer Y *et al.* Longitudinal symptom dynamics of COVID-19 infection. *Nat Commun* 2020;**11**:6208

70 Nallasamy K, Angurana SK, Jayashree M, Mathew JL, Bansal A, Singh MP *et al.* Clinical profile, hospital course and outcome of children with COVID-19. *Indian J Pediatr* 2021;**88**:979–84

71 Ma N, Li P, Wang X, Yu Y, Tan X, Chen P *et al.* Ocular manifestations and clinical characteristics of children with laboratory-confirmed COVID-19 in Wuhan, China. *JAMA Ophthalmol* 2020;**138**:1079–86

72 Nanavati R, Mascarenhas D, Goyal M, Haribalakrishna A, Nataraj G. A single-center observational study on clinical features and outcomes of 21 SARS-CoV-2-infected neonates from India. *Eur J Pediatr* 2021;**180**:1895–906

73 Nathan N, Prevost B, Sileo C, Richard N, Berdah L, Thouvenin G *et al.* The wide spectrum of COVID-19 clinical presentation in children. *J Clin Med* 2020;**9**:2950

74 Ozkan EA, Erdeniz EH. Evaluation of children followed up for Covid-19 in a tertiary hospital. *J Exp Clin Med* (*Turkey*) 2021;**38**:125–31

75 Parri N, Lenge M, Cantoni B, Arrighini A, Romanengo M, Urbino A *et al.* COVID-19 in 17 Italian pediatric emergency departments. *Pediatrics* 2020;**146**:e20201235

76 Peng X, Guo Y, Xiao H, Xia W, Zhai A, Zhu B *et al.* Overview of chest involvement at computed tomography in children with coronavirus disease 2019 (COVID-19). *Pediatr Radiol* 2021;**51**:222–30

77 Pérez-Gaxiola G, Flores-Rocha R, Valadez-Vidarte JC, Hernández-Alcaraz M, Herrera-Mendoza G, Real-Lugo MÁD. Clinical and epidemiological characteristics of children with SARS-CoV-2 infection: a case series in Sinaloa. *Bol Med Hosp Infant Mex* 2021;**78**:18–23

78 Pourakbari B, Mahmoudi S, Mahmoudieh Y, Eshaghi H, Navaeian A, Rostamyan M *et al.* SARS-CoV-2 RNAaemia in children: an Iranian referral hospital-based study. *J Med Virol* 2021;**93**:5452–7

79 Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis* 2020;**20**:689–96

80 Otto WR, Geoghegan S, Posch LC, Bell LM, Coffin SE, Sammons JS *et al.* The epidemiology of severe acute respiratory syndrome coronavirus 2 in a pediatric healthcare network in the United States. *J Pediatr Infect Dis Soc* 2020;**9**:523–9

81 Rabha AC, Oliveira Junior FI, Oliveira TA, Cesar RG, Fongaro G, Mariano RF *et al.* Clinical manifestations of children and adolescents with Covid-19: report of the first 115 cases from Sabará Hospital Infantil. *Rev Paul Pediatr* 2020;**39**:e2020305

82 Ramteke S, Tikkas R, Goel M, Mandraha S, Shrivastava J. Paediatric COVID-19: milder presentation--a silver lining in dark cloud. *J Trop Pediatr* 2021;**67**:fmaa106

83 Ranabothu S, Onteddu S, Nalleballe K, Dandu V, Veerapaneni K, Veerapandiyan A. Spectrum of COVID-19 in children. *Acta Paediatr* 2020;**109**:1899–900

84 Rouger-Gaudichon J, Thébault E, Félix A, Phulpin A, Paillard C, Alimi A *et al.* Impact of the first wave of COVID-19 on pediatric oncology and hematology: a report from the French Society of Pediatric Oncology. *Cancers* (*Basel*) 2020;**12**:3398

85 Rusetsky Y, Meytel I, Mokoyan Z, Fisenko A, Babayan A, Malyavina U. Smell status in children infected with SARS-CoV-2. *Laryngoscope* 2021;**131**:E2475–80

86 Sarangi B, Reddy VS, Oswal JS, Malshe N, Patil A, Chakraborty M *et al.* Epidemiological and clinical characteristics of COVID-19 in Indian children in the initial phase of the pandemic. *Indian Pediatr* 2020;**57**:914–17

87 Sena GR, Lima TPF, Vidal SA, Duarte M do CMB, Bezerra PGM, Fonseca Lima EJ *et al.* Clinical characteristics and mortality profile of COVID-19 patients aged less than 20 years old in Pernambuco - Brazil. *Am J Trop Med Hyg* 2021;**104**:1507–12

88 Shahbaznejad L, Rouhanizadeh H, Navaeifar MR, Hosseinzadeh F, Movahedi FS, Rezai MS. Clinical characteristics and outcomes of COVID-19 in children in Northern Iran. *Int J Pediatr* 2021;**2021**:e5558287

89 Sharma AK, Chapagain RH, Bista KP, Bohara R, Chand B, Chaudhary NK *et al.* Epidemiological and clinical profile of Covid-19 in Nepali children: an initial experience. *J Nepal Paediatr Soc* 2020;**40**:202–9

90 Siddiqui M, Gültekingil A, Bakırcı O, Uslu N, Baskın E. Comparison of clinical features and laboratory findings of coronavirus disease 2019 and influenza A and B infections in children: a single-center study. *Clin Exp Pediatr* 2021;**64**:364–9

91 Somekh I, Yakub Hanna H, Heller E, Bibi H, Somekh E. Age-dependent sensory impairment in COVID-19 infection and its correlation with ACE2 expression. *Pediatr Infect Dis J* 2020;**39**:e270–2

92 Song X, Delaney M, Shah RK, Campos JM, Wessel DL, DeBiasi RL. Comparison of clinical features of COVID-19 vs seasonal influenza A and B in US children. *JAMA Netw Open* 2020;**3**:e2020495

93 Sousa BLA, Sampaio-Carneiro M, de Carvalho WB, Silva CA, Ferraro AA. Differences among severe cases of Sars-CoV-2, influenza, and other respiratory viral infections in pediatric patients: symptoms, outcomes and preexisting comorbidities. *Clinics* (*Sao Paulo*) 2020;**75**:e2273

94 Soysal A, Gönüllü E, Arslan H, Kibar BS, Pop S, Yurttaş GN *et al.* Comparison of clinical and laboratory features and treatment options of 237 symptomatic and asymptomatic children infected with SARS-CoV-2 in the early phase of the COVID-19 pandemic in Turkey. *Jpn J Infect Dis* 2020;**74**:273–9

95 Sun D, Zhu F, Wang C, Wu J, Liu J, Chen X *et al.* Children infected with SARS-CoV-2 from family clusters. *Front Pediatr* 2020;**8**:386

96 Szépfalusi Z, Schmidthaler K, Sieber J, Kopanja S, Götzinger F, Schoof A *et al.* Lessons from low seroprevalence of SARS-CoV-2 antibodies in schoolchildren: a cross-sectional study. *Pediatr Allergy Immunol* 2021;**32**:762–70

97 Temel H, Gündüz M, Arslan H, Ünal F, Atağ E, Cömert M *et al.* Evaluation of the clinical features of 81 patients with COVID-19: an unpredictable disease in children. *J Pediatr Infect Dis* 2021;**16**:47–52

98 Tripathi S, Gist KM, Bjornstad EC, Kashyap R, Boman K, Chiotos K *et al.* Coronavirus disease 2019-associated PICU admissions: a report from the Society of Critical Care Medicine Discovery Network Viral Infection and Respiratory Illness Universal Study Registry. *Pediatr Crit Care Med* 2021;**22**:603–15

99 Wu Q, Xing Y, Shi L, Li W, Gao Y, Pan S *et al.* Coinfection and other clinical characteristics of COVID-19 in children. *Pediatrics* 2020;**146**:e20200961

100 Xia W, Guo Y, Tian Z, Luo Y, Hu D, Shao J *et al.* Clinical features and temporal changes of RT-PCR and chest CT in COVID-19 pediatric patients. *Front Pediatr* 2020;**8**:579512

101 Xiong X, Chua GT, Chi S, Kwan MYW, Sang Wong WH, Zhou A *et al.* A comparison between Chinese children infected with coronavirus disease-2019 and with severe acute respiratory syndrome 2003. *J Pediatr* 2020;**224**:30–6

102 Xu H, Liu E, Xie J, Smyth RL, Zhou Q, Zhao R *et al.* A follow-up study of children infected with SARS-CoV-2 from western China. *Ann Transl Med* 2020;**8**:623

103 Yilmaz K, Gozupirinççioğlu A, Aktar F, Akin A, Karabel M, Yolbas I *et al.* Evaluation of the novel coronavirus disease in Turkish children: preliminary outcomes. *Pediatr Pulmonol* 2020;**55**:3587–94

104 Zhamankulov A, Rozenson R, Morenko M, Shnayder K, Akhmetova U, Tyo A. COVID-19 and recurrent respiratory infections in children of Kazakhstan. *Russ Open Med J* 2021;**10**:e0104

https://doi.org/10.1017/S0022215122000536 Published online by Cambridge University Press

105 Zhang C, Gu J, Chen Q, Deng N, Li J, Huang L *et al*. Clinical and epidemiological characteristics of paediatric SARS-CoV-2 infections in China: a multicenter case series. *PLoS Med* 2020;**17**:e1003130
106 Zhang Y, Xie RM, He YL, Xing LH, Dong L, Zhang JZ *et al*. Clinical and imaging features of pediatric COVID-19. *Ital J Pediatr* 2020;**46**:153
107 Zhang L, Huang S. Clinical features of 33 cases in children infected with SARS-CoV-2 in Anhui Province, China -- a multi-center retrospective cohort study. *Front Public Health* 2020;**8**:255
108 Zheng G, Wang B, Zhang H, Xie C, Zhang Y, Wen Z *et al*. Clinical characteristics of acute respiratory syndrome with SARS-CoV-2 infection in children in South China. *Pediatr Pulmonol* 2020;**55**:2419–26
109 Cui X, Zhao Z, Zhang T, Guo W, Guo W, Zheng J *et al*. A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). *J Med Virol* 2021;**93**:1057–69
110 Qiu J, Yang X, Liu L, Wu T, Cui L, Mou Y *et al*. Prevalence and prognosis of otorhinolaryngological symptoms in patients with COVID-19: a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol* 2022;**279**:49–60
111 Bruno C, Locatello LG, Cilona M, Fancello G, Vultaggio A, Maltagliati L *et al*. Seasonal allergic rhinitis symptoms in relation to COVID-19. *Allergy Rhinol* (*Providence*) 2020;**11**:2152656720968804
112 Nguyen NN, Hoang VT, Lagier J-C, Raoult D, Gautret P. Long-term persistence of olfactory and gustatory disorders in COVID-19 patients. *Clin Microbiol Infect* 2021;**27**:931–2
113 Moein ST, Hashemian SM, Tabarsi P, Doty RL. Prevalence and reversibility of smell dysfunction measured psychophysically in a cohort of COVID-19 patients. *Int Forum Allergy Rhinol* 2020;**10**:1127–35
114 Yan Q, Qiu D, Liu X, Guo X, Hu Y. Prevalence of smell or taste dysfunction among children with COVID-19 infection: a systematic review and meta-analysis. *Front Pediatr* 2021;**9**:686600
115 Kilic O, Kalcioglu MT, Cag Y, Tuysuz O, Pektas E, Caskurlu H *et al*. Could sudden sensorineural hearing loss be the sole manifestation of COVID-19? An investigation into SARS-COV-2 in the etiology of sudden sensorineural hearing loss. *Int J Infect Dis* 2020;**97**:208–11
116 Elibol E. Otolaryngological symptoms in COVID-19. *Eur Arch Otorhinolaryngol* 2021;**278**:1233–6
117 Bhatta S, Sharma S, Sharma D, Maharjan L, Bhattachan S, Sah MK *et al*. Study of hearing status in COVID-19 patients: a multicentered review. *Indian J Otolaryngol Head Neck Surg* 2021. Epub 2021 Jul 12
118 Al-Ani RM, Rashid RA. Prevalence of dysphonia due to COVID-19 at Salahaddin General Hospital, Tikrit City, Iraq. *Am J Otolaryngol* 2021;**42**:103157
119 Azzam AAA, Samy A, Sefein I, ElRouby I. Vocal disorders in patients with COVID 19 in Egypt. *Indian J Otolaryngol Head Neck Surg* 2021. Epub 2021 May 28
120 Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. *Ann Intern Med* 2020;**173**:362–7
121 Syangtan G, Bista S, Dawadi P, Rayamajhee B, Shrestha LB, Tuladhar R *et al*. Asymptomatic SARS-CoV-2 carriers: a systematic review and meta-analysis. *Front Public Health* 2020;**8**:587374
122 Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z *et al*. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis* 2020;**20**:911–19
123 Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. *JAMA* 2020;**323**:2427–9
124 Fialkowski A, Gernez Y, Arya P, Weinacht KG, Kinane TB, Yonker LM. Insight into the pediatric and adult dichotomy of COVID-19: age-related differences in the immune response to SARS-CoV-2 infection. *Pediatr Pulmonol* 2020;**55**:2556–64

https://doi.org/10.1017/S0022215122000536 Published online by Cambridge University Press