Received: 11 March 2023 | Revised: 16 May 2023 | Accepted: 23 May 2023

DOI: 10.1111/apa.16855

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

BRIEF REPORT

Antibiotics and uncertainty of diagnosis in viral respiratory infections: Point-prevalence survey across 15 European countries

Acute respiratory infections (ARI) are the most common reason for unscheduled health care visits during childhood.[1] These visits also account for the majority of inappropriate antibiotic prescriptions.[2] We aimed to identify whether certainty of aetiological diagnosis was associated with differences in testing strategies, prescription of antibiotics, prescription in accordance with presumed aetiology and inpatient referral.

Patient consultations were documented prospectively at 70 primary care (PC) centres of different sizes (including facilities with a single medical practitioner), similar to previous rounds of this recurrent point-prevalence audit survey (PPAS) and for the first time four paediatric hospital emergency departments (EDs) between January and March 2022.[3] Consecutive consultations for either: symptoms of a lower or upper respiratory tract infection (≤14 days) or suspicion of COVID-19 were documented, unless the main presentation were ear infections or allergic symptoms, which led to exclusion. The PPAS protocol, including the anonymous case report form, is available as a supplement to this letter (Appendix S2). The project was considered an audit; therefore, no ethics committee approval was required. This was confirmed by investigators against local regulations. The project reported here was a secondary analysis of the audit data. For this analysis, only first presentations in any episode of illness were selected. Certainty of aetiological diagnosis was re-grouped as 'high' for responses '(very) certain' and 'low' for 'moderate' or lower. Comparisons between groups were done, where relevant, using chi-square testing.

We collected data on 1160 consultations in 15 countries (61.3% PC and 38.7% EDs). Per country, between 5 and 167 consultations in varying numbers of PC centres in each country and between 82 and 146 consultations in ED (4 countries only) were recorded. Patients seen in primary care were older on average and patients seen in ED had higher proportions of more acute respiratory symptoms including tachypnoea (21% vs. 2%), shortness of breath (12% vs. 4%) and wheeze (24% vs. 7%). Accordingly, oxygen saturation was measured in 88% of ED patients but only in 39% of primary care patients. In both settings, aetiology of the illness episode was thought to be viral in approximately 90% of cases. Certainty of the care provider regarding this aetiology was higher in EDs (82% high certainty compared to 76% in primary care, $p = 0.014$). While SARS-CoV-2 tests were ordered equally frequently, other pathogen testing including, but not restricted to influenza virus and group A streptococci, C-reactive protein testing, oxygen saturation measurement and chest X-rays all occurred more frequently in EDs.

Approximately 10% of patients received antibiotics, which were from the Access group of the WHO Essential Medicines List's AWaRe classification in at least 88% (PC) and 82% (ED) of cases.

Table 1 shows testing and management (both as decided by a responsible clinician) by presumed aetiology and certainty thereof. Pathogen testing was used most frequently in children presumed to have SARS-CoV-2 infection (>70% in both settings). When other viruses or bacteria were suspected, pathogen testing was done for less than half of the children.

Fewer (81% vs. 93%, $p = 0.063$) children with presumed bacterial causes (who might benefit) received antibiotics when certainty of aetiology was low. In contrast, slightly more (5% vs. 2%, $p = 0.028$) with presumed viral causes (who would likely not benefit) received antibiotics when certainty was low.

87% of prescribers were (very) confident that the patient would benefit from antibiotic treatment if they presumed a bacterial aetiology. However, 40% were (very) confident if they considered a non-bacterial aetiology most likely. When certainty was low, referral for inpatient treatment was more common for presumed viral (15% vs. 6%, $p < 0.001$) and possibly also for bacterial (13% vs. 5%, $p = 0.204$) aetiology.

Conclusions may be limited by some imbalance of available resources for testing and inpatient admissions between countries in which PC and ED visits were documented, which may have enhanced the trend for more investigations in EDs because ED visits were documented in countries with higher income levels. In addition, although the association between uncertainty and testing in presumed viral infection seems to suggest that more testing was

PPAS4 Paediatric Group members are listed in Appendix S1.

TABLE 1 Testing and management by presumed aetiology and certainty regarding aetiological diagnosis.

	Certainty of aetiology		Risk ratio (95%-CI)	*p*
	High	Low		
Presumed bacterial aetiology				
N	74	32		
SARS-CoV-2 test <14 days	21 (28.4)	9 (28.1)	1.01 (0.52, 1.96)	0.979
Tests at this visit				
Pathogen testing	33 (44.6)	11 (34.4)	0.84 (0.61, 1.17)	0.327
CRP	9 (12.2)	5 (15.6)	0.78 (0.28, 2.14)	0.629
Both of these	9 (12.2)	5 (15.6)	0.78 (0.28, 2.14)	0.629
Neither of these	41 (55.4)	21 (65.6)	0.84 (0.61, 1.17)	0.327
Antibiotic prescribed	69 (93.2)	26 (81.3)	1.15 (0.96, 1.37)	0.063
Hospital referral/ admitted	4 (5.4)	4 (12.5)	0.43 (0.12, 1.62)	0.204
Presumed SARS-CoV-2				
N	272	59		
SARS-CoV-2 test <14 days	142 (52.2)	14 (23.7)	2.20 (1.37, 3.53)	<0.001
Tests at this visit				
Pathogen testing	196 (72.1)	46 (78.0)	1.27 (0.76, 2.13)	0.354
CRP	14 (5.2)	0 (0.0)	–	0.075
Both of these	14 (5.2)	0 (0.0)	–	0.075
Neither of these	76 (27.9)	13 (22.0)	1.27 (0.76, 2.13)	0.354
Antibiotic prescribed	6 (2.2)	2 (3.4)	0.65 (0.13, 3.14)	0.591
Hospital referral/ admitted	14 (5.2)	2 (3.4)	1.52 (0.35, 6.50)	0.568
Presumed other viral aetiology				
N	592	126		
SARS-CoV-2 test <14 days	104 (17.6)	31 (24.6)	0.71 (0.50, 1.02)	0.067
Tests at this visit				
Pathogen testing	181 (30.6)	58 (46.0)	1.29 (1.09, 1.52)	<0.001
CRP	28 (4.7)	9 (7.1)	0.66 (0.32, 1.37)	0.266
Both of these	28 (4.7)	9 (7.1)	0.66 (0.32, 1.37)	0.266
Neither of these	411 (69.4)	68 (54.0)	1.29 (1.09, 1.52)	<0.001
Antibiotic prescribed	12 (2.0)	7 (5.6)	0.36 (0.15, 0.91)	0.025
Hospital referral/ admitted	34 (5.7)	19 (15.1)	0.38 (0.22, 0.65)	<0.001

Abbreviation: CRP, C-reactive protein.

ordered when uncertainty was high, we did not document whether uncertainty preceded testing or whether more testing, especially for pathogens, may have increased uncertainty.

In summary, we observed a high proportion of pathogen testing for children with ARI suspected to be caused by SARS-CoV-2. This may likely have been to confirm these infections and initiate appropriate public health measures. The overall low proportion of antibiotic treatment may be caused by a shift in perceived risk of bacterial infection due to the ongoing pandemic.[4] For children with suspected bacterial or other viral ARI, pathogen testing, referral to hospital and receipt of potentially inappropriate antibiotics (i.e. discordant to presumed aetiology) was more common when clinicians

were less certain of presumed aetiology. This finding is in agreement with management reasoning described in a qualitative study on primary care for children in the UK.[5] We therefore conclude that tools reducing uncertainty of aetiological diagnosis have some potential to avert unnecessary antibiotic prescription and hospitalisation.

AUTHOR CONTRIBUTIONS

Conceptualisation: MKV, TV, CCB, AWvdV, JAB. Formal Analysis: MKV, JAB. Funding acquisition: TV, HG, CCB, AWvdV. Investigation: MKV, LK, DI, MGM, LA, EF, HR, MNN, RS, EB, RA, AB, FB, SCh, SCo, AGS, HG, CL, SvdL, LM, JP, AT, AV. Methodology: MKV, TV, CCB, AWvdV, JAB. Resources: MGM, HR, MNN, EB, RA, AB, FB, SCh, SCo, AGS, HG, CL, SvdL, LM, JP, AT, AV, HG, JAB. Supervision: AWvdV, JAB. Visualisation: MKV. Writing – original draft: MKV, CCB, AWvdV, JAB. Writing – review & editing: LK, DI, MGM, LA, EF, HR, MNN, RS, EB, RA, AB, FB, SCh, SCo, AGS, HG, CL, SvdL, LM, JP, AT, AV, TV, HG.

FUNDING INFORMATION

This work was supported by the Innovative Medicine Initiative 2 Joint Undertaking (grant number 820755, VALUE-Dx) and by the Horizon 2020 research and innovation programme (grant number 101003589, RECOVER).

CONFLICT OF INTEREST STATEMENT

The authors have no potential conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Raw data can be obtained from the RECOVER consortium upon request to the Primary Care Studies Team via the corresponding author. Any requests for access to raw data will be welcomed as long as they are scientifically valid, appropriate consent for the requested level of data sharing has been obtained from participants and as long as the planned data use does not conflict with ongoing analyses by the Primary Care Studies Team.

PPAS4 Paediatric Group

Correspondence

Malte Kohns Vasconcelos, Antimicrobial Resistance Research Group, Centre for Neonatal and Paediatric Infection, St. George's, University of London, Cranmer Terrace, London SW17 0RE, UK.

Email: mkohns@sgul.ac.uk

REFERENCES

1. Schneider A, Cabral C, Herd N, et al. Reducing primary care attendance intentions for pediatric respiratory tract infections. Ann Fam Med. 2019;17(3):239-249.
2. Little P, Francis NA, Stuart B, et al. Antibiotics for lower respiratory tract infection in children presenting in primary care in England (ARTIC PC): a double-blind, randomised, placebo-controlled trial. Lancet. 2021;398(10309):1417-1426.
3. van der Velden AW, Bax EA, Bongard E, et al. Primary care for patients with respiratory tract infection before and early on in the COVID-19 pandemic: an observational study in 16 European countries. BMJ Open. 2021;11(7):e049257.
4. Barbieri E, Liberati C, Cantarutti A, et al. Antibiotic prescription patterns in the Paediatric primary care setting before and after the COVID-19 pandemic in Italy: an analysis using the AWaRe metrics. Antibiotics. 2022;11(4):457.
5. Horwood J, Cabral C, Hay AD, Ingram J. Primary care clinician antibiotic prescribing decisions in consultations for children with RTIs: a qualitative interview study. Br J Gen Pract. 2016;66(644):e207-e213.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.