WHAT’S KNOWN ON THIS SUBJECT: Quantitative real-time polymerase chain reaction allows sensitive detection of respiratory viruses. The clinical significance of detection of specific viruses is not fully understood, however, and several viruses have been detected in the respiratory tract of asymptomatic children.

WHAT THIS STUDY ADDS: Our results indicate that quantitative real-time polymerase chain reaction is limited at distinguishing acute infection from detection in asymptomatic children for rhinovirus, bocavirus, adenovirus, enterovirus, and coronavirus.

abstract

BACKGROUND: Acute respiratory illness (ARI) accounts for a large proportion of all visits to pediatric health facilities. Quantitative real-time polymerase chain reaction (qPCR) analyses allow sensitive detection of viral nucleic acids, but it is not clear to what extent specific viruses contribute to disease because many viruses have been detected in asymptomatic children. Better understanding of how to interpret viral findings is important to reduce unnecessary use of antibiotics.

OBJECTIVE: To compare viral qPCR findings from children with ARI versus asymptomatic control subjects.

METHODS: Nasopharyngeal aspirates were collected from children aged ≤5 years with ARI and from individually matched, asymptomatic, population-based control subjects during a noninfluenza season. Samples were analyzed by using qPCR for 16 viruses.

RESULTS: Respiratory viruses were detected in 72.3% of the case patients (n = 151) and 35.4% of the control subjects (n = 74) (P = .001). Rhinovirus was the most common finding in both case patients and control subjects (47.9% and 21.5%, respectively), with a population-attributable proportion of 0.39 (95% confidence interval: 0.01 to 0.62). Metapneumovirus, parainfluenza viruses, and respiratory syncytial virus were highly overrepresented in case patients. Bocavirus was associated with ARI even after adjustment for coinfections with other viruses and was associated with severe disease. Enterovirus and coronavirus were equally common in case patients and control subjects.

CONCLUSIONS: qPCR detection of respiratory syncytial virus, metapneumovirus, or parainfluenza viruses in children with ARI is likely to be causative of disease; detection of several other respiratory viruses must be interpreted with caution due to high detection rates in asymptomatic children. Pediatrics 2014;133:e538–e545

AUTHORS: Samuel Rhedin, MB BChir,a Ann Lindstrand, MD, MPH,b Maria Rotzén-Östlund, MD-PhD,c,d Thomas Tolfvenstam, MD-PhD,e Lars Öhrmalm, MD-PhD,a Malin Ryd Rinder, MD-PhD,f Benita Zweygberg-Wiigard, MD-PhD,g Ake Ortvquist, MD-PhD,g Birgitta Henriques-Normark, MD-PhD,b,c,d Kristina Broiiden, MD-PhD,a and Pontus Naucker, MD-PhD,a,e

aDepartment of Medicine Solna, Unit of Infectious Diseases, Center for Molecular Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden; bSwedish Institute for Communicable Disease Control, Stockholm, Sweden; cDepartment of Clinical Microbiology, dDepartment of Infectious Diseases, eDepartment of Medicine Solna, Infectious Diseases Unit, fDepartment of Communicable Disease Control and Prevention, Stockholm Karolinska University Hospital, Stockholm, Sweden; gDepartment of Clinical Science and Education, South General Hospital, Karolinska Institutet, Sachs’ Children and Youth Hospital, Stockholm, Sweden; hDepartment of Microbiology Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden

KEY WORDS: children, case-control study, etiology, respiratory illness, viral infections

ABBREVIATIONS
ARI—acute respiratory illness
CI—confidence interval
HAdV—human adenovirus
HBoV—human bocavirus
HCoV—human coronavirus
HEV—human enterovirus
hMPV—human metapneumovirus
HRV—human rhinovirus
OR—odds ratio
PAP—population-attributable proportion
PIV—parainfluenza virus
qPCR—quantitative real-time polymerase chain reaction
RSV—respiratory syncytial virus
URTI—upper respiratory tract infection

The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the funding agency.

(Continued on last page)
Although acute respiratory illness (ARI) in children accounts for a large part of all visits to pediatric health facilities and is a great economic burden on society, our tools to diagnose the etiologic agents have until recently been limited. Treatment with antibiotics induces development of antibiotic resistance in bacteria and has a negligible effect on most ARIs, which generally are of viral origin. Nevertheless, antibiotics are frequently prescribed due to lack of clinically valid diagnostic tests verifying a viral etiology. Sensitive methods, such as quantitative real-time polymerase chain reaction (qPCR) analyses on nasopharyngeal samples, for a number of viruses have been introduced in the clinic as a sensitive diagnostic tool among children with respiratory tract infection. However, whereas detection of some viruses, such as influenza virus and respiratory syncytial virus (RSV), clearly is predictive for respiratory disease, the clinical significance upon detection of several other viruses needs further investigation. The interpretation of a viral detection is complicated by the fact that infections with multiple viruses are common in children with ARI and that many viruses have lately been reported to be found also in asymptomatic children.

Numerous case series investigating respiratory viruses in hospitalized children with ARI have been published. However, data are available from only a few case-control studies that examined to what extent specific respiratory viruses cause disease. Furthermore, these studies had limitations in that they used hospital-based control subjects, which might have biased the results. To address these issues, we conducted a matched case-control study outside the influenza season to compare viral qPCR findings in nasopharyngeal aspirates from children with ARI versus population-based asymptomatic control subjects matched on age and calendar time.

**METHODS**

**Study Population**

A matched case-control study was conducted with case patients consecutively enrolled at the pediatric emergency department at Sachs’ Children and Youth Hospital (Stockholm, Sweden) between September 1, 2011, and January 30, 2012. Case patients were children aged $\leq 5$ years with $\geq 1$ of the following symptoms: coryza (rhinorrhea or nasal congestion), sore throat, earache, cough, sputum production, or dyspnea. Children were only included once in the study. One matched control subject for each case subject according to calendar time (±14 days) and age (±6 months) was selected from an ongoing population-based study of pneumococcal carriage. In that study, children were enrolled at the time of their routine visits to child welfare centers in Stockholm for vaccination within the childhood immunization program (covering $\sim 99.6\%$ of the population in Sweden). If no control subject was found, intervals were expanded to calendar time (±30 days) and age (±12 months). Children who were reported to have had episodes of respiratory disease within the last 7 days were not eligible as control subjects. Written informed consent was collected from the parents of all included children before sampling.

Information from both case patients and control subjects regarding chronic diseases, vaccination, and sociodemographic status was collected by using a standardized questionnaire. Chronic diseases were categorized into 2 groups: (1) “asthma” (including both allergic and nonallergic asthma); and (2) “other” (Table 1). Clinical parameters of case patients were registered at admission. Elevated breathing frequency was defined as $\geq 50$ breaths per minute in children aged $<1$ year and $\geq 40$ breaths per minute in children aged 1 to 5 years. Tachycardia was defined as a pulse $\geq 160$ beats per minute in children aged $<1$ year and $\geq 120$ beats per minute in children aged 1 to 5 years. Fever was defined as a body temperature $\geq 38.0^\circ$C. Information about treatment, outcome, and routine biochemical, microbiologic, and radiologic analyses were collected from medical records. Children with reported regular (>3 times a month) inhalation of $\beta_2$-adrenergic agents and/or glucocorticoids but without reported chronic disease were designated as having asthma. Discharge diagnoses were categorized according to International Classification of Diseases, 10th Revision, codes...
(Fig 1). The study was approved by the regional ethical review board in Stockholm.

**Sampling and Microbiologic Analyses**

Nasopharyngeal aspirates from case patients and control subjects were obtained by using an identical aspiration technique and were diluted in 3 mL of saline. qPCR was performed at the Clinical Microbiological Laboratory at Karolinska University Hospital, which is accredited by the Swedish Board for Accreditation and Conformity Assessment (ISO 15189:2007). Sixteen different viruses were included in the panel: influenza A seasonal as well as H1N1pdm09, influenza B, human adenovirus (HAdV), human bocavirus (HBoV), human coronavirus serotypes 229E, NL63, OC43, and HKU1 (HCoV), human enterovirus (HEV), human metapneumovirus (hMPV), human rhinovirus (HRV), parainfluenza virus (PIV) 1 to 3, and RSV.24 Due to cross-reactivity between HRV and HEV, samples positive for both viruses were further analyzed by using an in-house qPCR for HEV.25

We used the term coinfection to represent detection of at least 2 viruses in the same individual (although detection by using qPCR does not necessarily equal ongoing infection, as emphasized).8

**Statistical Analyses**

Data were analyzed by using Stata version 12.1 (StataCorp, College Station, TX). Paired t tests, Wilcoxon signed-rank tests, and McNemar’s test were used on paired data as appropriate.26 Within-group analyses of categorical data were performed by using \( \chi^2 \) tests and Fisher’s exact test, and independent continuous data were analyzed by using the Mann-Whitney U test. Unadjusted and multivariate odds ratios (ORs) were calculated with conditional logistic regression to assess the association between viruses and ARI. Because the risk associated with 1 virus can be confounded by coinfection with other viruses, we adjusted for infection with other viruses by including virus-specific data as single variables in a multivariate regression model. Two multivariate models were constructed in which the first model included age and viruses, and the second model included age, viruses, and clinical and sociodemographic variables. Selection of variables for the second model was performed in the following way. First, all variables that were associated with ARI in univariate analyses \((P < 2)\) were included in the model. Second, variables with a \( P \) value \( \geq 2 \) in the multivariate model were removed from the model. Finally, we removed variables that caused large drifts of ORs due to small sample bias.27 To estimate how much specific viruses attributed to ARI in the population, population-attributable proportion (PAP) for viruses that were significantly associated with ARI was calculated as follows: exposure among case patients \( \times \) (adjusted OR – 1)/adjusted OR, with 95% confidence intervals (CIs).28

**RESULTS**

**Characteristics of Study Subjects**

During the study period, 229 case patients with ARI were enrolled. Due to limited inclusion of control subjects during the holiday season, control
subjects were not found for 20 case patients in December and January. These case patients were excluded in all matched case-control analyses. Characteristics of study subjects are listed in Table 1. Case patients were significantly more likely to attend day care ($P = .03$) and less likely to be breastfed ($P = .01$) at the time of inclusion. Moreover, 10.0% of the case patients suffered from a chronic disease, predominantly asthma ($n = 16$ (7.7%)), compared with 1.9% in control subjects ($P < .001$), and case patients were to a larger extent receiving current treatment with antibiotics ($P = .006$) or had received antibiotic treatment within the last year ($P < .001$). Finally, parents with a university degree were more common among control subjects ($P = .04$). The 20 case patients who were excluded from the matched analyses due to lack of control subjects were significantly older and to a larger extent positive for RSV and HRV compared with the included case patients ($P = .04$, $P = .03$, and $P = .02$, respectively) (Supplemental Table 4).

In total, 24 case patients (10.5%) were admitted to an inpatient ward, and 48 patients (21.0%) were treated with antibiotics (Supplemental Table 5).

**Viruses Associated With ARI**

HRV was detected most frequently from September through November and was found at substantially lower levels in December and January (Fig 2). This finding was true for both case patients and control subjects. hMPV, HBoV, and RSV also followed an epidemic pattern, increasing in December and January; all RSV episodes in case patients were detected in late December through January. No influenza viruses or HCoV serotype 229E was detected during the study period.

One or more respiratory virus was detected in 151 (72.3%) of the case patients and 74 (35.4%) of the control subjects (Table 2). PIV (compiled), PIV1, RSV, and hMPV had the highest ORs for ARI, followed by HBoV and HRV. PIV was detected in 7.7% of the case patients compared with 0.5% of the control subjects, with PIV1 detected in 4.3% of case patients. PIV2 and PIV3 were only detected among case patients (2 and 5 case patients, respectively). RSV was detected in 5.3% of case patients and 0.5% of control subjects, and hMPV was detected in 4.8% of case patients and 1.0% of control subjects. HBoV was detected in 15.8% of case patients but was also detected relatively often among control subjects (4.3%). HRV, the most prevalent virus in the study population, was detected in 47.9% of case patients and 21.5% of control subjects. Nevertheless, HCoV serotype OC43 was only found in case patients ($n = 4$). The ORs were fairly stable for the 2 adjusted models were compared. Serving as an estimate of the fraction of children that would have been prevented from having respiratory disease if the specific virus had not been present, PAP was calculated for the most frequently detected viruses (based on ORs from model 2). HRV, HBoV, and PIV (compiled) accounted for the largest PAP: 0.39 (95% CI: 0.01 to 0.62), 0.12 (95% CI: −0.06 to 0.28), and 0.08 (95% CI: −0.13 to 0.24), respectively.

**Viral Association With Clinical Presentation and Diagnosis**

In an attempt to clinically distinguish the different viral infections, clinical parameters, symptoms, and discharge diagnoses were compared between case patients positive for a specific virus versus case patients negative for that specific virus. hMPV infection was associated with fever ($P = .003$), increased respiratory rate ($P = .035$), tachycardia ($P = .01$), and decreased $\text{O}_2$ saturation ($P = .05$) (Table 3). HAdV was associated with decreased $\text{O}_2$ saturation ($P = .05$); HBoV was associated with increased respiratory rate ($P = .003$), tachycardia ($P = .01$), and reported coughing ($P = .017$); HRV was associated with coryza ($P = .04$) and absence of fever ($P = .008$); and RSV was associated with increased respiratory rate ($P = .04$) and wheezing ($P = .03$).

Case patients with croup, bronchitis, and asthma were most likely to test positive for $\geq 1$ virus (all, 88%). Case patients diagnosed as having pneumonia, acute upper respiratory tract infection (URTI),
and otitis tested positive in 58%, 64%, and 74%, respectively. Viral findings in relation to discharge diagnosis are shown in Fig 1. HCoV was negatively associated with a diagnosis of acute URTI (P = .005). Furthermore, patients diagnosed with group were more likely to test positive for PIV (P < .001), and patients with bronchitis were more likely to be infected with HBoV (P = .04).

To assess the independent effect of specific viral infections, viruses that were significantly associated with the aforementioned clinical findings were stratified into single infections and coinfections. No significant differences were found between patients with single infections compared with coinfected patients (data not shown). However, there was a tendency that increased respiratory rate was more common in HBoV coinfection compared with HBoV single infection (P = .08), and fever was reported more commonly in HRV coinfection compared with HRV single infection (P = .08).

Clinical Impact of Coinfections

In 42 (20.1%) case patients, >1 virus was detected. Of these, 32 (15.3%) were positive for 2 viruses, 9 case patients (4.3%) were positive for 3 viruses, and 1 case patient (0.5%) was positive for 4 concurrent viruses (Table 2). Coinfections of viruses were more common in case patients compared with control subjects (20.1% and 5.3%, respectively) and were associated with a higher risk of ARI (OR: 12.3 [95% CI: 5.0 to 30.4]) compared with single infections (OR: 4.3 [95% CI: 2.6 to 7.1]). RSV, HADV, and HBoV were the viruses most frequently detected in coinfection with other viruses among the case patients (in 80%, 74%, and 69%, respectively), and the most common virus pairs were HBoV/HRV, HADV/HRV, and HBoV/RSV (n = 13, n = 11, and n = 9) (Supplemental Table 6). Case patients with coinfections had more severe disease compared with case patients with single infections, with the following being more prevalent: increased respiratory rate (P = .009), tachycardia (P = .05), decreased O2 saturation (P = .04), reported fever (P = .05), discharge diagnosis of pneumonia (P = .006), and bronchitis (P = .02), as well as decreased probability of a diagnosis of acute URTI (P = .01).

**DISCUSSION**

A better understanding of the etiologic role of viruses in respiratory diseases is needed to develop new targeted therapies and reduce overconsumption of antibiotics. In this matched case-control study, we assessed how specific respiratory viruses can be attributed to ARI by investigating viral qPCR data in children with ARI and in matched asymptomatic control subjects. The strength of our study was the unique population-based asymptomatic control subjects who were sampled consecutively from different areas of Stockholm, thus serving as a good estimate of the background prevalence of the different viruses in the source population. Proper control selection is of highest importance for garnering valid information regarding the clinical interpretation of respiratory virus detection in children. Moreover, the study design allowed adjustments for important confounders such as age, calendar time, and viral coinfections.

We report that 1 or more respiratory virus was detected in 72.3% of the case
TABLE 3 Clinical Parameters and Symptoms Associated With Viral Infections in Case Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All (n = 229)</th>
<th>HAdV (n = 19)</th>
<th>HBoV (n = 39)</th>
<th>HCoV (n = 13)</th>
<th>hMPV (n = 13)</th>
<th>PIV (n = 17)</th>
<th>HRV (n = 104)</th>
<th>RSV (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms on examination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased respiratory rate (breathe per min)</td>
<td>73 (33)</td>
<td>7 (37)</td>
<td>20 (56)</td>
<td>6 (48)</td>
<td>8 (62)</td>
<td>7 (41)</td>
<td>28 (29)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>97 (46)</td>
<td>9 (50)</td>
<td>25 (66)</td>
<td>3 (23)</td>
<td>10 (83)</td>
<td>8 (53)</td>
<td>39 (42)</td>
<td>8 (53)</td>
</tr>
<tr>
<td>O₂ saturation &lt;95%</td>
<td>26 (11)</td>
<td>5 (28)</td>
<td>7 (18)</td>
<td>1 (7)</td>
<td>4 (31)</td>
<td>1 (6)</td>
<td>1 (12)</td>
<td>4 (27)</td>
</tr>
<tr>
<td>Body temperature ≥38.0°C</td>
<td>67 (30)</td>
<td>9 (47)</td>
<td>16 (41)</td>
<td>4 (29)</td>
<td>9 (69)</td>
<td>5 (29)</td>
<td>21 (20)</td>
<td>7 (47)</td>
</tr>
<tr>
<td>Chest wall retractions</td>
<td>38 (17)</td>
<td>2 (11)</td>
<td>6 (15)</td>
<td>3 (21)</td>
<td>3 (23)</td>
<td>3 (19)</td>
<td>21 (21)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Nasal flare</td>
<td>4 (2)</td>
<td>—</td>
<td>2 (5)</td>
<td>—</td>
<td>1 (8)</td>
<td>—</td>
<td>2 (2)</td>
<td>—</td>
</tr>
<tr>
<td>Grunting</td>
<td>3 (1)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2 (2)</td>
<td>—</td>
</tr>
<tr>
<td>Wheezing</td>
<td>30 (13)</td>
<td>1 (6)</td>
<td>9 (23)</td>
<td>3 (23)</td>
<td>2 (15)</td>
<td>1 (6)</td>
<td>14 (14)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Affected general status</td>
<td>30 (13)</td>
<td>5 (26)</td>
<td>4 (11)</td>
<td>2 (14)</td>
<td>4 (31)</td>
<td>1 (6)</td>
<td>12 (12)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Admitted to inpatient ward</td>
<td>24 (10)</td>
<td>2 (11)</td>
<td>6 (15)</td>
<td>1 (7)</td>
<td>2 (15)</td>
<td>1 (6)</td>
<td>12 (12)</td>
<td>4 (27)</td>
</tr>
<tr>
<td>Reported symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coryza</td>
<td>194 (85)</td>
<td>18 (95)</td>
<td>32 (82)</td>
<td>11 (79)</td>
<td>7 (54)</td>
<td>12 (71)</td>
<td>93 (81)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>63 (28)</td>
<td>7 (37)</td>
<td>10 (26)</td>
<td>4 (29)</td>
<td>3 (23)</td>
<td>4 (24)</td>
<td>24 (24)</td>
<td>4 (27)</td>
</tr>
<tr>
<td>Earache</td>
<td>31 (14)</td>
<td>3 (16)</td>
<td>6 (15)</td>
<td>3 (21)</td>
<td>3 (23)</td>
<td>3 (16)</td>
<td>14 (14)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Coughing</td>
<td>204 (90)</td>
<td>16 (84)</td>
<td>39 (100)</td>
<td>14 (100)</td>
<td>13 (100)</td>
<td>17 (100)</td>
<td>94 (92)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Fever</td>
<td>148 (65)</td>
<td>16 (84)</td>
<td>30 (77)</td>
<td>9 (64)</td>
<td>13 (100)</td>
<td>13 (77)</td>
<td>58 (55)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>126 (56)</td>
<td>11 (53)</td>
<td>23 (59)</td>
<td>10 (71)</td>
<td>6 (46)</td>
<td>11 (63)</td>
<td>60 (59)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Trouble feeding/drinking</td>
<td>83 (37)</td>
<td>10 (53)</td>
<td>18 (46)</td>
<td>3 (21)</td>
<td>3 (23)</td>
<td>4 (24)</td>
<td>32 (21)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>122 (53)</td>
<td>11 (58)</td>
<td>17 (44)</td>
<td>10 (71)</td>
<td>5 (33)</td>
<td>9 (53)</td>
<td>50 (48)</td>
<td>7 (47)</td>
</tr>
</tbody>
</table>

* P < .05 **P < .01 ***P < .001.

1. >50 breaths per minute for children aged <1 year, >60 breaths per minute for children aged 1 to 5 years.
2. Significant differences between case patients positive and negative for the specific virus.
3. >160 beats per minute for children aged <1 year, >120 beats per minute for children aged 1 to 5 years.
4. Presence of wheezing or rhonchi on pulmonary auscultation.
5. Symptoms reported by parents.

patients with ARI and 35.4% of the control subjects. These findings are in line with previous studies that have reported viral findings in 54% to 72% of children with ARI and 19% to 40% in asymptomatic children, emphasizing the need for adequate control subjects when assessing the etiologic fraction of different respiratory viruses. PIV, hMPV, and RSV were associated with high relative risks for ARI and were only rarely detected in control subjects, which is concordant with previous studies. These viruses all seem to be rapidly cleared from the respiratory tract after an infection, making qPCR a suitable diagnostic method. Interestingly, hMPV was associated with severe disease presentations such as fever, decreased O₂ saturation, increased respiratory rate, and tachycardia. Recent reports support that hMPV is a significant respiratory pathogen capable of causing severe disease in children, yet the clinical pattern of disease is not fully understood. In view of our findings that RSV, PIV, and hMPV were strongly associated with ARI and reports of nosocomial transmission of these viruses, further studies of control interventions such as cohort nursing are warranted for these infections.

HBoV is reportedly commonly detected in coinnfection with other viruses, and its pathogenicity in humans has been debated. In our study, HBoV was associated with ARI even after adjustment for coinfection with other viruses, and HBoV was associated with tachycardia, increased respiratory rate, and coughing (which suggest lower respiratory tract infection). However, both HBoV and HRV were detected at such a high frequency in control subjects that it might be hard to interpret the clinical significance of a positive qPCR finding. Our data indicate that 39% (95% CI: 1 to 62) of ARI in this population could be attributed to HRV, however.

HEV and HCoV were detected at equal levels in both case patients and control subjects. However, HCoV serotype OC43 was only detected in case patients, but due to limited sample size, we could perform only grouped analyses of these viruses; it is likely that different HEV serotypes have different disease-causing potential. Nevertheless, our results indicate that the current qPCR method needs to be more specific to have a clinical value for differential diagnostic purposes.

The clinical importance of viral coinnfections is not fully understood. In our data, coinnfections were associated with increased risk of ARI compared with single infections, and they were also associated with more severe disease. However, we did not have sufficient power to fully address how different respiratory viruses interact in the development of ARI, which is of great importance when assessing the potential impact of targeted interventions.

We performed sampling of control subjects from multiple child welfare centers at the time of routine vaccination to obtain a representative
sample of the background prevalence of respiratory viruses in the child population. However, the frequency of parents having a university degree was higher among control subjects compared with the general population of 20- to 40-year-olds in Stockholm (68.1% vs 49.7%). Although the populations were not perfectly comparable, it might indicate that our control selection failed to include all socio-economic groups. Moreover, study subjects were not followed up with consecutive sampling. Hence, we could not assess if viral findings in control subjects represent early detection of an infection, asymptomatic carriage, low-virulent infection, or prolonged shedding. In addition, samples were not systematically collected on all study subjects to assess bacterial infections, and some case patients are likely to have suffered from bacterial or mixed infection rather than solely from a viral infection. This possibility is indeed a limitation to the current study that impairs the translation of the findings into decision-making policies regarding antibiotic treatment. However, the diagnostics of bacterial infections in children with respiratory infections are difficult because blood culture results are rarely positive, sputum samples or bronchoalveolar lavage are difficult to obtain, and the clinical significance of bacterial diagnostics from the nasopharynx in children with ARI is limited due to high rates of colonization of common bacterial pathogens. Finally, the qPCR method used in our study was not appropriate to adequately assess viral load, which has been found to be associated with severity of disease.

CONCLUSIONS

Our study indicates that a qPCR finding of RSV, hMPV, or PIV is likely to be causative of disease in children with ARI. In contrast, detection of several other viruses such as HBoV, HRV, HAdV, HCoV, and HEV must be interpreted with caution due to high detection rates among healthy children. Future studies should focus on how to improve differential diagnostics with refined molecular techniques of the latter viruses to further characterize their pathogenicity in humans.

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