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## Concise Communication

# Respiratory virus coinfections with severe acute respiratory coronavirus virus 2 (SARS-CoV-2) continue to be rare one year into the coronavirus disease 2019 (COVID-19) pandemic in Alberta, Canada (June 2020–May 2021)

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### Abstract

To assess the burden of respiratory virus coinfections with severe acute respiratory coronavirus virus 2 (SARS-CoV-2), this study reviewed 4,818 specimens positive for SARS-CoV-2 and tested using respiratory virus multiplex testing. Coinfections with SARS-CoV-2 were uncommon (2.8%), with enterovirus or rhinovirus as the most prevalent target (88.1%). Respiratory virus coinfection with SARS-CoV-2 remains low 1 year into the coronavirus disease 2019 (COVID-19) pandemic.

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As the coronavirus disease 2019 (COVID-19) pandemic has progressed, multiple reports have highlighted the marked decrease in the incidence of other cocirculating respiratory viruses except rhinovirus.[1] The most impressive finding is the near absence of cocirculating seasonal influenza.[2,3] The principal hypothesis for the observed declines are the public health and social measures implemented to help control the spread of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

During the first 3 months of the pandemic in Alberta, Canada (March–May 2020), when all specimens submitted for SARS-CoV-2 testing also underwent respiratory viral multiplex testing, only 3.4% of those positive for SARS-CoV-2 were found to have a coinfecting respiratory virus.[4] The most prevalent of these respiratory viruses was either enterovirus or rhinovirus (ERV); the viral panel utilized could not distinguish them.

Despite the reported low prevalence of concomitant respiratory virus coinfections with SARS-CoV-2, infection control and public health concerns remain that undetected seasonal respiratory viruses could lead to hospital or long-term-care outbreaks. In this study, we assessed changes in frequency of respiratory virus coinfections with SARS-CoV-2 in adult and pediatric patients to determine whether routine on-demand multiplex respiratory virus testing in SARS-CoV-2 positive patients is beneficial later in the coronavirus disease 2019 (COVID-19) pandemic.

## Methods

Retrospectively, respiratory virus testing data were extracted from a centralized provincial laboratory information system at the Alberta Public Health Laboratory for samples subjected to both SARS-CoV-2 and a multiplex respiratory virus panel testing on the same sample between June 1, 2020, and May 31, 2021, in

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**Table 1.** Characteristics of COVID-19 Patients Tested for Additional Respiratory Viruses

| Variable | Adults | Pediatric[a] | Total | *P* Value[b] |
|---|---|---|---|---|
| **Concomitant testing, no. (%)** | | | | |
| Total | 4,569 (94.8) | 249 (5.2) | 4,818 | <.01 |
| Sex, male | 2,415 (52.9) | 137 (55.0) | 2,552 (53.0) | .52 |
| Sex, female | 2,143 (46.9) | 110 (44.2) | 2,253 (46.8) | .41 |
| Sex, unknown | 11 (0.2) | 2 (0.8) | 13 (0.2) | .05 |
| **Age, y** | | | | |
| Mean | 57.4 | 9.1 | 54.9 | |
| Median | 57.0 | 11 | 56.0 | |
| Range | 18–107 | 0–17 | 0–107 | |
| **Patient setting, no. (%)** | | | | |
| Community | 2,266 (49.6) | 165 (66.3) | 2,431 (50.5) | <.01 |
| Emergency | 1,130 (24.7) | 67 (26.9) | 1,197 (24.8) | .43 |
| Inpatient, non-ICU | 859 (18.8) | 16 (6.4) | 875 (18.2) | <.01 |
| ICU | 154 (3.4) | 1 (0.4) | 155 (3.2) | <.01 |
| Nursing home | 160 (3.5) | 0 | 160 (3.3) | <.01 |
| **Coinfections detected, no. (%)** | | | | |
| Total | 109 (2.4) | 25 (10.0) | 134 (2.8) | <.01 |
| Influenza A | 0 | 0 | 0 | . . . |
| Influenza B | 0 | 0 | 0 | . . . |
| RSV | 3 (2.9) | 1 (4.0) | 4 (3.0) | .77 |
| hCoV NL63 | 2 (1.8) | 0 | 2 (1.5) | .50 |
| hCoV HKU1 | 1 (0.9) | 0 | 1 (0.7) | .63 |
| hCoV OC43 | 0 | 0 | 0 | . . . |
| hCoV 229E | 0 | 0 | 0 | . . . |
| HMPV | 2 (1.8) | 0 | 2 (1.5) | .50 |
| PIV 1-4 | 1 (0.9) | 1 (4.0) | 2 (1.5) | .25 |
| ERV | 98 (89.9) | 20 (80.0) | 118 (88.1) | .17 |
| Adenovirus | 2 (1.8) | 3 (12.0) | 5 (3.7) | .01 |
| **Patient setting of coinfections, no. (%)** | | | | |
| Community | 42 (38.5) | 13 (52.0) | 55 (41.0) | .21 |
| Emergency | 33 (30.3) | 7 (28.0) | 40 (29.9) | .81 |
| Inpatient, non-ICU | 26 (23.9) | 4 (16.0) | 30 (22.4) | .40 |
| ICU | 6 (5.5) | 1 (4.0) | 7 (5.2) | .76 |
| Nursing home | 2 (1.8) | 0 (0) | 2 (1.5) | .50 |

Note. ERV, enterovirus/rhinovirus; hCoV, human coronavirus; HMPV, human metapneumovirus; ICU, intensive care unit; PIV, parainfluenza virus; RSV, respiratory syncytial virus.
[a]Pediatric patients are defined as ≤17 years of age; adults are defined as ≥18 years of age.
[b]Comparison of adult and pediatric groups.

Calgary and Edmonton, Alberta, Canada. Combined, these cities constitute ~70% of the 4.4 million provincial population.

Details regarding sample types and SARS-CoV-2 testing in the province have been published previously.[5] Multiplex testing was conducted using the NxTAG Respiratory Pathogen Panel (RPP, Luminex, Austin, TX). This multiplex assay reports out results for influenza viruses A/B, respiratory syncytial virus (RSV), parainfluenza viruses (PIV 1–4), human metapneumovirus (HMPV), adenovirus, human coronaviruses (hCoVs; NL63, HKU1, OC43, and 229E), and ERV (a combined target). During the study period, multiplex respiratory virus testing was conducted only upon request of the ordering clinicians, public health, or hospital infection control, and not on all SARS-CoV-2 test requests. Further information is detailed in the Supplementary Methods (online).

This study was approved by the Human Research Ethics Board (HREB) at the University of Alberta (study identifier Pro00105658).

## Results

During the 12-month study, 125,571 individuals were diagnosed with COVID-19 from the 2 geographic regions examined: 101,793 (81.1%) were adults and 23,778 (18.9%) were children. Among them, 4,818 (3.8%) also had concomitant RPP testing performed on the same sample: 4,569 (94.8%) were adults and 2,552 (53.0%) were male (Table 1). The median age was 56 years (range, 0–107). Half of those with concomitant respiratory virus testing were outpatients and ~20% required hospital admission (3% were admitted to critical care). Significantly more adults required hospital (and critical care) admission than pediatric patients ($P < .01$).

Respiratory viral coinfections occurred in 134 (2.8%; 95% confidence interval [CI], 2.4%–3.3%) of 4,818 COVID-19 cases, with significantly more in the pediatric group compared to adults: 10.0% (95% CI, 6.9%–14.4%) versus 2.4% (95% CI 2.0-2.9%), respectively ($P < .01$) (Table 1). Of the 134, the most common viral target identified among other tested respiratory viruses, 118 (88.1%) were ERV. RSV, PIV, ERV, and adenovirus were detected among both age categories. ERV was observed more significantly in pediatric patients: 12.0% versus 1.8% ($P = .01$) (Table 1). We did not detect a statistically significant difference for coinfections in different patient settings ($P = .08$) (Supplementary Table S1).

Based on respiratory virus surveillance data from Edmonton and Calgary (Fig. 1), a decline in circulating viruses began at epidemiologic week 11 (2020), coinciding with introduction of pandemic restrictions in Alberta. Prior to this, RSV, PIV, HMPV, hCoVs, and influenza A displayed a consistent seasonal variation. After the start of the pandemic, while ERV transmission reached a nadir between epidemiologic weeks 21 and 25 (2020), it was the only RPP target detected in a seasonal pattern (Fig. 1). Near absence of influenza viruses was noted by epidemiologic week 15 (2020).

Review of historic data from between 2016 and 2019 demonstrated that ERV has been detected as a coinfection with every other respiratory virus tested at our center (Supplementary Table S2). ERV coinfection generally occurred at a lower rate with influenza viruses (0.1%–4.4%) than with other respiratory viruses (3.3%–30.8%).

## Discussion

In this retrospective study, we have demonstrated that SARS-CoV-2 coinfection with other respiratory viruses remains uncommon >1 year into the COVID-19 pandemic. Coinfection was observed ~3% of the time, more commonly in children, with ERV being the most prevalent assay target identified.

Our findings are consistent with reports from Australia, Hong Kong, Japan, South Korea, and the United States, where reductions in influenza of 44%–65% and coinfection rates <5% have been recorded.[1,2,6] Notably, although earlier studies did show higher coinfection rates (10%–22%), these were from earlier in the pandemic (January–May 2020), during the tail end of the 2019–2020 influenza and respiratory virus season, and less effect of early

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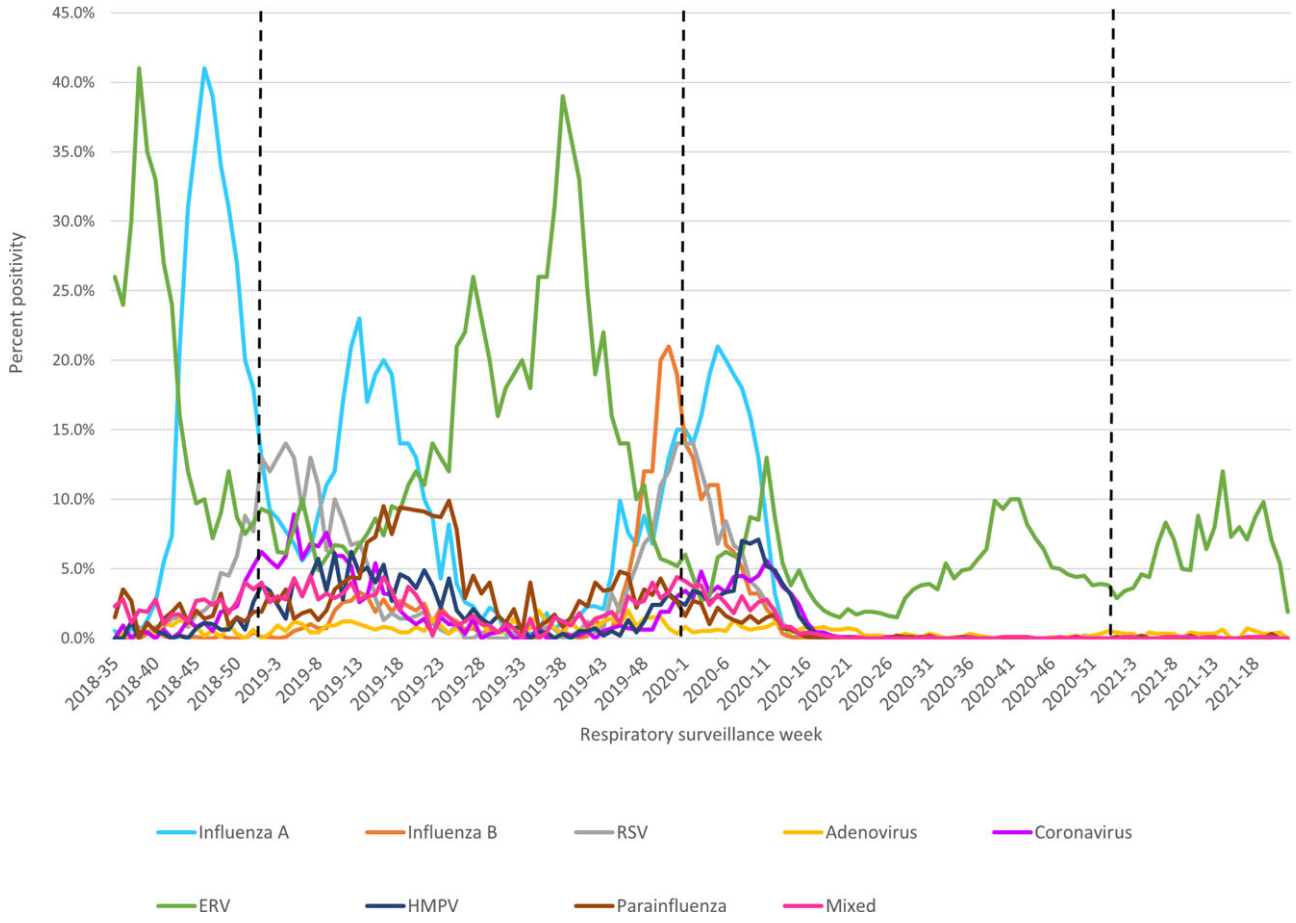


**Fig. 1.** Non–SARS-CoV-2 respiratory virus positivity over the 2018–2019, 2019–020, and 2020–2021 respiratory seasons (through epidemiologic week 22), from Calgary and Edmonton Zones, Alberta, Canada. The vertical axis represents the percent positivity for samples submitted for non-SARS-CoV-2 respiratory virus testing. Vertical lines indicate the start of each respiratory virus surveillance season (ie, 2019 week 1 (2019-1); 2020 week 1 (2020-1); and 2021 week 1 (2021-1).

public health restrictions.[1] This study now extends our knowledge to June 2021, demonstrating continued low prevalence of most respiratory virus and SARS-CoV-2 coinfection across adult and pediatric groups.

As with other regions, ERV was the most common additional respiratory virus detected among SARS-CoV-2–positive samples,[2] which is consistent with our observations earlier in the pandemic.[4] As ERV is a common single target on multiplex respiratory assays, many studies have not been able to differentiate them. However, published data from Australia, Austria, Canada, and the United Kingdom have demonstrated rhinovirus as the predominant seasonal circulating respiratory virus since the SARS-CoV-2 pandemic started[1,7,8]; therefore, we speculate that rhinovirus is likely predominant here. Rhinovirus starkly contrasts with other normally circulating respiratory viruses (including enteroviruses), in which circulation has significantly dropped across the globe during the pandemic.[1] The reasons for rhinovirus persistence with SARS-CoV-2 are not entirely clear, though speculation has included physical distancing measures,[2] similar modes of transmission (droplets and self-inoculation of the eyes and nose),[9] and indirect negative virus–virus interaction through cellular interferon signaling in the infected host (as has been reported between rhinovirus and influenza).[10] The latter may also explain the historically lower proportion of coinfections observed between ERV and influenza viruses versus other respiratory viruses in Table S2.

This study had several limitations. It was retrospective nature and was biased toward individuals seeking health care, which may have led to overrepresentation of symptomatic and more ill patients. Furthermore, additional respiratory virus testing was performed on a small proportion of COVID-19 patients (3.8% of all SARS-CoV-2–positive specimens). This factor reflects province-wide changes in further respiratory virus testing on SARS-CoV-2–positive specimens, due to the limited use of broader testing early in the pandemic. Finally, we focused on coinfection at the time of COVID-19 diagnosis and could therefore miss subsequent respiratory virus superinfection, which has been reported to occur with a low frequency (4%).[1]

In general, active transmission of respiratory viruses with SARS-CoV-2 that were previously common appears to be infrequent, except for ERV. Further study is important to identify clinical scenarios where multiplex viral testing may be most beneficial, given ongoing pressure on clinical laboratories during the pandemic. Maintenance of public health respiratory virus surveillance is critical to understanding changing epidemiology in the face of gradual lifting of public health and travel restrictions, as well as rising COVID-19 and influenza vaccination rates.

**Supplementary material.** For supplementary material accompanying this paper visit https://doi.org/10.1017/ice.2021.495

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