Circulation of Respiratory Viruses in Hospitalized Adults before and during the COVID-19 Pandemic in Brescia, Italy: A Retrospective Study

Maria Antonia De Francesco 1,2,*, Caterina Pollara 2, Franco Gargiulo 2, Mauro Giacomelli 2 and Arnaldo Caruso 1,2

Abstract: Different preventive public health measures were adopted globally to limit the spread of SARS-CoV-2, such as hand hygiene and the use of masks, travel restrictions, social distance actions such as the closure of schools and workplaces, case and contact tracing, quarantine and lockdown. These measures, in particular physical distancing and the use of masks, might have contributed to containing the spread of other respiratory viruses that occurs principally by contact and droplet routes. The aim of this study was to evaluate the prevalence of different respiratory viruses (influenza viruses A and B, respiratory syncytial virus, parainfluenza viruses 1, 2, 3 and 4, rhinovirus, adenovirus, metapneumovirus and human coronaviruses) after one year of the pandemic. Furthermore, another aim was to evaluate the possible impact of these non-pharmaceutical measures on the circulation of seasonal respiratory viruses. This single center study was conducted between January 2017–February 2020 (pre-pandemic period) and March 2020–May 2021 (pandemic period). All adults >18 years with respiratory symptoms and tested for respiratory pathogens were included in the study. Nucleic acid detection of all respiratory viruses was performed by multiplex real time PCR. Our results show that the test positivity for influenza A and B, metapneumovirus, parainfluenza virus, respiratory syncytial virus and human coronaviruses decreased with statistical significance during the pandemic. Contrary to this, for adenovirus the decrease was not statistically significant. Conversely, a statistically significant increase was detected for rhinovirus. Coinfections between different respiratory viruses were observed during the pre-pandemic period, while the only coinfection detected during pandemic was between SARS-CoV-2 and rhinovirus. To understand how the preventive strategies against SARS-CoV-2 might alter the transmission dynamics and epidemic patterns of respiratory viruses is fundamental to guide future preventive recommendations.

Keywords: circulation; seasonality; prevention; pandemic; respiratory viruses

1. Introduction

Different respiratory viruses, including influenza viruses (FLU), rhinovirus (RV), respiratory syncytial virus (RSV), human metapneumovirus (hMPV), human coronaviruses (CoV), adenoviruses (AdV), and parainfluenza viruses (PIV) contribute to significant morbidity [1] and mortality [2] in adult persons, especially in older adults and in those with underlying comorbidities [3–8]. Furthermore, they are responsible for massive economic costs annually worldwide [9].

Although FLU viruses, RSV and common coronaviruses had a seasonal pattern with a peak in the winter months, and RV circulates year-round with a peak incidence in spring and fall, all the other respiratory viruses circulate throughout the entire year. No preventive
measures, except for the influenza vaccination, are undertaken to limit the occurrence of these viruses that are accepted as inevitable.

The appearance of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China in December 2019, and its sudden pandemic spread forced the governments to adopt different non-pharmacological public health preventive measures, such as wearing masks, social distancing, and hand hygiene, to mitigate the diffusion of SARS-CoV-2.

Furthermore, to contain COVID-19 infections, the Italian government used a system based on risk color [10,11], which was updated weekly by using a combination of different criteria among which were hospitalization numbers and the new positive cases numbers.

Following this criterion, the 20 Italian regions may exhibit a very low risk (blank), a low risk (yellow), medium risk (orange) and high risk (red). On the basis of the color risk stratification, different commercial activities might be closed and some activities might be prohibited.

These preventive strategies, in particular physical distancing and the use of masks, may have contributed to reducing the circulation of other respiratory viruses besides SARS-CoV-2 [12,13]. Different studies show that social restrictions had an impact on the spread of both seasonal influenza [14–18] and other respiratory viruses [19–22].

Only limited data are available in Italy about the prevalence of respiratory viruses during SARS-CoV-2 pandemic [23,24]. Therefore, the aims of this study were:

(a) To evaluate the prevalence of different respiratory viruses (FLU A and FLU B, RV, RSV, hMPV, AdV, PIV and human CoVs) during the COVID-19 pandemic period, in samples collected from hospitalized adults, compared to that observed in the three years before the pandemic period;

(b) To correlate the possible impact of non-pharmaceutical measures, recommended in response to the COVID-19 pandemic, on the circulation of seasonal respiratory viruses.

2. Materials and Methods

2.1. Study Design and Patients

This retrospective study was conducted at the Laboratory of Microbiology and Virology, Spedali Civili Hospital, Brescia, Italy. This is a 1650-bed tertiary hospital and is one of the biggest medical centers in Lombardy, in northern Italy. Inclusion criteria were: hospitalized patients aged ≥18 years, and the presence of one or more respiratory symptoms such as shortness of breath, sore throat, cough and fever ≥37.5 °C. We collected data on respiratory virus and/or SARS-CoV-2 testing performed from January 2017 to May 2021 defining two periods as pre-pandemic (January 2017–February 2020) and during pandemic (March 2020–May 2021). The first positive SARS-CoV-2 test and first COVID-19 case admitted to Spedali Civili Hospital occurred on 24 February 2020. Samples collected included nasopharyngeal swabs, bronchoalveolar lavage (BAL) and bronchial aspirate (BAS). Swabs samples were stored at 4 °C until processing.

2.2. Detection of Respiratory Viruses and SARS-CoV-2

Total nucleic acid extraction for SARS-CoV-2 was performed by using Seegene Nimbus (Seegene Inc., distributed by Arrow Diagnostics, Genoa, Italy), while total nucleic acid extraction for respiratory viruses was performed by using NucliSENSE® EasyMAG® (BioMérieux Italia, Florence, Italy). Detection of SARS-CoV-2 was performed using a real time reverse polymerase chain reaction (Allplex TM 2019-nCoV assay, Seegene Inc., distributed by Arrow Diagnostics, Genoa, Italy). This single tube assay identified firstly three SARS-CoV-2 gene targets: E, RdRP and N genes, updated then to identify further the S gene.

A multiplex real time PCR was performed to detect all the viruses under investigation in this study (FTD Respiratory pathogens 21, Fast Track Diagnostics, Siemens Healthcare, Milan, Italy).
Upon medical request for specific respiratory pathogens, laboratory diagnosis was performed with the following assays:

(a) Respiratory Viral ELITe MGB\textsuperscript{®} Panel (ELITech Italy, Turin, Italy) for influenza viruses (A and B) and RSV detection;

(b) FTD HAdV/HMPV/HBoV (Fast Track Diagnostics) for human metapneumovirus A and B and human adenovirus detection;

(c) FTD HPIV for PIV (serotypes 1, 2, 3 and 4) detection;

(d) FTD (Fast Track Diagnostics) for human endemic coronaviruses (HKU1, NL63, 229 and OC43) detection.

2.3. Statistical Analysis

Descriptive statistics were applied to describe patient characteristics. Comparisons between categorical variables were performed by using the Fisher’s exact test with Yates’ correction and the chi-square test as appropriate. Continuous data were analyzed by t-test. The significance level was set at 0.05.

3. Results

During the study period, 12,483 patients were tested for different respiratory viruses. Of these, 10,121 were analyzed from January 2017 to February 2020 and 2362 from March 2020 to the end of this study (May 2021). Patient characteristics were summarized in Table 1.

Table 1. Characteristics of patients tested for respiratory viruses other than SARS-CoV-2 during the study period (January 2017–May 2021).

|                         | January 2017–February 2020 (Pre-Pandemic) | March 2020–May 2021 (During Pandemic) | January 2017–February 2020 (Pre-Pandemic) | March 2020–May 2021 (During Pandemic) | p   |
|------------------------|-------------------------------------------|----------------------------------------|-------------------------------------------|----------------------------------------|-----|
| Samples tested (N\textsuperscript{a}) | 10,121                                    | 2362                                   |                                           |                                        |     |
| Positive (N\textsuperscript{a})          | 1475                                      | 63                                     |                                           |                                        |     |
| Frequency (%)            | 14.6                                      | 2.7                                    |                                           |                                        |     |

Total population tested

|                         |                                           |                                        |                                           |                                        |     |
|------------------------|-------------------------------------------|----------------------------------------|-------------------------------------------|----------------------------------------|-----|
| Demographic characteristics |                                           |                                        |                                           |                                        |     |
| Male, n (%)            | 5098 (50.3)                               | 1341 (55.5)                            | 878 (59.5)                               | 41 (65)                                | 0.4 |
| Mean Age               | 65.1                                      | 63.5                                   | 64.02                                    | 59.9                                   | 0.07|
| Age in years, n (%)    | 18–44                                     | 1355 (13.2)                            | 261 (11)                                 | 240 (16.2)                             | 0.02|
|                         | 45–64                                     | 3012 (29.7)                            | 940 (39.7)                               | 414 (28)                               | 0.01|
|                         | 65–79                                     | 3561 (35.1)                            | 838 (35.4)                               | 524 (35.5)                             | 0.79|
|                         | ≥80                                       | 2193 (21.6)                            | 323 (13.6)                               | 297 (20)                               | 0.001|

\textsuperscript{a} Bold character indicates statistical significance.

As the number of COVID-19 infections increased from March 2020 (Figure 1), the number of tests required from clinicians during the pandemic for the other respiratory viruses decreased by less than a quarter, compared to the pre-pandemic period (2362 vs. 10,121) (Table 1).

Moreover, the overall test positivity for them was lower during the pandemic than in the previous years (2.7% vs. 14.6%, \( p < 0.0001 \)) (Table 1). Demographic characteristics show that in the adult population tested during pandemic period, male gender was more prevalent (55.5% vs. 50.3%, \( p < 0.0001 \)) and the median age was lower (63.5 vs. 65.1, \( p < 0.0001 \)) compared to that tested during the pre-pandemic period. No statistical difference for gender was found between subjects positive for respiratory viruses analyzed during the two periods.
Figure 1. Monthly positive cases of respiratory pathogens in the pandemic period (March 2020–May 2021) in comparison with monthly positive cases in the pre-pandemic period (January 2017–February 2020). Reported positive cases of SARS-CoV-2 are displayed for comparison.
Group 45–64 years was more prevalent during the pandemic period compared to that in the pre-pandemic period (39.7% vs. 29.7%, \( p < 0.0001 \)), while the \( \geq 80 \) years group accounted for 21.6% of adult patients in pre-pandemic period, compared to that present during the pandemic (13.6%, \( p < 0.0001 \)) (Table 1). The same results were obtained when virus respiratory positive subjects were stratified for age (Table 1).

The rate of positivity for each respiratory virus analyzed during the study period is shown in Table 2. The test positivity for FluA, FluB, MPV, PIV, RSV and human CoVs decreased with statistical significance (0.2 vs. 7.6%, \( p < 0.0001 \); 0.06% vs. 3%, \( p < 0.0001 \); 0.28% vs. 1.1%, \( p = 0.04 \); 1.4% vs. 7.3%, \( p < 0.0001 \) and 0.14% vs. 5%, \( p < 0.0001 \), respectively). On the contrary, for AdV the decrease was not statistically significant. Conversely, an increase statistically significant of positivity percentage was detected for RV (3.8% vs. 5.7%, \( p = 0.02 \)).

Table 2. Comparison of positivity rates of respiratory viruses other than SARS-CoV-2 between January 2017–February 2020 (pre-pandemic period) and March 2020–May 2021 (during pandemic period).

| Virus                  | January 2017–February 2020 (Pre-Pandemic) | March 2020–May 2021 (During Pandemic) |
|------------------------|-------------------------------------------|---------------------------------------|
| Influenza A virus      | 523/6881 (7.6)                             | 3/1628 (0.18)                         | \(<0.0001 \) ^a |
| Influenza B virus      | 210/6881 (3)                               | 1/1628 (0.06)                         | \(<0.0001 \) |
| Respiratory syncytial virus | 238/3240 (7.3)                     | 10/734 (1.4)                          | \(<0.0001 \) |
| Metapneumovirus        | 38/3240 (1.1)                              | 2/734 (0.27)                          | 0.04 |
| Adenovirus             | 48/3240 (1.4)                              | 4/734 (0.6)                           | 0.08 |
| Parainfluenza viruses  | 131/3240 (4)                               | 1/734 (0.14)                          | \(<0.0001 \) |
| Rhinovirus             | 123/3240 (3.8)                             | 41/734 (5.6)                          | 0.02 |
| Coronavirus             | 164/3240 (5)                               | 1/734 (0.14)                          | \(<0.0001 \) |

^a Bold character indicates statistical significance.

During the seasons analyzed previous the pandemic, we diagnosed 523 influenza A cases and 210 influenza B cases, for an average of 244 combined cases per season. During the pandemic period, only three cases of influenza A and one case of influenza B were detected. The peak for influenza viruses was always reached in the period pre-pandemic in January and February (Figure 1) with a decline of cases in March. However, the decrease in positive tests observed already in late February and March 2020 was maintained in January and February 2021, without the seasonal pattern present in the pre-pandemic period.

Among specimens tested for PIV, hCoVs and MPV, the percentage with a positive result declined in March 2020 and remained suppressed until May 2021, without the seasonal increases that occurred during the pre-pandemic period (Table 2). During the pre-pandemic period, PIV reached a peak during fall (October–November) and spring (March–May) (Figure 1), while during the pandemic period only 1 case of PIV was detected.
The peak circulation of human coronaviruses occurred between January and February during the pre-pandemic period and ranged from 8.1% to 12.5% (Figure 1), disappearing completely during the pandemic period.

The circulation of RSV occurred from winter to spring, reaching a peak between January and February and a positivity rate of 7.3% during the pre-pandemic period, while in the pandemic period it was detected only in March 2020, with a total absence of positive cases in the next months.

Only two cases of human metapneumovirus were detected from March 2020 to May 2021, while during the previous years it circulated mostly from January to April.

From March 2020 to May 2021, adenovirus circulate to lower ranges (0.6%) than those observed during the pre-pandemic period (1.4%).

Contrary to this, the positivity rate of Rhinovirus during the pandemic period increased respect to that observed during the previous years.

In addition, some coinfections were also detected (Table 3). During the pre-pandemic period, RSV was the virus most found in coinfections (7/12, 58.3%). During the pandemic period, the only coinfection observed was between Rhinovirus and SARS-CoV-2 (6 cases).

Table 3. Patients with >1 positive respiratory virus detection during the study period (January 2017–May 2021).

| Virus detected                  | January 2017–February 2020 (Pre-Pandemic) | March 2020–May 2021 (During Pandemic) |
|---------------------------------|-------------------------------------------|---------------------------------------|
| RhV and RSV                     | 1                                         | 0                                     |
| PIV and RSV                     | 1                                         | 0                                     |
| Coronavirus and RSV             | 2                                         | 0                                     |
| AdV and RSV                     | 1                                         | 0                                     |
| Coronavirus and PIV             | 1                                         | 0                                     |
| FluA and RSV                    | 1                                         | 0                                     |
| FluA and Coronavirus            | 2                                         | 0                                     |
| FluA, FluB and Coronavirus      | 1                                         | 0                                     |
| FluB and RSV                    | 1                                         | 0                                     |
| FluA and PIV                    | 1                                         | 0                                     |
| SARS-CoV-2 and RhV              | 0                                         | 6                                     |

Abbreviations: RhV, Rhinovirus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus, FluA, influenza A virus; FluB, Influenza B virus; AdV, Adenovirus.

4. Discussion

The non-pharmaceutical interventions, such as social distancing, wearing face masks and increased hand hygiene, used to limit the spread of COVID-19 might also help to prevent other respiratory virus infections, which are transmitted in a similar way to SARS-CoV-2.

According to other studies [16–22,25,26], our results show that the circulation of respiratory viruses was disrupted during the pandemic, even if the magnitude of this effect was different between the viruses analyzed.

We found that the frequency of influenza and other respiratory viruses (human metapneumovirus; parainfluenza virus 1, 2, 3 and 4; and human coronaviruses) was significantly reduced during the COVID-19 pandemic.

We demonstrated seasonality and sequential seasonal epidemic patterns for these viruses in the previous years analyzed, but with the appearance of SARS-CoV-2, the epidemic patterns of respiratory viruses have undergone a profound change.

After March 2020, influenza virus circulated at very low levels with detection of few cases also in 2021 season. In according with these results, a study from the USA showed a great decrease in the positivity rate during the lockdown and it remained low during the inter-seasonal circulation [27].

The persistence of the effect of the preventive measures against SARS-CoV-2 on respiratory circulation of respiratory viruses is unrecognized. However, the low levels of
circulation of influenza viruses during the 2020–2021 seasons might influence the severity of the next influenza season, due to a decreased population immunity owing to the absence of a natural exposure to influenza viruses during these years.

In fact, a study based on mathematical modelling suggests the possibility of a hard rebound, marked by increased morbidity and mortality in the winter of 2021/22 [28], for countries that have experienced years without influenza.

Furthermore, interactions between the SARS-CoV-2 virus and endemic viruses may be very complex. Immunological relationships between viruses, both competitive and cooperative, may have extensive consequences for future infection dynamics [29].

Therefore, with the advent of autumn season, it might be advisable to recommend influenza vaccination to prevent a more widespread disease when influenza virus circulation will restart.

In addition to influenza viruses, parainfluenza viruses, metapneumovirus, human coronaviruses and adenovirus also showed a change in their epidemic patterns, with a marked reduction in their circulation.

Moreover, the positivity rate of respiratory syncytial decreased significantly during the pandemic period. This result was in agreement with other studies that show that positive RSV tests also decreased notably [30–33], and in disagreement with others that demonstrate a resurgence of RSV circulation [34,35].

Interestingly, a temporal association was observed between the introduction of preventive strategies against COVID-19 (mainly the use of facemasks) and the rate of positive cases for all the above respiratory viruses. All of them had a peak between January and February 2020, but the community mitigation measures were mandatory around mid-March 2020; following that date, we noticed a low circulation of influenza viruses, parainfluenza viruses, metapneumovirus, human coronaviruses, adenovirus and respiratory syncytial virus underlining the possible impact of these preventive strategies on their spread. Our study evidenced that while there was a decline in the positivity rates of other respiratory viruses, the diffusion of rhinovirus seems not to be affected, and it was frequently detected during the pandemic. We observed an increase in its circulation; a finding confirmed by other studies [36–38]. The different pattern might be due to their greater stability under environmental conditions (e.g., heat, desiccation, and pH values) than enveloped viruses. Furthermore, a study of Leung et al. [10] showed that facemasks are more effective in filtering out enveloped viruses such as influenza virus and coronavirus than non–enveloped viruses such as rhinovirus.

Rhinovirus is responsible for the common cold, but may cause pulmonary complications in some patients [39]. The signs and symptoms of this infection might be severe and resemble that of COVID-19 in patients with underlying disease [40]. To discriminate between the two viruses is, therefore, important.

Similar results were obtained by a recent study [41], conducted in Shanghai, China on a different study population. Liu et al. found that interventions adopted during the COVID-19 pandemic contributed to the significant reduction of other respiratory viral infections, including RSV, PIV, FluA, FluB, MPV and ADV, except for rhinovirus in a pediatric hospitalized population.

In the pre-pandemic period, we have detected some mixed viral infections where the respiratory syncytial virus was the virus more involved in these coinfections.

Then, during the pandemic, we found only coinfections between SARS-CoV-2 and rhinovirus probably because these are the more frequent circulating viruses. Previous reports have described co-infections between SARS-CoV-2 and common respiratory viruses including rhinovirus, influenza virus, metapneumovirus, parainfluenza virus and respiratory syncytial virus [42–44]. Even if it is not clear whether these coinfections are associated with severe disease, determining the coinfection rate and eventual clinical impact on the disease course is important.

This study has some limitations. It was performed at a single center and the reduced hospital accession due to concerns about COVID-19, particularly from persons with milder
symptoms might have influenced the number of laboratory confirmed cases for respiratory viruses.

5. Conclusions

This study underlines that face coverings, together with social distancing and hand hygiene against COVID-19, are crucial in containing airborne transmitted infections and, therefore, should be implemented during public health emergencies and pandemics or for the future management of respiratory infections. Our data show that these non-pharmaceutical interventions altered the typical seasonal circulation patterns of different respiratory viruses, and that some of them might resurge with the mitigation of these preventive measures, increasing the importance of testing for multiple respiratory pathogens.

Author Contributions: Conceptualization, M.A.D.F. and A.C.; methodology, C.P.; formal analysis, C.P., F.G., M.G.; data curation, C.P., F.G., M.G., M.A.D.F.; writing—original draft preparation, M.A.D.F.; writing—review and editing, A.C.; supervision, A.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study did not require ethical approval as it did not involve a prospective evaluation. The samples were leftovers from the routine investigation and were used anonymously.

Informed Consent Statement: Formal consent was not required due to the retrospective format of the study according to Italian law.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. James, S.L.; Abate, D.; Abate, K.H.; Abay, S.M.; Abbafati, C.; Abbasi, N.; Abbastabar, H.; Abd-Allah, F.; Abdelha, J.; Abdelalim, A.; et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018, 392, 1789–1858. [CrossRef]

2. Roth, G.A.; Abate, D.; Abate, K.H.; Abay, S.M.; Abbafati, C.; Abbasi, N.; Abbastabar, H.; Abd-Allah, F.; Abdelha, J.; Abdelalim, A.; et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: A systematic analysis for the Global Burden of disease Study 2017. Lancet 2018, 392, 1736–1788. [CrossRef]

3. Blackburn, R.; Zhao, H.; Pebody, R.; Hayward, A.; Warren-Gash, C. Laboratory-confirmed respiratory infections as predictors of hospital admission for myocardial infarction and stroke: Time series analysis of English data for 2004–2015. Clin. Infect. Dis. 2018, 67, 8–17. [CrossRef]

4. Mohan, A.; Chandra, S.; Agarwal, D.; Guleria, R.; Broor, S.; Gaur, B.; Pandey, R.M. Prevalence of viral infection detected by PCR and RT-PCR in patients with acute exacerbations of COPD: A systematic review. Respiratory 2010, 15, 536–542. [CrossRef] [PubMed]

5. Widmer, K.; Zhu, Y.; Williams, J.V.; Griffin, M.R.; Edwards, K.M.; Keipp, T.H. Rates of hospitalizations for respiratory syncytial virus, human metapneumovirus, and influenza virus in older adults. J. Infect. Dis. 2012, 206, 56–62. [CrossRef] [PubMed]

6. Van Asten, L.; van den Wijngaard, C.; van Pelt, W.; van de Kassteele, J.; Meijer, A.; van der Hoek, W.; Kretzschmar, M.; Koopmans, M. Mortality attributable to 9 common infections: Significant effect of influenza A, respiratory syncytial virus, influenza B, norovirus, and parainfluenza in elderly persons. J. Infect. Dis. 2012, 206, 628–639. [CrossRef]

7. Lim, Y.K.; Kweon, O.J.; Kim, H.R.; Kim, T.H.; Lee, M.K. Clinical features epidemiology, and climatic impact of genotype-specific human metapneumovirus infections: Long-term surveillance of hospitalized patients in South Korea. Clin. Infect. Dis. 2020, 70, 2683–2694. [CrossRef]

8. Falsey, A.R.; Hennessey, P.A.; Formica, M.A.; Cox, C.; Walsh, E.E. Respiratory syncytial virus infection on elderly and high-risk adults. N. Engl. J. Med. 2005, 352, 1749–1759. [CrossRef] [PubMed]

9. Fendrick, A.; Monto, A.S.; Nightengale, B.; Sarnes, M. The economic burden of non-influenza-related viral respiratory tract infection in the United States. Arch. Intern. Med. 2003, 163, 487–494. [CrossRef] [PubMed]

10. Covid-19, Situation in Italy. Available online: salute.gov.it (accessed on 7 April 2021).

11. Prevention and Response to COVID-19: Evolution of Strategy and Planning in the Transition Phase for the Autumn-Winter Season. Available online: https://www.iss.it/documents/5430402/1/COVID+19+strategyISSMoH+%281%29.pdf/0d91693c7ce-880b-e554-643c049e0f3?b=1604675609974 (accessed on 11 December 2020).

12. Leung, N.H.L.; Chu, D.K.W.; Shiu, E.Y.C.; Chan, K.H.; McDevitt, J.J.; Hau, B.J.P.; Yen, H.L.; Li, Y.; Ip, D.K.M.; Peiris, J.S.M.; et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. Nat. Med. 2020, 26, 676–680. [CrossRef] [PubMed]
13. Wu, D.; Lu, J.; Liu, Y.; Zhang, Z.; Luo, L. Positive effects of COVID-19 control measures on influenza prevention. *Int. J. Infect. Dis.* 2020, 95, 345–346. [CrossRef]

14. Sakamoto, H.; Ishikane, M.; Ueda, P. Seasonal influenza activity during the SARS-CoV-2 outbreak in Japan. *JAMA* 2020, 323, 1960–2212. [CrossRef] [PubMed]

15. Cowling, B.J.; Ali, S.T.; Ng, T.W.Y.; Tsang, T.K.; Li, J.C.M.; Fong, M.W.; Liao, Q.; Kwan, M.Y.; Lee, S.L.; Wu, J.T.; et al. Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: An observational study. *Lancet Public Health* 2020, 5, e279–e288. [CrossRef]

16. Olsen, S.J.; Winn, A.K.; Budd, A.P.; Prill, M.M.; Steel, J.; Midgley, C.M.; Kniss, K.; Burns, E.; Rowe, T.; Foust, A.; et al. Changes in influenza and other respiratory virus activity during the COVID-19-pandemic—United States, 2020–2021. *MMWR Morb. Mortal. Wkly. Rep.* 2021, 70, 1013–1019. [CrossRef]

17. Lee, H.; Lee, H.; Song, K.H.; Kim, E.S.; Park, J.S.; Jung, J.; Ahn, S.; Jeong, E.K.; Park, H.; Kim, H.B. Impact of public health interventions on seasonal influenza activity during the SARS-CoV-2 outbreak in Korea. *Clin. Infect. Dis.* 2021, 73, e132–e140. [CrossRef]

18. Fricke, L.M.; Glöckner, S.; Dreier, M.; Lange, B. Impact of non-pharmaceutical interventions targeted at COVID-19 pandemic on influenza burden- a systematic review. *J. Infect.* 2021, 82, 1–35. [CrossRef]

19. Hatoun, J.; Correa, E.T.; Donahue, S.M.A.; Vernacchio, L. Social distancing for COVID-19 and diagnoses of other infectious diseases in children. *Pediatrics* 2020, 146, e2020006460. [CrossRef] [PubMed]

20. Kim, M.C.; Kweon, O.J.; Lim, Y.K.; Choi, S.H.; Chung, J.W.; Lee, M.K. Impact of social distancing on the spread of common respiratory viruses during the coronavirus disease outbreak. *PLoS ONE* 2021, 16, e0252963. [CrossRef]

21. Park, K.Y.; Seo, S.; Han, J.; Park, J.Y. Respiratory virus surveillance in Canada during the COVID-19 pandemic: An epidemiological analysis of the effectiveness of pandemic-related public health measures in reducing seasonal respiratory viruses test positivity. *PLoS ONE* 2021, 16, e0253451. [CrossRef]

22. Rodgers, L.; Sheppard, M.; Smith, A.; Dietz, S.; Jayanthi, P.; Yuan, Y.; Bull, L.; Wotiz, S.; Schwans, T.; Azondekon, R.; et al. Changes in seasonal respiratory illnesses in the United States during the coronavirus disease 2019 (COVID-19) pandemic. *Clin. Infect. Dis.* 2021, 73, S110–S117. [CrossRef]

23. Calderaro, A.; De Conto, F.; Buttrini, M.; Piccolo, G.; Montecchini, S.; Maccari, C.; Martinelli, M.; Di Maio, A.; Ferraglia, F.; Pinardi, F.; et al. Human respiratory viruses, including SARS-CoV-2, circulating on the winter season 2019-2020 in Parma, Northern Italy. *Int. J. Infect. Dis.* 2021, 102, 79–84. [CrossRef]

24. Sberna, G.; Amendola, A.; Valli, M.B.; Carletti, F.; Capobianchi, M.R.; Bordi, L.; Lalle, E. Trend of respiratory pathogens during the COVID-19 epidemic. *J. Clin. Virol.* 2020, 129, 104470. [CrossRef] [PubMed]

25. Satia, I.; Cusack, R.; Greene, J.M.; O’Byrne, P.; Killian, K. Prevalence and contribution of respiratory viruses in the community to rates of emergency department visits and hospitalizations with respiratory tract infections, chronic obstructive pulmonary disease and asthma. *PLoS ONE* 2020, 15, e0228544. [CrossRef] [PubMed]

26. Parry, F.; Shah, A.K.; Sestovic, M.; Salter, S. Precipitous fall in common respiratory viral infections during COVID-19. *Open Forum Infect. Dis.* 2020, 7, ofaa511. [CrossRef]

27. Olsen, S.J.; Azziz-Baumgartner, E.; Budd, A.P.; Brammer, L.; Sullivan, S.; Pineda, R.F.; Cohen, C.; Fry, A.M. Decreased influenza activity during the SARS-CoV-2 outbreak in Korea. *Clin. Infect. Dis.* 2020, 70, 1013–1019. [CrossRef]

28. Baker, R.E.; Park, S.W.; Yang, W.; Vecchi, G.A.; Metcalf, C.J.E.; Grenfell, B.T. The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic States. *Proc. Natl. Acad. Sci. USA* 2020, 117, 30547–30553. [CrossRef]

29. Nickbakhsh, S.; Mair, C.; Matthews, L.; Reeve, R.; Johnson, P.C.D.; Thorburn, F.; von Wissmann, B.; Reynolds, A.; McMenamin, J.; Gunson, R.N.; et al. Virus–virus interactions impact the population dynamics of influenza and the common cold. *Proc. Natl. Acad. Sci. USA* 2019, 116, 27142–27150. [CrossRef]

30. Hsieh, C.; Lin, C.; Wang, W.Y.C.; Paulleen, D.J.; Chen, J.V. The outcome and implications of public precautionary measures in Taiwan. Declining respiratory disease case in the COVID-19 pandemic. *Int. J. Environ. Res. Public Health* 2020, 17, 4877. [CrossRef]

31. Partridge, E.; McCleery, E.; Cheema, R.; Nakra, N.; Lakshminrusmha, S.; Tancredi, D.J.; Blumberg, D.A. Evaluation of seasonal respiratory virus activity before and after the statewide COVID-19 shelter-in-place order in North California. *JAMA Netw. Open* 2021, 4, e2035281. [CrossRef] [PubMed]

32. Yeoh, D.K.; Foley, D.A.; Minney-Smith, C.A.; Marin, A.C.; Mace, A.O.; Sikazwe, C.T.; Le, H.; Levy, A.; Blyth, C.C.; Moore, H.C. The impact of COVID-19 public health measures on detection of influenza and respiratory syncytial virus in children during the 2020 Australian winter. *Clin. Infect. Dis.* 2020, 72, 2199–2202. [CrossRef]

33. Varela, E.H.; Scotta, M.C.; Polese-Bonatto, M.; Sartor, I.T.S.; Ferreira, C.F.; Fernandes, I.R.; Zavaglia, G.O.; Ferreira de Almeida, W.A.; Arakaki-Sanchez, D.; Pinto, L.A.; et al. Absence of detection of RSV and influenza during the COVID-19 pandemic in a Brazilian cohort: Likely role of a lower transmission in the community. *J. Glob. Health* 2021, 11, 05007. [CrossRef]

34. Agh, R.; Avner, J.R. Delayed seasonal RSV surge observed during the COVID-19 pandemic. *Pediatrics* 2021, 148, e2021052089. [CrossRef]

35. Lavoie, P.M.; Reicherz, F.; Solimano, A.; Langley, J.M. Potential resurgence of respiratory syncytial virus in Canada. *CMAJ* 2021, 193, E1140–E1141. [CrossRef] [PubMed]
36. Takashita, E.; Kawakami, C.; Momoki, T.; Saikusa, M.; Shimizu, K.; Ozawa, H.; Kimazaki, M.; Usuku, S.; Tanaka, N.; Okubo, I.; et al. Increased risk of rhinovirus infection in children during the coronavirus disease-19 pandemic. *Influenza Other Respir. Viruses* 2021, 15, 488–494. [CrossRef] [PubMed]

37. Watanabe, Y.; Kamioka, Y.; Seki, M. Rhinovirus infected patients in the COVID-19 pandemic period. *Infect. Drug Resist.* 2021, 14, 609–611. [CrossRef] [PubMed]

38. Kiymet, E.; Bonc, E.; Sahinkaya, S.; Cem, E.; Celebi, M.Y.; Dugzol, M.; Kara, A.A.; Otiken, K.; Aikan, K.O.; Aydin, T.; et al. Distribution of spreading viruses during COVID-19 pandemic: Effect of mitigation strategies. *Am. J. Infect. Control* 2021, 49, 1142–1145. [CrossRef] [PubMed]

39. To, K.K.W.; Yip, C.C.Y.; Yuen, K.Y. Rhinovirus—from bench to bedside. *Formos Med. Assoc.* 2017, 116, 496–504. [CrossRef]

40. Jacobs, S.E.; Lamson, D.; St George, K.; Walsh, T.J. Human rhinoviruses. *Clin. Microbiol. Rev.* 2013, 26, 135–162. [CrossRef]

41. Liu, P.; Xu, M.; Cao, L.; Su, L.; Lu, L.; Dong, N.; Jia, R.; Zhu, X.; Xu, J. Impact of COVID-19 pandemic on the prevalence of respiratory viruses in children with lower respiratory tract infections in China. *Virol. J.* 2021, 18, 1–7. [CrossRef]

42. Lai, C.C.; Wang, C.Y.; Hsueh, P.R. Co-infections among patients with COVID-19: The need for combination therapy with non-anti—SARS-CoV-2 agents? *J. Microbiol. Immunol. Infect.* 2020, 53, 505–512. [CrossRef]

43. Hazra, A.; Collison, M.; Pisano, J.; Kumar, M.; Oehler, C.; Ridgway, J.P. Coinfections with SARS-CoV-2 and other respiratory pathogens. *Infect. Control Hosp. Epidemiol.* 2020, 41, 1228–1236. [CrossRef]

44. Kim, K.W.; Deveson, I.W.; Pang, C.N.; Yeang, M.; Naingm, Z.; Adikari, T.; Hammond, J.M.; Stevanovski, I.; Beukers, A.G.; Verich, A.; et al. Respiratory viral co-infections among SARS-CoV-2 cases confirmed by virome capture sequencing. *Sci. Rep.* 2021, 11, 3934. [CrossRef] [PubMed]