A living review examining the impact of COVID-19 pandemic on Influenza and Respiratory Syncytial Virus activity

Week 30.08.2021 to 05.09.2021

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Purpose of the review

The aim of this review was to examine the impact of a novel virus, SARS-CoV-2, on the activity of Influenza virus and Respiratory Syncytial Virus (RSV) in the human population. Understanding their co-existence will help inform clinical guidelines and public policy to protect public health and prevent health services from becoming overwhelmed.

Key themes

1) Seasonality: the seasonality and circulating strains of influenza virus and RSV.
2) Epidemiology/ surveillance: The epidemiology and surveillance activity of influenza virus and RSV. This includes disruptions to and adaptations for end-to-end integrated influenza/RSV and COVID-19 surveillance, change in surveillance standards (type of specimens processed, sampling strategy, testing algorithms, data reporting) and lessons from sentinel surveillance for SARS-CoV-2.
3) Public health measures and COVID-19 vaccinations: Effect of COVID-19 related public health measures and availability of COVID-19 vaccines on influenza and RSV activity.
4) Health Systems: The health systems, the reallocation of health resources such as poor availability of flu vaccines due to prioritization of health resources for COVID.

Table 1: Summary table of study characteristics and main findings

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
Seasonality	Foley et al., 2021a	Retrospective cohort study	Australia (WPR)	A tertiary paediatric hospital	1st January 2019 to 31st December 2020	• *Hypothesis*: SARS-CoV-2-related public health measures also reduced the circulation of RSV, altering this seasonality. • In children <16 years, RSV-positive admissions peaked during early summer in 2020, following an absent winter season. • December 2020 was the peak month, contributing almost 75% of RSV-positive admissions, 2.5 times higher that that of the 2019 peak. • The 2020 RSV season was in summer, with a larger than expected peak. There was an increase in RSV-positive non-bronchiolitis admissions, consistent with infection in older RSV-naïve children.
	Wiliams et al., 2021	Protocol	UK, Ireland (EUR)	Unclear	Unclear	*Hypothesis*: When RSV returns to the UK and Ireland in 2021, it will not follow its usual predictable seasonal pattern, especially if lockdown measures are lifted.
			Australia (WPR)	Britton et al., 2020	1st January 2015 – 30th June 2020	In 2020 when NPIs were implemented, the prevalence of RSV (type A and B) detection, admission to hospital for bronchiolitis, and emergency department attendance for acute illnesses in children younger than 16 years was lower compared to previous years.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
			New Zealand (WPR)	Huang et al., 2021	May – September 2020 (Exact dates not specified)	• The hospital-based SARI surveillance (by population of 1 million people) showed a reduction in cases than the reference period of 2015–2019. • There was no influenza-associated SARI was identified. • For influenza, there was 67.7% reduction during the lockdown and 99.9% after the lockdown compared with the reference period of 2015- 2019. • For RSV, there were 81.2% reduction during the lockdown and 98.0% reduction after the lockdown compared with the reference period of 2015- 2019.
			Australia (WPR), Chile (AMR), and South Africa (AFR)	Olsen et al., 2020	(i) April-July in 2017-2019 (ii) April – July 2020	• Since NPIs were implemented, there were 33 influenza cases amongst 60,031 tested in Australia, 12 cases out of 21,178 tested of Influenza in Chile, 6 cases out of 2098 specimens tested in South Africa during April-July 2020: Total 51 cases (0.06%, 95%CI: 0.04%- 0.08%) of influenza were observed. • During the April- July period in 2017-2019, a total of 4,512 influenza cases were detected amongst 178,690 tested specimens (13.7%, 95% CI: 13.6%–13.9%) in the three countries.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
Epidemiology / surveillance	Grant et al., 2021a *	Presentation from Starship and Kidz Hospitals Auckland: included data from several studies in particular Huang QS et al. 2021 for New Zealand and Wellington.	New Zealand (WPR)	Surveillance programme (SHIVERS – see main findings) and laboratory data from Wellington	RSV and Influenza in 2020 and 2021 (dates from other studies). Laboratory data from week 22 to 33 of 2021 on RSV in Wellington.	• *Hypothesis*: COVID-19 pandemic resulted in changes to the rates of RSV in 2020 and 2021 and typical age distribution of infections, therefore it is likely to affect influenza seasonality and may affect different ages. • The post lockdown period had of 99.9% reduction in Influenza and 98% in RSV in New Zealand. • A study using community cohort in Wellington showed an increase in influenza and RSV in July 2021. Data from six laboratories in Wellington showed a rapid increase in numbers of RSV from weeks 22 to 33 of 2021 with a change in age distribution of RSV infection. Children aged 12-48 months had a five hold higher increase in 2021 compared to 2019 and children under 12 months a two-fold increase.
	Osorio-López et al., 2021	Cross-sectional study	Mexico (AMR)	Influenza surveillance databases and electronic medical records	2008 to March 2021 (Exact dates not specified)	• *Hypothesis:* The public health measures implemented due to the COVID-19 pandemic would lead to a lower rate of nosocomial infections in cancer patients • There were no hospital-acquired influenza cases in 2020 compared to the period 2015-2019. • Influenza vaccination in health care workers increased to 95.3% in 2020 compared to 54.6% in the 2015 to 2019 period.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Yu et al., 2021	Ecological study	China (WPR)	Influenza tests in paediatric outpatient department in Zhongnan Hospital in Wuhan	Four-month period (September to December) in 2018, 2019 and 2020 (Exact dates not specified)	• *Hypothesis*: The public health measures introduced to combat COVID-19 transmission can lead to decreased levels of influenza in children. • Average influenza positive rate in 2018 was 14%, in 2019 28.7% and in 2020 4.3%. • Lower rates in 2020 were seen in all age groups (0-2,3-6,7-10). • However, the number of outpatient attendances in 2020 was noticeably lower than in 2018 and 2019 which may have affected the results.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
Public health measures and COVID-19 vaccinations	Campos-Outcalt, 2020	Practice alert	USA (AMR)	Recommendations of the Advisory Committee on Immunization Practices—United States, 2020-21 Influenza Season and CDC guidelines	2017-2021 (Exact dates not specified)	• *Hypothesis*: COVID-19 and influenza overlap can present opportunities for synergistic preventive measures. • Approximately 410,000 to 740,000 hospitalisations and 24,000 to 62,000 deaths were attributable to influenza in 2019-2020. An increase in patient visits was recorded for ILI in late November and early December 2017-2018, 2018-2019 and 2019-2020 remaining above baseline for 4 months in each season. • Recommendation for influenza vaccines for 2020-2021 year's flu season is that the composition be different for 3 of the 4 antigens: A/H1N1, A/H2N2 and B/Victoria. • It is recommended that individuals with ILI be tested for both influenza virus and SARS-CoV-2 if testing is available. • All household contacts of individuals with ILI should be vaccinated against influenza. Unvaccinated contacts and those at high risk who have been recently vaccinated, should consider influenza antiviral prophylaxis. • Keeping the potential for adverse interaction between COVID-19 and influenza vaccines, it is important that influenza vaccine be given by mid- to late-October to avoid such an interaction. • Family physicians should encourage influenza vaccination uptake among patients during office visits.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Kobayashi and Noguchi, 2021	Letter to the Editor	Japan (WPR)	Ministry of Health, Labor and Welfare of Japan, and Infectious Disease Surveillance Center of Japan	2012 to 2021 (January through March every year) (Exact dates not specified)	• Japan recorded a minimal number of influenza cases during the 2021 winter season, despite influenza vaccination rates remaining at similar levels in recent years. • It is likely that wearing masks with improved hygiene practices contributed to the significant reduction in influenza and thereby co-infections.
	Rachiotis et al., 2021	Cross-sectional study (online survey)	Greece (EUR)	Online survey among the members of the Larissa, (Thessaly, Central Greece) Medical, Dentists, and Pharmacists	2020-2021 (Exact dates not specified)	• *Hypothesis*- COVID-19 pandemic had a positive impact on influenza vaccination among healthcare workers (HCWs). • Influenza vaccination coverage among HCWs was found to be 74%. • Acceptance of COVID-19 vaccination was higher among HCWs who were vaccinated against influenza as compared to their counterparts who were not (78% vs. 59%; p-value = 0.001) • Acceptance of COVID-19 vaccination showed independent association with the likelihood of influenza vaccination coverage (OR = 2.06; 95% CI=1.15–3.67).
	Rubin, 2021	Medical news and Perspectives	United States of America (AMR)	US Centers for Disease Control and Prevention (CDC)	3rd October 2020 to 24th July 2021	Of the 1.3 million specimens tested, 2136 were positive for influenza virus, and 748 deaths were coded as influenza.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
			Australia (WPR)	Foley et al., 2021b	2012 to 2020 (Exact dates not specified)	A delayed seasonal RSV surge was observed in Australia in late September 2020 as NPIs were relaxed. A similar trend was observed at a New York city hospital.
	Tunaligil et al., 2021	Data simulation and computational modelling (Four simulations run for a COVID-19 and seasonal-influenza overlap, with/without adequate flu-vaccination, with higher/fewer number of personal contacts)	Unclear	Global indicator of infectious diseases	Unclear	• *Hypothesis*: Vaccination against influenza and limiting contacts is an affordable preventive measure to tackle the threat of COVID-19 and seasonal flu overlap. • Outcomes ('never infected', 'vaccinated', 'infected symptomatic', 'infected asymptomatic', 'recovered symptomatic', 'recovered asymptomatic' and 'deceased') were most favourable in scenario 1 corresponding to '60% vaccinated for seasonal flu, 10 contacts'- (higher number of vaccinated with lesser number of contacts). Between scenario 2 &3, scenario 2 comprising of higher vaccination rate but same number of contacts had a noteworthy reduction in deaths. • Scenario 4 with lower flu-vaccination rate and higher number of personal contacts, had the worst outcomes.
	Sanz-Muñoz et al., 2021	Communication	Not applicable	Unclear	Unclear	NPIs implemented against COVID-19 also limited RSV and influenza activity.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
Health Systems	No studies identified	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

*** The presentation reviewed here is based on an editorial which was published on 13th August and can be found here Grant et al. 2021b**

Abbreviations:
SARI: Severe acute respiratory illness
NPI: Non-pharmaceutical interventions
ILI: influenza like illness
EUR: European Region
WPR: Western Pacific Region
AMR: Region of the Americas
AFR: African Region

Summary of findings

A total of 11 studies were included in this rapid review. Of these, two studies reported data on seasonality and three reported data on epidemiology/ surveillance theme. We found six studies focussing on the public health measures and COVID-19 vaccinations theme. Our search did not identify any studies focusing on health system changes. Table 1 summarises the study characteristics and findings of each study by themes, with Table 2 providing quality assessment of the included studies.

1. Seasonality

Foley et al. 2021a observed a rapid resurgence of RSV admissions amongst children in late 2020, during the southern hemisphere summer season, with more than 2.5 times the admissions compared with the winter peak. In 2019, 271 of 454 (59.7%) RSV-positive bronchiolitis admissions were reported, followed by 113 of 454 (24.9%) RSV-positive admissions for other acute lower respiratory tract infection (OALRI). In 2020, there were 181 of 445 (40.7%) RSV-positive bronchiolitis and 145 of 445 (32.6%) RSV-positive OALRI admissions. Although there were no clinically important differences in length of stay or disease severity, the proportion of RSV-positive OALRI admissions was statistically significantly greater in 2020 (32.6% vs 24.9%, p=0.01). In contrast, RSV-positive bronchiolitis admissions significantly decreased in 2020 (p<0.001). When comparing the peak months for July 2019 and December 2020, the total number of RSV-positive admissions in December 2020 was more than 2.5-fold that of July 2019.

Williams et al. (2021) propose a prospective study in the UK and Ireland. Their supportive evidence demonstrated that the circulation of RSV and influenza in Australia, New Zealand, Chile, and South Africa was dramatically reduced since NPIs were implemented. However, the usual predictable seasonal pattern of RSV can be expected to change with delayed or summer epidemics and with different age distributions as NPIs are relaxed.

Rubin, 2021 reported a delayed seasonal RSV surge in Australia that was observed in the study by Foley et al., 2021b. However, this change in the seasonality pattern was attributed to the relaxation of NPIs.

2. Epidemiology/ surveillance

Grant et al. 2021a, is a video presentation of the affect of pandemic on influenza and RSV in 2020 and 2021 with a particular focus on the surge in RSV in 2021. The presentation is based on an editorial published on the 13th August (Grant et al. 2021b). The presentation uses data from Huang QS et al. 2021, community influenza surveillance cohort in Wellington and laboratory data in Auckland. It shows a marked reduction of influenza and RSV in 2020 and increases seen in July 2021. They particularly note a high number of RSV infections from weeks 22 to 33 in 2021 and note a difference in age distribution post pandemic. Five-fold higher rates of RSV in 12-24month olds in 2021 compared to 2019 versus a two-fold increase in 12 months olds in 2021 compared to 2019.

Osorio-López. 2021 conducted a cross-sectional study looking at the electronic medical records of patients admitted with cancer (both solid organ and haematological) to the Oncology referral centre in Mexico City. Only 30 of the 289 patients developed nosocomial influenza between 2008 and March 2021. The authors found a sharp decrease of nosocomial influenza (NI) cases in 2020 (n=0) compared to 2015-2019 (9 NI of a total 222 influenza cases). In addition, vaccination for influenza in healthcare workers increased in 2020 compared to the 2015-2019 period (54.64% from 2015 to 2019 vs 95.3% in 2020).

Yu et al. 2021 undertook an ecological study to investigate influenza testing and positivity in children attending outpatient department in Zhonghan hospital in Wuhan over a four-month period (September to December) in 2018, 2019 and 2020. Though lower influenza positivity rate was found in 2020 compared to 2018 and 2019 in all age groups, the number attending the outpatient clinics were lower in 2020 in respect to other years.

3. Public health measures and COVID-19 vaccinations

Evidence from several countries suggests that influenza and RSV cases have declined during the COVID-19 pandemic while NPIs were implemented (Kobayashi and Noguchi, 2021, Rubin, 2021, Sanz-Muñoz et al., 2021). Rubin, 2021 concluded that it is currently hard to exactly say which NPIs were most effective in controlling the influenza cases. However, all the measures- mask wearing, social distancing, handwashing, restrictions on international travel and school closures are likely to have contributed. Conversely, as schools re-open, an increased influenza activity can be expected.

However, it is suggested a sharp rise in cases can be expected as NPIs are relaxed (Rubin, 2021, Sanz-Muñoz et al., 2021). Multiple factors have been suggested to be contributing to this rise in influenza and RSV cases in the future.

The immune response in terms of duration and the type of protection conferred by natural infection is variable for different organisms and additionally depends on the person and their clinical condition and a lack of exposure to RSV and influenza can be harmful. Limited circulation of a virus like influenza would lower the antigenic drift and can lead to a lower immune scape of the virus. Limited influenza activity also creates a greater pool of susceptible people during the next season resulting from a drop in herd immunity (Sanz-Muñoz et al., 2021).

Another aspect to consider is that there are relatively few viruses available for characterisation as most countries were unable to effectively maintain influenza surveillance at the face of the pandemic (Rubin, 2021). This could mean that some viral characteristics were undetected and are likely to pose a threat during the next season as vaccines are recommended every year depending on the circulating virus strains in the previous seasons.

Different mask wearing rules have been put in place in different parts of the world or in different regions of the USA as schools re-open. However, people should be recommended to wear masks when using public transport or in crowded places or while experiencing flu symptoms (Rubin, 2021). Importantly, those in high-risk groups (for example-immunocompromised people) should also continue wearing masks during the flu season (Rubin, 2021).Profound reforms in health systems, adaptation of health systems to situations of increased demand and providing surveillance systems with greater capacity to predict such situations, improving the influenza vaccine production and coverage, awareness campaigns for vaccination and targeted efforts towards vaccination of children are needed to reduce the proportion if susceptible individuals in the community and to limit the consequences of a potentially higher and earlier circulation of influenza (Sanz-Muñoz et al., 2021).

Kobayashi and Noguchi, 2021 strongly recommend flu vaccination and continued mask wearing practices for the successful prevention of co-infection of influenza and COVID-19.

A computational modelling study (Tunaligil et al., 2021) showed best outcomes corresponding to a scenario of higher number of vaccinated individuals with lesser number of contacts in COVID-19 and seasonal flu overlap. The reverse scenario of lesser numbers vaccinated with

higher number of personal contacts had worst outcomes and could disrupt provision of essential health services within the community. Higher vaccination rate was independently associated with lesser number of deaths. Therefore, the authors concluded that the strategy of enhanced influenza vaccination combined with reduction in number of personal contacts is critical during the COVID-19 pandemic to prevent negative public health consequences. However, reduction in health seeking behaviour coupled with a shift to telemedicine along with reallocation of funds towards fighting the pandemic may have had a negative impact on vaccination rates. Therefore, it is essential that health care systems be reshaped to prevent dual outbreaks.

A cross-sectional study (Rachiotis et al.,2021) based on an online survey found that the acceptance of influenza vaccination was higher among HCWs in response to the COVID-19 pandemic. Also, the acceptance of COVID-19 vaccination can be considered as a surrogate indicator for perceived risk of COVID-19 infection.

A review of recommendations for the overlap of influenza and COVID-19 season (Campus-Outcalt, 2020), concluded that the overlap period between COVID-19 and influenza may present opportunities for synergistic preventive measures including encouraging higher uptake of influenza vaccination.

4. Health Systems

Our search did not identify any studies presenting data on health systems changes in response to the COVID-19 pandemic that may have impacted influenza or RSV activity.

Table 2: Quality of evidence of included studies

Theme	Number of studies	Quality of evidence*	Comments
Seasonality	N= 2 (Foley et al. 2021a,Williams et al. 2021,)	Not applicable to Moderate	1. Cohort study (N=1): Foley et al. 2021a • Limited generalisability of findings. • Clinical data not captured for the entire delayed season as the RSV season was ongoing at the time of the research. • RSV testing results at other providers, especially negative results, not captured unless ICD-10-AM RSV-related code used; testing rates and negatives are therefore expected to be higher than reported 2. Protocol (N=1): Wiliams et al. 2021 • It is not possible to assess the study quality based on protocol. • However, the supportive evidence (Britton et al. 2020, Huang et al. 2021, Olsen et al. 2020) were high quality studies: large sample sizes in multiple countries, and appropriate statistical analysis comparing with the pre-NPI or pre-pandemic
Epidemiology / Surveillance	N=3 (Grant et al. 2021, Osorio-López. 2021 Yu et al. 2021)	Low	1. Video presentation (N=1) Grant et al. 2021a • A recorded presentation which includes data from various sources, and some from studies • The quality of studies included in the presentation not assessed. The editorial Grant et al. 2021b was not assessed in this rapid review as it was published in August. 2.Cross-sectional study (N=1): Osorio-López. 2021 • Presented as a letter to the Editor with minimal information about study design and methods. • Limited sample size • Confounding factors not identified and adjusted for in the analysis • Generalisability of findings is limited. 3. Ecological study (N=1): Yu et al. 2021 • Results cannot be generalised to other cities and countries and to the entire paediatric population in Wuhan. • Though lower influenza positivity rates were found in 2020 compared to 2018 and 2019 lower number of outpatients and test were conducted in 2020 compared to previous years.

Theme	Number of studies	Quality of evidence*	Comments
Public Health measures and COVID-19 vaccine availability	N=6 (Campos-Outcalt, 2020, Kobayashi and Noguchi, 2021, Rachiotis et al., 2021, Rubin, 2021, Sanz-Muñoz et al., 2021, Tunaligil et al., 2021)	Very low	• Communication/ letter to the Editor/ Medical news and perspectives/ Practice alert (N= 4) Campos- Outcalt, 2020, Kobayashi and Noguchi, 2021, Rubin, 2021, Sanz-Muñoz et al., 2021 • Did not contain primary data. However, supported their claims with data from other sources and countries. • Did not directly estimate the impact of specific NPIs on influenza or RSV cases. 2. Cross-sectional study (N=1) Rachiotis et al., 2021 • Small sample not representative of the nationwide healthcare population. • Attitudes of individuals towards COVID-19 vaccination was assessed by a separate questionnaire but not for influenza vaccination. 3. Modelling study (N=1) Tunaligil et al., 2021 • Generalisability to different real-world scenarios limited • Limited by assumption of modelling studies
Health systems	N=0	Not applicable	Not applicable

*Quality appraisal tool not used

Limitations of the review

We identified a few limitations in this review. There might be some levels of risk of bias because data were extracted, and quality assessment of the studies were conducted by a single reviewer. The studies included in this review were reported from different countries and regions of the world and at variable time points. The heterogeneity across the included studies does not enable us to generalise the findings to all populations and settings.

We did not exclude any papers because of their study designs or on the grounds of poor quality as we were keen on providing a maximally inclusive synthesis of available evidence. However, this may have reduced the quality of evidence generated from this review.

Importantly, this should not be considered a comprehensive literature review of the effect of the ongoing COVID-19 pandemic on influenza and RSV activity since our literature search was restricted to dates from 30.08.2021 to 05.09.2021.

However, this review was planned and undertaken as a rapid review with a quick turnaround to provide a quick summary of the literature for the week between 30.08.2021 to 05.09.2021. We aim to update this review and summarise the existing literature weekly.

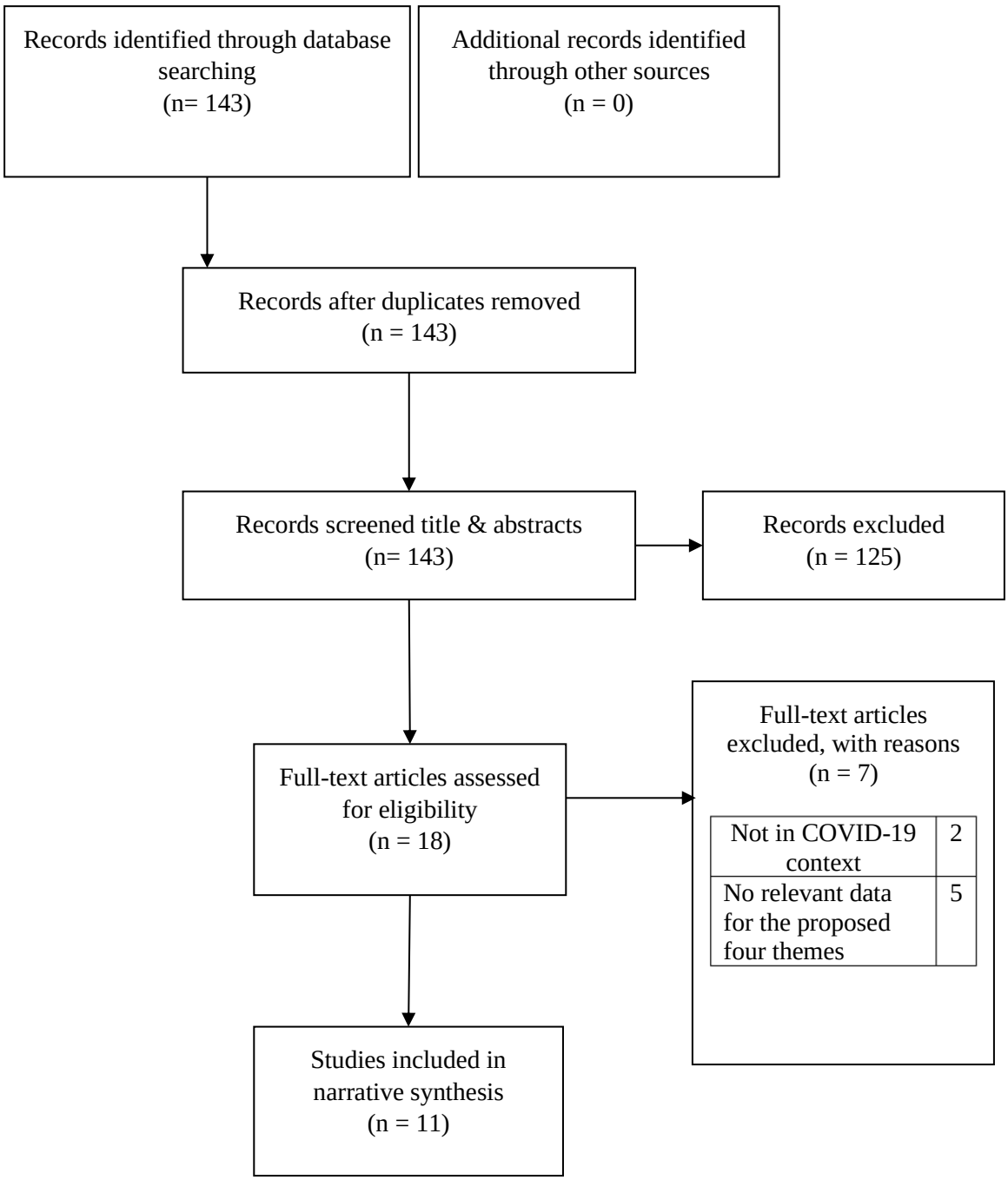
Conclusions

A change in the seasonality pattern of RSV was observed in different countries in the context of the COVID-19 pandemic. During the COVID-19 pandemic, a decline in number of influenza and RSV cases was reported. Public health measures implemented against COVID-19 seem to be effective in reducing the transmission of influenza and RSV. However, a rise in influenza and RSV cases can be expected after the relaxation of these public health measures. It is therefore, recommended that vaccinations against flu and mask wearing should be continued as preventive measures against influenza. Vaccination against influenza can also be a synergistic preventive measure during dual outbreaks. There was limited evidence regarding the impact of changes in health system changes on influenza and RSV activity. Heterogeneity across available studies does not allow further generalisation of findings.

Methods

This rapid review was guided by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA-2020) protocols statement (Page et al., 2021) and a study protocol was developed (see appendices). We designed a search strategy by developing a search string that included terms related to influenza and RSV (shown in appendices). The COVID-19 literature database was searched on 6th September 2021 for studies published between 30th August 2021 and 05th September 2021, and results were imported to Covidence (COVIDENCE, 2021) after deduplication in EndNote. Within Covidence we then performed a further deduplication. Two reviewers from the review team performed independent screening of the titles and abstracts of all the records followed by independent screening of full-texts of the studies selected for full-text review. Disagreements at any stage were reconciled by discussion within team members. A single reviewer performed data extraction for each included study. Figure 1 illustrates the flow of study selection at each stage.

Figure 1: PRISMA flow chart



Data extracted were study type and methods, country and WHO region, sources of data, period of data collection, and study findings. Four themes were used to synthesise the available literature on influenza virus and RSV:

1) The seasonality and circulating strains of influenza virus and RSV.
2) The epidemiology and surveillance activity of influenza virus and RSV. This includes disruptions to and adaptations for end-to-end integrated influenza/RSV and COVID-19 surveillance, change in surveillance standards (type of specimens processed, sampling strategy, testing algorithms, data reporting) and lessons from sentinel surveillance for SARS-CoV-2.
3) Effect of COVID-19 related public health measures and availability of COVID-19 vaccines on influenza and RSV activity.
4) The health systems, the reallocation of health resources such as poor availability of flu vaccines due to prioritization of health resources for COVID.

We were unable to conduct a formal quality assessment of individual studies, owing to time constraints. However, we commented on the general quality of evidence available for each theme.

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Appendices

Appendix 1- Study protocol

Review title

A living review examining the impact of the COVID-19 pandemic on influenza and respiratory syncytial virus (RSV) activity in the human population

Rationale

Since its emergence in December 2019, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has heavily impacted influenza and respiratory syncytial virus (RSV) activity. Non-pharmaceutical interventions (NPIs) implemented to prevent SARS-CoV-2 transmission might have affected transmission dynamics of influenza and other respiratory viruses due to commonality in modes of transmission. Also, widespread lockdowns and restriction of movement may have increased virus–virus interactions. Moreover, there might have been a reduction in healthcare seeking behavior for respiratory viruses among the general population. Furthermore, lifting restrictions might result in a surge of cases or alteration of seasonality.

Research Questions

How has the COVID-19 pandemic affected influenza and RSV activity in the human population in terms of-

a) The seasonality and circulating strains of the influenza virus and RSV
b) The epidemiology of the influenza virus and RSV
c) The surveillance activity of the influenza virus and RSV (disruptions, adaptations for end-to-end integrated influenza/RSV and COVID-19 surveillance, change in surveillance standards – type of specimens processed, sampling strategy, testing algorithms, data reporting, lessons from sentinel surveillance for SARS-CoV-2)
d) Effect of COVID-19 related public health measures on influenza and RSV activity
e) The health systems (reallocation of health resources- poor availability of flu vaccines due to prioritization of health resources for COVID)
f) The impact of availability of COVID-19 vaccines on influenza and RSV activity

Methods

Eligibility criteria

Inclusion

- **Population**- Individuals of all age groups
- **Exposure -** RSV or Influenza in the context of the COVID-19 pandemic
- **Diagnosis-** RSV or influenza infections diagnosed with standard, valid laboratory based, or laboratory confirmed tests (for example, reverse transcriptase-polymerase chain reaction (RT-PCR), antigen testing, viral culture, serology, immunofluorescence assays, influenza nucleic acid amplification etc.) or ICD-9 or ICD-10 codes
- **Comparator**- Studies comparing different time points (pre-pandemic vs post pandemic) or studies comparing different health systems or epidemiological features by regions /countries.

- **Outcome**- Reporting data on at least one of our research questions
- No geographical restrictions
- **Language**- Studies published in English language
- **Publication type**
  - Academic literature published in peer-reviewed journals
  - Pre-prints
- **Study design**
  - Observational studies
  - Modelling studies
  - Publication date: 1st December 2019 onwards

Exclusions

- Studies that focus on clinical features or immunology
- Interventional studies such as drug or vaccine trials
- Environmental studies (transmission dynamics in different environments)
- Studies not reporting data for the pandemic period and only reporting data for the period before 31st December 2019 (pre-COVID-19 pandemic)
- Studies published in languages other than English

Search strategy

Database searches will be conducted in the WHO COVID-19 database to identify studies investigating influenza or RSV related activity during the COVID-19 pandemic period to-date.

Searches will be conducted weekly using a pre-designed search strategy for weekly updates.

Search terms- We will include two main strings comprising influenza and RSV, and COVID related terms.

(lnfluenza OR RSV) AND COVID

We will not apply any language restrictions for searches. However, considering time constraints, translations may not be possible for every non-English paper.

Study selection and data extraction

This study will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 checklist. Studies retrieved from searches will be imported into Covidence after deduplication in Endnote. Studies retrieved will be screened for eligibility using pre-defined inclusion/ exclusion criteria independently by pairs of reviewers for both title and abstract screening as well as full-text screening. Any disagreement will be resolved by mutual discussion, however, if unresolved a third reviewer will assess the final decision. Information from included studies will be extracted into a pre-piloted excel extraction sheet and the following variables will be extracted: the name of the author, publication year, study site, setting, WHO region, aims and objectives, study design and methods, sample description/population, outcome measures, main finding, method of assessment of quality and quality score.

The risk of bias and quality of individual studies will be assessed using JBI critical appraisal tools appropriate for each type of study included in the review. Two reviewers will independently assess the risk of bias and quality of included studies.

Data synthesis

We will synthesise the available data narratively. However, if comparable data emerge, we will consider undertaking a meta-analysis to report pooled estimates (for example, odds ratios or incidence rates).

Appendix 2- Search strategy

The search covers the week 30/08/2021 - 05/09/2021 inc.

"respiratory virus" OR "respiratory viruses" OR "acute respiratory infection" OR "acute respiratory infections" OR "respiratory tract infection" OR "respiratory tract infections" OR "respiratory tract disease" OR "respiratory tract diseases" OR "respiratory distress syndrome" OR influenza OR influensa OR flu OR grippe OR ili OR rsv OR "Respiratory Syncytial Virus" OR "Respiratory Syncytial Viruses" OR alphainfluenzavirus) AND (entry_date:20210830 OR entry_date:20210831 OR entry_date:20210901 OR entry_date:20210902 OR entry_date:20210903 OR entry_date:20210904 OR entry_date:20210905)