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

Week 06.09.2021 to 12.09.2021

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Date of review: 22nd September 2021

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 prioritisation 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	De la Puerta et al. 2021	Prospective cross-sectional study	Spain (EUR)	CSRV survey registry for allo-HSCT recipients with respiratory symptoms at the hematology division of the Hospital Universitari i Politècnic La Fe in Valencia, Spain	01st Feb 2018-30th Sep 2018 (P1), 01st Feb 2019 -30th Sep 2019 (P2), and 01st Feb 2020 - 30th Sep 2020 (P3)	• *Hypothesis:* NPI measures for COVID-19 led to a reduction in CSRV infections and its complications in allo-HSCT patients. • Over the three periods, 406 PCR tests conducted of which 145 (35.7%) were done in P1, 187 (46.1%) in P2, and 74 (18.2%) in P3 ($p < 0.001$). Of these, 115 (79.3%), 145 (77.5%), and 40 (54%) tested positive for one or more CSRV, respectively ($p < 0.001$). • Significant decline noted in lab confirmed RSV (93.3%) and influenza (80%) cases, respectively. • Between April and September 2020 no cases of RSV or influenza were detected in allo-HSCT recipients. • A reduction in absolute numbers of lower respiratory tract disease (68.1%), co-infections (91.7%), and hospitalisations (72.6%) was recorded during P3.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Delestrain et al.,2021	Cross-sectional study	France (EUR)	National data from three networks: emergency departments (ED) hospitals, general practitioners (GP), and hospital laboratories for bronchiolitis in children <2 years of age, and percentage of RSV positive tests	2018-2019 (P1), 2019-2020 (P2), 2020-2021 (P3)	• *Hypothesis:* Restrictions imposed in view of COVID-19 pandemic have altered the natural course of RSV infections • Acute bronchiolitis epidemics in metropolitan France in the years 2018-2019 and 2019-2020 commenced in October (Weeks 43 and 44), attaining a peak in early December (Weeks 49 and 50), and ended in early March (Weeks 9 and 10). • In 2020-2021, the epidemic threshold for bronchiolitis in children less than 2 yrs old was reached 12 weeks later than usual in Feb 2021 (week 05). • Total number of cases of bronchiolitis were lower in 2020-2021 than that recorded in previous years.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Sunagawa S et al. 2021	Ecological study	Japan (WPR)	Two datasets with different time periods (1) Nationwide surveillance by RAT and/or ILI in 55 sentinel healthcare sites in Okinawa (2) RAT from four hospitals in capital city in Okinawa for Influenza A and B	Four time periods for dataset (1) From 36th epidemiological week of the first year to the 35th week of the 2nd year in these years: 2015-2016 2016-2017 2017-2018 2018-2019 2019-2020 Dataset (2) only used the most time period 2019-2020	• *Hypothesis:* NPI measures lead to the loss of summer influenza season in Okinawa. • The epidemic curve in 2019/2020 showed a peak of influenza cases in the 38th week of 2019 falling in the 40th week which was not present in previous time periods. There were much lower levels in the winter of 2019/2020 and loss of the summer influenza peak. • A similar pattern was found in the number of RAT tests and positivity rate from the four hospitals. • NPIs such as mask wearing, travel restrictions and school closures may have resulted in the changes in influenza seasonality.
Epidemiology / surveillance	Boschi et al., 2021	Ecological Published	France (EUR)	Laboratory data from four University hospitals in Marseille	01st Mar 2020 to 30th April 2020	• *Hypothesis: co-infection of respiratory viruses and SARS-CoV-2 is possible but depends on overlap of their epidemic periods* • This small study (n=4,222) of throat swabs results showed 15.2% (n=1,095) were positive for SARS-CoV-2, of which 4.2% had co-infection with another respiratory virus (n=27). • RSV was found in 1.3% (n=22) of all swabs alone with no co-infection. • Influenza A and B were found in swab results in 12.4% (n=212) and 13.7% (n=235) of all cases respectively

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
						with 7.4% (n=2) coinfection with SARS-CoV-2 for both. • The authors state their study results justify using syndromic diagnostic strategy through use of multiplex PCR assay in laboratories
	Covin and Rutherford 2021	Literature review	Worldwide search	No details given – written as a commentary		• *Hypothesis*: coinfection of SARS-CoV-2 and Influenza may lead to more severe pulmonary disease. • The review found 16 reports (n=35 patients) of coinfection with SARS-CoV-2 and influenza from Brazil, Japan, Germany, Spain, Italy and USA. • Most cases of coinfection were with influenza A (n=18), followed by both influenzae A and B (n=10) and unspecified in 6. • A review of hospitalised patients with SARS-CoV-2 reported that the aetiology of coinfection was viral in 3% of cases. • Analyses of 530 Chinese patients in 2019 from three studies observed 286 (54%) had coinfection with influenza. • Coinfection leads to greater pulmonary damage, also shown by in vitro evidence in hamsters who had been inoculated with both viruses.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Giraud-Gatineau et al., 2020	Short communication	France (EUR)	real-time surveillance of all infections in public hospitals in Marseille, Southeastern France performed by The University Hospital Institute Méditerranée Infection	Between week 47 of 2018 and week 14 of 2019 (P1) and between week 47 of 2019 and week 14 of 2020 (P2)	• *Hypothesis:* SARS-CoV-2 infections had an impact on the all-cause mortality among hospitalized patients. • There was a decrease in the proportion of influenza A positive cases (19.2% v/s 9.7%) and proportion of deaths among influenza A positive patients (1.7% v/s 0.5%) in 2019 compared to 2018. • In case of influenza B, the proportion of positive cases were higher in 2019 when compared to 2018 (0.1% v/s 7.8%). The proportion of deaths among influenza B positive patients were also high in 2019 (0% v/s 0.2%). • There was a decrease in the proportion of RSV positive cases (9.6% v/s 6.5%) and proportion of deaths among RSV positive patients (1.1% and 0.7%) in 2019 compared to 2018.
	Haddadin et al., 2021	multicenter, population-based ARI surveillance	USA (AMR)	New Vaccine Surveillance Network	December 2016 to April 2017, and October to April each year from 2017 to 2020	• *Hypothesis*: The proportions of acute respiratory infections testing positive for RSV and influenza during the COVID-19 mitigation period in 2020 would be lower than in prior seasons. • There were no RSV or influenza cases in children reported in 2020, about 2 to 4 weeks after NPIs were implemented, in weeks 11 to 13, which contrasted with predictions based on data from previous seasons when mitigation measures were not in effect.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Sherman et al. 2020	Retrospective cohort study	USA(AMR)	Medical records of all inpatient and outpatient adults who underwent testing for respiratory viruses at Emory Healthcare system (EHC) in Atlanta and the Mass General Brigham (MGB) Healthcare System in Boston	01st Sep 2015 to 30th May 2020	• *Hypothesis*: SARS-CoV-2 pandemic had an impact on rates of infection of seasonal respiratory viruses. • Effective Rt declined below 1 in week 12 for Influenza A and below zero for influenza B in week 13 in Atlanta whereas influenza A Rt dipped below 1.0 on week 7 and fell to 0 at week 14 and influenza B Rt was consistently below 1.0 at week 11 in Boston in 2019-2020 season. • Reduction in cases coincided with the restriction of large gatherings, bar closures, and stay-at-home orders (weeks 12-13). • In previous seasons the effective Rt did not consistently drop below 1.0 prior to week 15 for Influenza A and Rt values decreased to <1.0 after week 15 for influenza B. • Rt values for RSV declined to <1.0 in week 13 during the current season and week 14 for previous seasons.
	Stowe, 2021	Ecological study	England, UK (EUR)	SGSS and RDMS	20th January 2020 to 25th April 2020	In influenza-positive cases, the risk of testing positive for SARS-CoV-2 was 58% lower than those with double negative (influenza and SARS-CoV-2). Coinfection with influenza and SARS-CoV-2 was associated with a higher risk of mortality (OR 5.92, 95%CI: 3.21 to 10.91) than those with double negative.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Edwards et al. 2020	Literature Review	USA (AMR), Brazil (AMR), and Australia (WPR)	No details given	Jan to Apr 2020	• *Hypothesis*: Declines in both RSV and influenza cases may be associated with mitigation strategies implemented in response to the SARS-CoV-2 in different regions of the world. • In the Yukon-Kuskokwim Delta (YKD) region of Alaska RSV cases were reported in late Feb 2020 but showed a sharp decline in late Apr following social distancing measures implemented in Mar 2020 for Covid-19, a change not observed in past 25 seasons. • A significant reduction in the number of hospitalizations for acute bronchiolitis in infants younger than one year was noted in Brazil, with a greater than 70% reduction when compared to earlier years. Brazil implemented social distancing, restrictions on business and non-essential services., and closure of schools from middle of Mar 2020. • Mitigation measures implemented in end Mar 2020 in Western Australia. Prior to mitigation measures, RSV and influenza cases in the first 13 weeks were comparable to earlier seasons. However, after mitigation efforts RSV detections were 98% lower and influenza detections 99 % lower than in earlier years. A sharp decline was noted which remained low, even in the face of school reopening.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
Public health measures and COVID-19 vaccinations	Hadler 2020	Editorial commentary	China (WPR)	China's outpatient hospital-based sentinel surveillance system (Lei et al., 2020)	October 2019 to May 2020	• The marked decline in influenza was associated in time with the implementation of NPIs- number of visits decreased dramatically over the 2 weeks following NPIs implementation, the percentage for ILI increased, and the percentage positive for influenza decreased. • The influenza rate reached nearly undetectable levels within 5 weeks and remained very low until mid-May.
			Southern Hemisphere countries	World Health Organisation, 2019, World Health Organisation, 2020	20th July 2020 to 02nd August 2020 and 22nd July 2019 to 04th August 2019	In 2020, 40 influenza isolates were made in the laboratories in the Global Influenza Surveillance and Response System laboratories with five times as many tests conducted in 2019. In 2019, there were 3660.
			Australia (WPR)	Australian Government Department of Health, 2020	1st June and 23rd August 2020	There were few laboratory tests and only 2 hospitalisations for laboratory confirmed influenza in sentinel hospitals in Australia with most schools being open during the winter.

Themes	Study	Study type	Country (WHO region)	Data sources	Time period for data collection	Main findings
	Madaniyazi et al., 2021	Interrupted time series (quasi-experimental)	Japan (WPR)	Infectious disease surveillance center, National Institute of Infectious Diseasse	1st week of 2016 to 53rd week of 2020	• *Hypothesis:* longer periods of NPI could increase the susceptibility of the population to RSV potentially causing larger outbreaks once control measures are lifted. • The authors conducted an interrupted time series analysis to examine the effects of NPI on RSV infections. Modelling assumed different reductions in transmission rate from 0-90% in 10% intervals. • NPI was introduced in Japan from 02/03/20 to 53rd week of 2020 (end of 2020) during which RSV activity declined by 97.9% (95% CI 94.8-99.2). • The analysis suggested there would be an outbreak in 2022-2023 which may be 5 times larger than previous outbreaks.
Health Systems	Sun and Gong, 2021	Commentary	China (WPR)			• The number of flu vaccinations has increased dramatically during the COVID-19 pandemic. • Due to influenza vaccination and improvement of medical services, China has not seen the same peak flu season as observed between 2015 and 2019 since February and March 2020.

Abbreviation:
NPIs: Non-pharmaceutical interventions, **RAT: Rapid Antigen Test**, **ILI: Influenza like illness**, **CSRV: Common seasonal respiratory virus**, **allo-HSCT: allogeneic stem cell transplant**, **PCR: polymerase chain reaction**, **SGSS: Second Generation Surveillance System**, **RDMS: Respiratory, DataMart System**, **95% CI: 95% confidence interval**, **Rt: Reproduction number**
EUR: European Region.
WPR: Western Pacific Region
SEAR: South-East Asian Region
AMR: Region of Americas

Summary of findings

A total of twelve English language studies and one Chinese language study were included in this rapid review. Three studies (De la Puerta et al. 2021, Delestrain et al.,2021, Sunagawa S et al. 2021) reported data on seasonality (theme 1). We identified six studies with data on epidemiology/ surveillance (theme 2) (Boschi et al., 2021, Covin and Rutherford 2021, Giraud-Gatineau et al., 2020, Haddadin et al., 2021, Sherman et al. 2020, Stowe, 2021). Our rapid review included three (Edwards et al. 2020, Hadler 2020, Madaniyazi et al., 2021) studies focussing on COVID-19 public health measures/ COVID-19 vaccines (theme 3). The Chinese study (Sun and Gong, 2021) discussed the impact of the pandemic on health systems (Theme 4). 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

Sunagawa S et al. 2021 was a cross-sectional study on Influenza patterns in Okinawa prefecture in Japan. The authors used surveillance from 55 sentinel healthcare facilities for rapid antigen tests (RAT) and/or influenza like symptoms, and RATs conducted with positivity for influenza A or B in four capital city hospitals. Comparing time periods before the pandemic (2015-2016, 2016-2017, 2017-2018, 2018-2019) to during the start of the pandemic (2019 -2020) there was a peak of cases in the 38th week of 2019 with a smaller peak of winter cases and no summer peak. In contrast, the other time periods had winter and summer peaks. The authors suggest NPIs due to the pandemic may have caused this change in seasonality.

De la Puerta et al. 2021 noted an overall reduction in the prevalence of CSRV (common seasonal respiratory virus) infections and its complications in allo-HSCT (allogeneic stem cell transplant) recipients in the SARS-CoV-2 pandemic overlap period. This could be a result of reduced transmission due to preventive measures instituted for SARS-CoV-2.

Delestrain et al.2021 reported a late start of the bronchiolitis outbreak in January 2021 with its peak shifted by almost three months and the total number of cases lower than in previous seasons. Also, an ongoing increase in RSV cases in the period corresponding to the end of the epidemic in previous seasons raised concerns regarding overburdening of the health system during the COVID-19 pandemic.

2. Epidemiology/ surveillance

Boschi et al.2021 was written as a letter to the editor but described a small study over a short period of two months (from 1st March to 30th April 2020). All throat swab results (n=4222) were examined to find proportions of respiratory viral infections and the number of co-infections with SARS-CoV-2. Both influenza A and B co-infection was found in two separate cases, which was 7.4% of those with co-infection. The majority of co-infections were with Rhinoviruses. The authors state co-infection is possible and syndromic diagnostic strategies should be used in laboratories, for example through use of multiplex PCR assays.

Covin and Rutherford 2021 give a commentary of a literature review of coinfection of SARS-CoV-2 and influenza. They identified 16 reports from various countries globally. The reports identified 35 patients with coinfection, influenza A being the commonest (n=18), followed by both influenza A and B (n=10) and remainder unspecified. They also comment on findings that viral coinfection occurred in 3% but do not give the population where this occurred only that it was hospitalized patients. In addition, three Chinese studies in 2019 reported very high proportion of coinfection (54%) with influenza A or B. They do not discuss why this figure is so high.

Giraud-Gatineau et al., 2020 assessed for proportion of deaths among patients positive for different respiratory viruses before (2018-2019) and during (2019-2020) the pandemic period. It was observed that there were fewer common respiratory virus-associated deaths in South-eastern France hospitals during 2019–2020 in comparison to 2018–2019. There was a decrease in influenza A virus ($p<0.001$) and RSV ($p=0.18$) associated death proportions in 2019-2020. The authors concluded that SARS-CoV-2 infections had a limited impact on the number of deaths from any cause among hospitalized patients. However, statistical analyses for number of influenza cases were not conducted and there was in fact a rise in influenza B cases during the 2019-2020 period compared to the 2018-2019 period. This finding contrasts with the findings of other studies reported in this review and previous weeks' reviews.

Haddadin et al., 2021 noted a decrease in eligible and enrolled acute respiratory infection cases after NPIs were introduced. In all sites except Seattle, the proportions of positive RSV and influenza in the 2020 NPIs period were lower than predicted. There was no RSV or influenza detection between 5th April 2020 and 30th April 2020 (week 15 to week 18) in all study sites including Seattle. Compared to 2016–2019, there were 63.9% and 45.8% lower

odds of testing positive for RSV and influenza, respectively, during the 2020 community mitigation period.

Stowe et al. 2021 assessed whether influenza is associated with a reduced risk of SARS-CoV-2 infection and whether coinfection with influenza and SARS-CoV-2 will lead to severe disease outcomes in England. They found that SARS-CoV-2 cases were observed 58% lower amongst influenza-positive cases and coinfection increased the risk of death compared to patients with neither influenza nor SARS-CoV-2 (OR 5.92, 95%CI: 3.21 to 10.91). Therefore, authors recommended to implementing double testing for influenza and SARS-CoV-2 and maximising influenza vaccination.

Sherman et al. 2020 reported an early decline in Rt of influenza A, B and RSV in 2019-2020 season as compared to the 4 last seasons and postulated that this decline could be attributable to NPI measures instituted for prevention of COVID-19 transmission.

3. Public health measures and COVID-19 vaccinations

Edwards et. al. 2020 reviewed reports of mitigation measures from Alaska (USA), Brazil and Western Australia and reported a sharp decline in influenza and RSV cases coinciding with the time period of implementation of COVID-19 restrictions in all these regions.

Hadler 2020 reported data from China, Australia and other southern hemisphere countries to demonstrate that COVID-19 NPIs have led to a marked decrease in influenza cases. However, it has also been warned that countries that have achieved a relative success in controlling the number of COVID-19 cases seem to be relaxing their NPIs to a greater extent. These countries may be considered to have the highest potential of a distinct seasonal influenza epidemic that can lead to the largest related healthcare burden. Vaccination against influenza, therefore, remains important and should be prioritised for high-risk groups such as young children, older adults, people with underlying medical conditions, and those in congregate settings that facilitate transmission.

Madaniyazi et al 2021This was an interrupted time series analysis using data from national surveillance in Japan for RSV. Using pre pandemic periods from 2016 to the end of 2020, so during the early pandemic when control measures were implemented (2nd March 2020 to end of the year 2020) they showed the number of RSV infections significantly fell. They used a variety of reduction rates from 0-90% reduction and hypothesized there may be an outbreak

of RSV in 2022-2023 and this could be due to the introduction of COVID-19 NPIs. Lack of circulating RSV might cause the population to be more susceptible to infection and the authors suggest the outbreak may be five times higher than previous outbreaks.

4. Health Systems

Sun and Gong, 2021 suggested that a combined outbreak of influenza and COVID-19 can cause greater difficulties for epidemic prevention and control. The analysis of influenza-like cases in Luohu District from 2015 to 2019 demonstrated that the number of such cases tend to increase significantly around February and March every year and reach a peak. However, the peak of influenza was not observed in 2020. The authors suggest that this decline in influenza cases may be attributed to improved influenza vaccinations and highlight the importance of influenza vaccines in controlling influenza cases.

Table 2: Quality of evidence of included studies

Theme	Number of studies	Quality of evidence*	Comments
Seasonality	N= 3 (De la Puerta et al. 2021, Delestrain et al. 2021, Sunagawa S et al. 2021)	Low	Ecological (N=1) Sunagawa S et al. 2021 • This was an ecological study that used nationwide surveillance data but combined rapid antigen test for influenza with people with unconfirmed influenza who had influenza like symptoms. • They did conduct any inferential analysis but only provided descriptive analysis and results cannot be generalised to other countries. Cross sectional study (N =2) De la Puerta et al. 2021, Delestrain et al. 2021 • Findings not generalisable as included specific population and specific countries. • Did not take into account the association between individual NPI measures and change in seasonality of CSRV infections.
Epidemiology / Surveillance	N= 6 Boschi et al.2021, Covin and	Moderate	Ecological (N=2) Boschi et al.2021, Stowe et al. 2021

Theme	Number of studies	Quality of evidence*	Comments
	Rutherford 2021, Delestrain et al. 2021, Sherman et al., 2020)		• Limited information on methods (Boschi et al.2021. This study also had a small sample size and as incidence of viruses can alter with seasons, a longer duration with a larger sample size is required to understand patterns of co-infection. • Large sample size with appropriate statistical analyses to achieve research objectives (Stowe et al. 2021) Commentary, short communication (N=2) Covin and Rutherford 2021, Giraud-Gatineau et al., 2020) • Little information on methods, there is no information how common coinfection is within the general population as a denominator was not provided in their descriptive statistics, and there is no information on the heterogeneity of incorporating data from various countries with different healthcare systems (Covin and Rutherford 2021). • Study conducted in south-eastern France and so findings may not be generalisable (Giraud-Gatineau et al., 2020). Cross – sectional study (N=1) Delestrain et al. 2021 • The study did not analyse the association between individual NPI measures and change in seasonality of CSRV infections. • Also, as NPIs were instituted at different time periods in different countries, the results are not generalisable. Retrospective cohort study (N= 1) Sherman et al., 2020 • Health seeking behaviour patterns for influenza and RSV could have changed during the pandemic, and number of cases might not be a true reflection of the number of infections in the community. • Each independent NPI variable and its effect was not evaluated

Theme	Number of studies	Quality of evidence*	Comments
Public Health measures and COVID-19 vaccine availability	N= 3 (Edwards et. al 2020, Madaniyazi et al 2021, Sherman et al 2020)	Low	Literature review (N= 1) Edwards et. al 2020 • Source of primary data not established. • Potential for selection bias as search strategies and selection criteria unclear. Editorial commentary (N= 1) Hadler 2020 • Does not contain primary data but reports data from other sources and several countries. • Does not estimate association of cases with with specific NPIs. Interrupted time series (N=1) Madaniyazi et al 2021 • Used data from National surveillance in Japan to estimate the effects of NPI on RSV activity. • Though they used an interrupted time series (ITS) data did not run past the intervention period (NPI duration) but stopped at the end of the intervention. • ITS are regarded as useful to evaluate interventions but need data pre and post intervention. • The paper did not mention effects of seasonality and autocorrection though the attempted to factor in population size and birth rate. • They do not provide any descriptive statistics on their data or clarify the NPI measures.
Health systems	N=1	low	• Does not have primary data. • Findings may not be generalisable.

*Quality appraisal tool not used

Limitations of the review

We identified a few limitations in this review. There may have been bias in data extraction and quality assessment of papers as these 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. We realise that some studies fit into more than one themes. If studies appear to report data on more than one theme, the theme that is most

closely associated with the primary aims or hypotheses of the study was used to classify that study. This might mean that data relevant to other theme/s may have been misclassified under other themes.

We have selected studies based on their entry dates. However, the data collection periods in the individual studies varies greatly and therefore, these findings cannot be considered to representing a snapshot of the short specific timeframe.

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 06.09.2021 to 12.09.2021. It was planned and undertaken as a rapid review with a fast turnaround to provide a brief summary. We aim to update this review and summarise the existing literature weekly.

Conclusions

A change in the seasonality pattern of RSV and influenza was observed in different countries in the context of the COVID-19 pandemic. During the pandemic, a decline in number of influenza and RSV cases was reported, except by one study from France that observed a rise in percent positive influenza B cases (Giraud-Gatineau et al., 2020). Public health measures implemented against COVID-19 seem to be effective in reducing the transmission of influenza and RSV. However, a rise in both influenza and RSV cases can be expected after the relaxation of these measures. It is therefore, recommended that vaccinations against influenza should be continued, with prioritisation of high-risk groups, to combat a possible rise in cases. Vaccination against influenza can also be a synergistic preventive measure during dual outbreaks. Evidence from China suggests that influenza vaccination rates may have been high in 2019 that helped control a dual epidemic situation (COVID-19 and influenza). 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 13th September 2021 for studies with entry dates between 6th September 2021 and 12th 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.

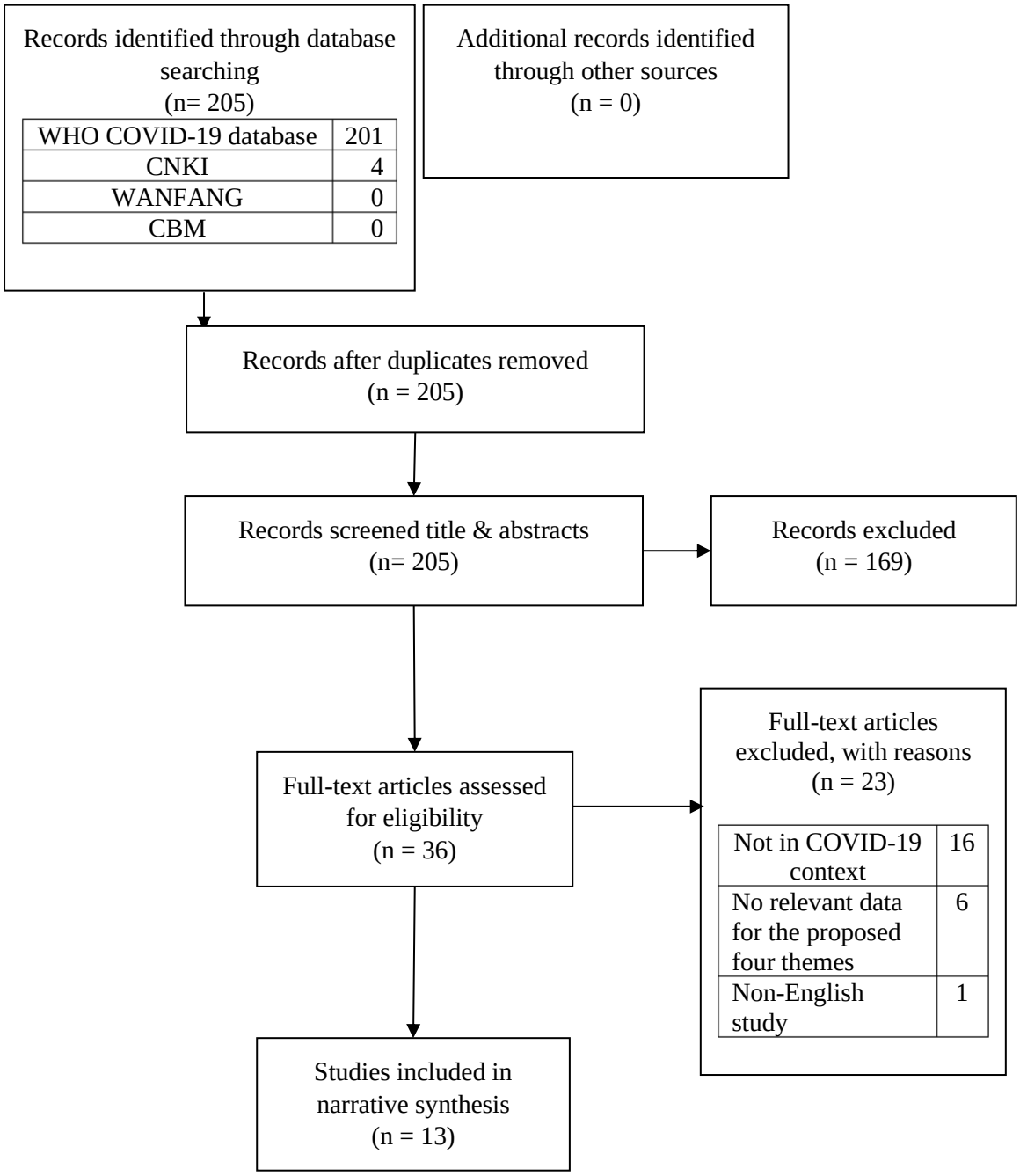
We also searched the following three Chinese literature databases- CNKI/ China National Knowledge Infrastructure, WANFANG Database and CBMdisc/China Biology Medicine disc. Search terms developed for English literature databases were translated into Chinese for literature databases.

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 prioritisation 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.

Figure 1: PRISMA flow chart



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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 prioritisation 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 or Chinese language
- **Entry date**- 06th September 2021 to 12th September 2021
- **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.

For studies published in Chinese literature databases, we will translate the search terms in Chinese language and run the searches in CNKI/ China National Knowledge Infrastructure, WANFANG Database and CBMdisc/China Biology Medicine disc. databases.

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

WHO COVID-19 literature database

The search covers the week 06/09/2021 - 12/09/2021 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:20210906 OR entry_date:20210907 OR entry_date:20210908 OR entry_date:20210909 OR entry_date:20210910 OR entry_date:20210911 OR entry_date:20210912)

CNKI:

(SU%=('呼吸道病毒' OR '呼吸系统病毒') OR SU%=('急性呼吸道感染' OR '急性呼吸系统感染') OR SU%=('呼吸道疾病' OR '呼吸系统疾病') OR SU%='呼吸窘迫综合征' OR SU%=('流感' OR '流行性感冒') OR SU%='呼吸道合胞病毒') AND SU%=('新冠' OR '新型冠状病毒' OR 'COVID-19' OR 'SARS-COV-2')

WANFANG DATA

(主题:("呼吸道病毒" or "呼吸系统病毒") or 主题:("急性呼吸道感染" or "急性呼吸系统感染") or 主题:("呼吸道疾病" or "呼吸系统疾病") or 主题:"呼吸窘迫综合征" or 主题:("流感" or "流行性感冒") or 主题:"呼吸道合胞病毒") and 主题:("新冠" or "新型冠状病毒" or "COVID-19" OR "SARS-COV-2") and Date:2021-*

CBM

("呼吸道病毒"[常用字段] OR "呼吸系统病毒"[常用字段] OR "急性呼吸道感染"[常用字段] OR "急性呼吸系统感染"[常用字段] OR "呼吸道疾病"[常用字段] OR "呼吸系统疾病"[常用字段] OR "呼吸窘迫综合征"[常用字段] OR "流感"[常用字段] OR "流行性感冒"[常用字段]) AND ("新冠"[常用字段] OR "新型冠状病毒"[常用字段] OR "COVID-19"[常用字段] OR "SARS-COV-2"[常用字段])

Appendix 3: List of included studies with publication dates

Sr. No.	Author names	Study title	Published date	Language
1.	Sunagawa et al., 2021	Disappearance of summer influenza in the Okinawa prefecture during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic	16 Nov 2020	English
2.	Boschi et al., 2021	Coinfections with SARS-CoV-2 and other respiratory viruses in Southeastern France: A matter of sampling time	17 Dec 2020	English
3.	Covin and Rutherford, 2021	Coinfection, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and Influenza: An Evolving Puzzle	15 Jun 2021	English

4.	De la Puerta et al., 2021	Common seasonal respiratory virus infections in allogeneic stem cell transplant recipients during the SARS-COV-2 pandemic	04 May 2021	English
5.	Delestrain et al.,2021	Impact of COVID-19 social distancing on viral infection in France: A delayed outbreak of RSV	02 Sep 2021	English
6.	Edwards et. al 2020	The Impact of Social Distancing for Severe Acute Respiratory Syndrome Coronavirus 2 on Respiratory Syncytial Virus and Influenza Burden	15 Jun 2021	English
7.	Giraud-Gatineau et al., 2020	Comparison of mortality associated with respiratory viral infections between December 2019 and March 2020 with that of the previous year in Southeastern France	Jul 2020	English
8.	Haddadin et al., 2021	Acute Respiratory Illnesses in Children During the sars-cov-2 Pandemic: A Prospective Multicenter Surveillance Study	31 Dec 2020	English
9.	Hadler 2020	Will Severe Acute Respiratory Syndrome Coronavirus 2 Prevention Efforts Affect the Coming Influenza Season in the United States and Northern Hemisphere?	07 Sep 2020	English
10.	Madaniyazi et al., 2021	Respiratory syncytial virus outbreaks are predicted after the COVID-19 pandemic in Tokyo, Japan	31 Aug 2021	English
11.	Sherman et al., 2020	The Effect of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Mitigation Strategies on Seasonal Respiratory Viruses: A Tale of 2 Large Metropolitan Centers in the United States	01 Mar 2021	English
12.	Stowe et al., 2021	Interactions between SARS-CoV-2 and influenza, and the impact of coinfection on disease severity: a test-negative design	30 Aug 2021	English
13.	Sun and Gong, 2021	Effective response to public health emergencies by compact medical consortium	09 Sep 2021	Chinese