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Medical Intelligence Report

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Topic: COVID-19 and Flu Season

Overview

As the seasons move towards fall, health officials have some concern about the convergence of flu season and the COVID-19 pandemic. On the positive side, because both viruses are spread mainly by droplets, measures to curtail COVID-19 transmission may also reduce the transmission of influenza. However, as influenza and pneumonia are already the eighth leading cause of death each year without a public health crisis, the additional risk from COVID-19 this fall and winter requires additional planning.

Continued Importance of Testing

While fall and winter are referred to as “flu season,” there are actually a number of different respiratory viruses that are commonly present. The flu, which is caused by infection with the influenza virus, is the most serious of the seasonal respiratory viruses, but the other viruses that circulate during cooler months have a large overlap of symptoms with the flu. Because the flu can progress to more serious complications such as pneumonia and because there are treatments available specifically for flu, there are tests available to diagnose influenza infections in order to differentiate between cold symptoms and flu symptoms.

The clinical symptoms of the flu and other seasonal respiratory viruses also overlap with the symptoms of COVID-19, making correct diagnosis even more complicated. The number of people experiencing symptoms of respiratory viruses will increase during the fall and winter, and being able to quickly differentiate between the different infections will put additional strain on the current measures to test for COVID-19. In a report from members of the House of Representatives, experts estimate that there could potentially be 100 million cases of “influenza-like symptoms” during the upcoming flu season, and differentiating the cause of symptoms would greatly overwhelm current testing capacity (Kovaleski, 2020).

With this in mind, many experts have been participating in discussions on how to continue to expand the COVID-19 testing program in the United States. One of the recommendations is to expand the types of tests being used to include antigen-based testing in addition to PCR-based tests. PCR-based tests detect viral RNA from an infection while antigen-based tests detect protein components of the virus. Both tests have advantages and disadvantages (listed in Table

1), but based on the level of testing that will be needed to distinguish between different infections, both will most likely be needed.

Table 1. Advantages and disadvantages for PCR and antigen-based testing.

PCR-Based Tests		Antigen-Based Tests	
Pros	**Cons**	**Pros**	**Cons**
• Very sensitive • Can amplify small amounts of viral DNA present for easier detection	• Labor intensive • Process is lengthy • Requires technical equipment • Requires trained operators • Sample collection includes transmission risk	• Quick results • Does not require specialized training • Less risk of transmission during sample collection • Inexpensive • Production of large quantities of tests is possible	• Less sensitive • No amplification of viral components

Distinguishing between the flu and COVID-19 is important for a number of reasons described in detail below (Solomon et al, 2020). However, the appropriate sequence of testing for flu has not yet been determined, and it is still unknown if testing for both infections at the same time or testing for flu after results are returned for COVID-19 will be more effective for diagnosis. Companies have developed and are evaluating tests that can detect SARS-CoV-2, influenza, and respiratory syncytial virus (or RSV, a virus that causes cold symptoms for most individuals, but can cause serious symptoms in some young children) using a single testing cartridge.

Differences in the priorities for testing children versus adults may emerge with the progression of flu season as the flu is normally more contagious and results in more symptoms for children compared to adults, and the reverse is true for COVID-19. Continued tracking of the effect of children on community transmission will be needed to determine if specific measures are required.

Difference in Treatments between the Flu and COVID-19

One reason it will be necessary to differentiate between the flu and COVID-19 is that the treatments for the two conditions differ. There are four FDA-approved medications for the flu, oseltamivir (Tamiflu), zanamivir (Relenza), peramivir (Rapivab), and baloxavir (Xofluza). There are two therapies that have been given Emergency Use Authorization by the FDA for treatment of COVID-19, remdesivir and convalescent plasma. Neither influenza nor SARS-CoV-2 are affected by the treatment for the other virus. Treatment with the medication for the wrong infection would not be expected to cause harm, but it would delay the initiation of useful treatment.

Identifying the correct treatment is also important because there have been drug shortages of remdesivir over the summer, and wasting doses on individuals with the flu who would not benefit from the therapy could worsen shortages.

One of the supportive treatments that has been found to be helpful for individuals with severe cases of COVID-19 is use of systemic corticosteroids, such as dexamethasone. However, use of corticosteroids for people hospitalized with the flu has been associated with increased mortality and is not recommended (Rubin, 2020). Other supportive treatments for severe flu and COVID-19 are similar, such as blood pressure management and oxygen supplementation, and can be used safely and with good effect for both the diseases.

Different Course of Infection after the Onset of Symptoms

Additionally, the disease course is different for COVID-19 and the flu. Severe symptoms appear at different time periods after the onset of symptoms, meaning that people at high risk for disease progression need to be monitored at different times. People with the flu experience the most acute symptoms during the first week of illness. Quick identification of the flu is also beneficial because the treatments are the most effective at the start of the infection. Individuals with COVID-19 do not typically have severe symptoms until the second or third week of illness, and therefore a longer observation period is needed to quickly identify serious complications.

Changes in Clinical Management

In a normal flu season, individuals with respiratory symptoms are typically managed based on clinical criteria with only those at high risk for complications getting tested for influenza infections.

However, researchers from the Division of Infectious Diseases at Brigham and Women's Hospital in Boston, Massachusetts recommend that any patient presenting with the nonspecific features of a respiratory viral infection should receive testing for SARS-CoV-2 at a minimum.

Once identified, symptoms can be managed based on the best practices determined by the CDC and other disease organizations.

Control of Transmission

One of the most important distinctions between the two infections are the measures necessary to prevent transmission of SARS-CoV-2.

Recommendations for quarantine or isolation are typically not issued for people with the flu. However, SARS-CoV-2 has been shown to be more contagious than influenza, and while both influenza and SARS-CoV-2 are mainly spread through droplets, there is additional evidence of airborne transmission associated with so-called superspreader events of SARS-CoV-2 (Solomon et al., 2020). Because of this difference, stringent quarantine and isolation protocols

are recommended to limit the spread of SARS-CoV-2 as well as the universal use of masks and social distancing.

Vaccination Recommendations during a Pandemic

Vaccination for influenza both protects the individual from becoming sick with the flu and reduces the viral reservoir in a population to reduce overall transmission (Solomon, 2020). Studies have shown that an increased vaccination rate in adults between the ages of 18 and 64 years leads to a reduction in influenza-related illness for adults over 65 years of age in their community due to an overall reduced transmission of the virus (Zanettini, 2020).

The CDC website states that annual influenza vaccination is recommended for all persons age 6 months and older to decrease morbidity and mortality caused by influenza.

This is the same recommendation that was in place last year for flu season, but the CDC added that "influenza vaccination will be paramount to reduce the impact of respiratory illnesses in the population and resulting burdens on the healthcare system during the COVID-19 pandemic."

While the recommendation for vaccination includes almost everyone, the CDC recommends that healthcare providers use every possible opportunity to extend influenza vaccination to

- **Essential workers**, such as healthcare personnel, nursing home staff, employees at long-term care facilities, pharmacy staff, and other critical infrastructure workforce
- **Individuals at increased risk for severe illness from COVID-19**, such as adults age 65 years and older, residents in a nursing home or long-term care facility, persons of all ages with certain underlying medical conditions, and members of ethnic and racial minority groups.
- **Persons at high risk for influenza complications**, such as infants and young children, children with neurologic conditions, pregnant women, adults age 65 years and older, and other persons with certain underlying medical conditions

For individuals who are currently ill from COVID-19, the CDC recommends waiting until the illness has resolved before receiving vaccination for the flu (CDC_Vaccination, 2020). The delay in vaccination is not due to risks for the patient, but rather to prevent transmission of COVID-19 to healthcare workers administering the vaccines and other individuals at the vaccination site.

Effectiveness of Flu Vaccine

The effectiveness of the flu vaccine varies from year to year because of changes in the strains circulating around the world. There are specific research groups who monitor the influenza strains during the flu seasons in the North and South Hemisphere in order to predict which

strains will be most important in the upcoming flu seasons. When conditions change quickly, the predictions can be less accurate. During the 2017-2018 flu season, the effectiveness of the flu vaccine for the year was found to be relatively low at 38%. However, it is estimated that even with a lower efficacy, vaccination prevented 7.1 million illnesses, 3.7 million medical visits, 109,000 hospitalizations, and 8,000 deaths in the United States (Grohskopf et al., 2020).

The risk reduction observed from influenza vaccination is higher for the elderly population who have chronic health conditions compared to those in the same age group without chronic conditions (Zanettini, 2020). A study showed that even when there was a poor match between the vaccine and circulating strains and in cases where the efficacy of the vaccine was only 10%, the risk reduction from the vaccine was 2 to 4-fold higher in those with chronic underlying conditions compared to the healthy population.

Rates of Vaccination

While the CDC and other public health officials have recommended vaccination for influenza for all individuals over the age of six months, the rate of vaccination in the United States and the rest of the world is normally low. The rate of flu vaccination in older adults, who are the main target in most countries, ranges between 2% to 72.8% based on the country of residence (Servick, 2020). In the United States, 45% of the adult population and 63% of children were vaccinated for flu during the 2018 and 2019 flu season (Jaklevic, 2020). The rate of vaccination was higher (68%) for those over the age of 65, the group with the highest flu mortality risk. Importantly, only 48% of young and middle aged adults who have conditions that increase the risk of complications from the flu were vaccinated during the 2018-2019 flu season. The conditions associated with higher risks from the flu include asthma, diabetes, heart disease, chronic obstructive pulmonary disease, and most cancers.

The CDC has emphasized the importance of vaccination of essential workers as well. Data from the 2018-2019 flu season indicates that only 68% of workers in long-term care facilities were vaccinated for flu in that period. As was evident early in the pandemic, control of viral transmission in nursing homes and long-term care facilities is vital for the health and safety of this vulnerable group, and increased flu vaccination would facilitate this goal. Conversely, 95% of people working in hospitals were vaccinated due to state and institutional requirements for employment in this environment.

Vaccine manufacturers have boosted production of flu vaccines by about 10% for the upcoming season. The CDC has also increased the amount of vaccine it normally purchases to supply to states and local health departments from 500,000 to 9.3 million adult doses. Health officials are reporting that they would be happy with an increase in vaccination to 60% of the eligible population, which corresponds to about 20 million more than in the 2018-2019 season (Rubin, 2020).

While the overall flu vaccination rate of the population in the United States is low, the number of ethnic and racial minorities that receive the flu vaccine each year is even lower (Grohskopf et al., 2020). A breakdown of the vaccination rates for different groups over the last two years is outlined in Table 2. The rates of vaccination were higher in the 2018 to 2019 season than in previous years, which was attributed to forecasts of a worse flu season than usual. Such

increases mainly occur after forecasts of a bad year with the lower rates, as during the 2017 to 2018 season, reemerging during the more typical forecasted years.

The trend of low vaccination rates for minority groups is specifically concerning because the effect of COVID-19 has already disproportionately affected this group of individuals in the United States. Increasing overall vaccination rates, or the rates for a specific group, will not directly reduce the effects of COVID-19, but the reduced stress from potential illness and reduced strain on the healthcare system can improve the response to circulation of two potentially serious respiratory viruses at the same time.

Table 2. Vaccination coverage of different groups in the United States.

Group	Vaccination Coverage	
	2017-2018 season	2018-2019 season
Overall	37.1%	45.3%
Non-Hispanic White	40.2%	48.7%
Non-Hispanic Black	32.3%	39.4%
Hispanic	28.4%	37.1%
Asian	42.0%	44.0%
American Indian or Alaskan Native	33.1%	37.6%
Other or multiple races	32.4%	39.7%

Circulation of a False Claim about the Influenza Vaccine

There has been dissemination of FALSE rumors that vaccination for the flu leads to an increased risk for COVID-19.

This rumor is not true, and instead there is some evidence that flu vaccination is associated with a lower risk of COVID-19 as described below. The false rumor was started by anti-vaccination groups, including a group called the Children's Health Defense. An incorrect post on social media platforms suggested that a Pentagon-backed study reported an increased risk of COVID-19 after vaccination for the flu.

While the study in question does look at influenza vaccinations, the interpretation of the results stated in the post was incorrect (Wolff, 2020a). First, the time period of the study was the 2017 and 2018 flu seasons, and the paper was submitted and published before SARS-CoV-2 existed. Therefore it is not possible to address the effects of influenza vaccination in the risk of COVID-19 from the information in the study.

The confusion over the conclusions in the study stems from the investigation of a potential effect from vaccination, called **virus interference**, that is still being investigated and has not been proven to lead to clinically relevant effects. Based on the current knowledge of the immune system, the concept of virus interference involves the possibility that vaccination may increase the risk of contracting other respiratory viruses. In the study by Wolff, personnel from the Department of Defense were evaluated to determine if there was an association between

influenza vaccination and other respiratory viruses. Based on the analysis of the study results, the author concluded that “Receipt of influenza vaccination was not associated with virus interference among our population.”

The study found no association with influenza vaccination and the overall risk of becoming infected with a respiratory virus.

When possible virus interference from influenza vaccination was evaluated for specific viruses, the author found that influenza vaccination led to protection from most influenza viruses as well as parainfluenza, RSV, and non-influenza virus coinfections. There was evidence of an increased odds of infection with the four seasonal, regularly circulating strains of coronavirus that cause cold symptoms (229E, NL63, OC43, and HKU1) and another virus called human metapneumovirus.

The author of the study, Greg G. Wolff, has written a letter to the editor of the journal that published the initial study rebutting the false claims on social media and reiterating that there is no known negative effect from the flu vaccine on SARS-CoV-2 (Wolff, 2020b).

Greg G. Wolff, the author of the paper stated the following in a Letter to the Editor,

“the results of this study cannot and should not be interpreted to represent any sort of relationship or association of influenza vaccination receipt and COVID-19 illness. Results from this study DO NOT support the anti-vaccination viewpoint of avoiding seasonal influenza vaccination, and in fact should be interpreted in the opposite manner, since significant protection against influenza was associated with vaccination receipt, and a slight decrease in the odds of infection from other respiratory viruses was also noted.

Results from this study should not be applied to or interpreted with COVID-19 in any way.”

Edward Belongia, a Senior Epidemiologist and Director at the Marshfield Clinic Research Institute in Marshfield, Wisconsin, stated in response to the rumors that the concept is potentially possible, but there has been little evidence to support virus interference in clinical studies, and there is no known clinical relevance of the effect at this time (Fichera, 2020). Dr. Belongia was an author of a clinical study published in 2013 refuting the concept of virus interference. The study indicated that influenza vaccination was not associated with an increased detection of non-influenza respiratory viruses in study participants. He also stresses that, while the report by Wolff mentions a possible association between seasonal coronaviruses that cause cold-like symptoms and vaccination with the flu, the study was not designed to prove what an association means. Specifically, the study did not include information on age groups or seasons that would change the risk of infection with one of the seasonal coronaviruses. Typically, researchers will discuss an observed, but unproven association from a study to promote further research in the field in future clinical studies.

Importantly, the study in question reports conclusive evidence of statistically significant protection by influenza vaccination against both multiple forms of the

influenza virus and other, serious non-influenza viruses, such as parainfluenza, Respiratory Syncytial Virus (RSV), and non-influenza virus coinfections.

Flu Vaccination and COVID-19 Risk

Two different research groups have found an association between flu vaccination and a reduction in risk of negative outcomes with COVID-19.

The authors of the two studies both mentioned that the erroneous conclusions circulated about the Wolff study led them to investigate if there was a connection between influenza vaccination and the outcome from COVID-19 (Rubin, 2020 and Fink et al., 2020).

Researchers at Johns Hopkins University, Cornell Medical School, and Harvard University investigated whether there was an association between the level of influenza vaccination coverage in people aged 65 years and older and the number of deaths from COVID-19 at a county-level in the United States (Zanettini et al., 2020). The investigation has been released on a pre-print server and is not yet published in a peer-reviewed journal, and the information from the preprint was discussed in a report in *JAMA* (Rubin, 2020). The study included information from 2034 counties in 50 states and the Washington DC between January 22 and June 10. The median vaccine coverage of individuals older than 65 years of age was 45%, and 1060 counties had a higher coverage than the median while 974 had lower coverage than the median. The death rate of the entire population included in the study was 18.9 per 100,000 people. When the death rate was assessed based on county, the counties with higher influenza vaccination coverage than the median had a death rate of 17.3 per 100,000 while the death rate was 20.5 per 100,000 in counties with a vaccine coverage under the median.

The researchers report that higher influenza vaccination coverage is associated with lower COVID-19 mortality.

Additionally they saw that for every 10% increase in vaccination coverage, there was a 28% decrease in the rate of mortality from COVID-19. Because data on testing was mainly reported on a state level rather than a county level, the researchers were not able to evaluate if there was a change in the SARS-CoV-2 infection rate with increased influenza vaccination.

The cause behind the association is not known. The authors speculate that it could be either due to a direct effect on the immune system or due to a lower rate of respiratory complications from influenza, resulting in a better baseline health condition, which has been shown to be an important factor in the risk for COVID-19. The authors also postulated that the effect could be due to the way the immune system responds to a vaccine compared to an active infection. Vaccination against influenza does not induce a strong killer T-cell response, but an active infection does, which leads to a reduction in T-cell diversity that would negatively affect a later response to SARS-CoV-2.

Influenza vaccination may reduce the effect on the immune system compared to infection with influenza, allowing for a more robust response after exposure to SARS-CoV-2.

Another study performed in Brazil also investigated the potential association between influenza vaccination and outcome from COVID-19 (Fink et al., 2020). This study was also released as a preprint and has not been evaluated by peer review, but was mentioned in the same JAMA report as the study by Zanetti and colleagues (Rubin, 2020). In this study, the medical records from 92,664 individuals across Brazil who had been diagnosed with COVID-19 as of June 9 were investigated to determine if there was an association with vaccination for influenza. Based on analysis of the records, 31% of the people diagnosed with COVID-19 had been vaccinated for influenza in the last vaccination campaign, which began on March 23 of 2020. The typical influenza season peaks between April and May in the northern regions of Brazil and between June and July in the southern regions.

The mortality from COVID-19 calculated in this study for people who were not vaccinated for influenza ranged from 14% in children under the age of 10 to 84% among individuals aged 90 or older. A reduction in the mortality associated with COVID-19 after vaccination for influenza was observed in all age groups, and the largest reduction occurred in individuals aged 10 to 19 (reduction of 17 percentage points) and the smallest reduction in people over the age of 90 (reduction of three percentage points). To offset potential differences in overall healthcare between locales, the researchers also investigated the association within specific institutions. Within a single healthcare institution, there was an 18% reduction in the odds of death from COVID-19 with influenza vaccination.

The reduction in mortality from COVID-19 was found to be statistically significant in all age groups over the age of 30 years, and there was an 18% reduction in the odds of death in people who were vaccinated.

The researchers also found that individuals who had been vaccinated for influenza had an 8% reduction in the odds of receiving intensive care, and a 19% reduction in the odds of receiving respiratory support. It was determined that the protective effect from vaccination was present in individuals who had been vaccinated in the campaign started in March of 2020, but not in those who had been vaccinated in previous seasons.

The authors conclude that concerns regarding potential negative side effects of influenza vaccination on SARS-CoV-2 infections are not warranted, and that individuals in Brazil had a statistically significant higher chance of surviving and less need for intensive hospital care than patients without recent influenza vaccination.

Again, the study was not able to investigate the cause of the improved outcome with vaccination, but the authors postulated many of the same methods of action listed by Zanetti and colleagues.

Reduced Flu Season in Southern Hemisphere

There has been an unusually small flu season in the Southern Hemisphere so far in 2020. Because the seasons are opposite from the Northern Hemisphere, in the south the flu season spans from May to October. South Africa's National Institute for Communicable Diseases (NICD), which is charge of monitoring cases of respiratory diseases, had only a single case of

flu reported between March and August. The average number of cases during this timeframe is usually 700 cases of flu (Servick, 2020). Some of the reduction was attributed to closure of clinics and avoidance behavior by those with mild symptoms of the flu, but officials also report that measures enacted in response to the COVID-19 pandemic, such as travel restrictions, school closures, social distancing, and mask wearing, have stopped flu from spreading in South Africa with similar reports from Australia, New Zealand, and some parts of South America.

> **Because lockdown conditions are no longer in place in most areas of the Northern Hemisphere, such a large reduction in transmission of the flu is not expected to occur during the fall and winter seasons in the North.**

However, because droplet transmission is the main form of spread for both viruses, measures for slowing the transmission of COVID-19 can be expected to slow the transmission of the flu as well.

Researchers in Qatar also reported that laboratory-confirmed cases of influenza decreased more than 30-fold after schools began closing on February 13, and all schools were closed as of March 14 (Perez-Lopez et al., 2020). Amazingly, there were no cases detected from samples tested between March 30 and June 11 at the Sidra Medicine hospital laboratory.

The WHO released their Influenza Update on August 31 where they describe that influenza activity was reported at lower levels than expected for this time of the year (WHO, 2020). The number of positive tests for influenza cases was very low even though there were similar levels, and in some cases increased levels, of testing taking place. Reports from the FluNet were used to compile the report and include information from 59 countries, areas or territories, and the last report included information from August 3 to August 16. During this time period, more than 198,148 specimens were tested, and 46 were positive.

While the reduced incidence of sickness in the Southern Hemisphere was a good sign for the residents of the area, it has led to complications for public health officials who normally monitor the flu season in the South to plan for it in the North. An important piece of data that is lacking this year was detailed information about the strains of influenza that are circulating, which is used to plan for the strains included in flu vaccines. Insufficient data from fewer patient samples could lead to a less effective vaccine.

Additionally, researchers had hoped to get more information on the effects on outcomes in individuals who are infected with both viruses, which is called **co-infection**. More details about co-infection is described below.

Co-Infection with Multiple Respiratory Viruses

One of the big questions still to be answered is if there is an effect on COVID-19 from co-infection with other viruses. There have been conflicting reports from the early part of the pandemic in Wuhan, China and the New York City area. The rate of co-infection in Wuhan is reported to be higher than that seen in New York City. The differences between different geographical regions could be caused by a difference in the local rates of respiratory virus circulation rather than a difference in the interaction between different viruses. Reports from the

influenza-like illness (ILI) surveillance data network coordinated by the CDC indicates that the number of confirmed influenza cases started decreasing in the middle of February, but testing of random samples remained at 30% until early March, suggesting there was some continued circulation of the virus (Flannery et al., 2020). Because the pandemic began at the end of the flu season in the Northern Hemisphere and the flu season was abnormally light in the Southern Hemisphere, it has been difficult for researchers to predict what to expect for the upcoming flu season.

> The other respiratory viruses which are included in a typical testing panel include Chlamydia pneumoniae, seasonal coronavirus, enterovirus or rhinovirus, human metapneumovirus, influenza A and B, Mycoplasma pneumoniae, parainfluenza, RSV, and adenovirus.

In the New York City region, researchers published an account of the clinical characteristics of individuals with COVID-19 who were treated at 12 hospitals from the Northwell Health system in in New York City, Long Island, and Westchester County, New York between March 1 and April 4 (Richardson et al., 2020). There were 5700 people in the analysis, and the rate of co-infection with another respiratory virus was 2.1%, and only one patient was infected with influenza as well as SARS-CoV-2.

The rate of co-infection was higher in a study performed in Northern California by researchers at Stanford University (Kim et al., 2020). In this study, 1217 specimens from 1206 different patients were tested for SARS-CoV-2 and other respiratory pathogens. The results of the testing indicated that 9.5% had a SARS-CoV-2 infection and 26.1% had other respiratory infections but were negative for SARS-CoV-2. Of those individuals who were positive for COVID-19, 20% were also found to have co-infection with another respiratory virus. Only one person had a co-infection with influenza. The most common viruses observed were RSV (6 people), rhinovirus (8 people), and seasonal coronaviruses (5 people). They also found that there was not a statistically significant difference in the age of participants with co-infection and those with only SARS-CoV-2 infection (46.9 years versus 51.1).

When the researchers at Stanford evaluated the participants, individuals with an infection with a respiratory virus were not more likely to have COVID-19 than people without, suggesting that infection with another virus does not make individuals more susceptible to SARS-CoV-2.

One of the initial reports from Wuhan, China describing the characteristics of 99 individuals infected with SARS-CoV-2 at the Huanan seafood wholesale market found that none of the participants had a co-infection with another respiratory virus (Chen et al., 2020). In another study from China, researchers investigated the characteristics of 544 patients treated for COVID-19 at Tongji Hospital in Wuhan between January 28 and February 18 (Yu et al., 2020). The prevalence of co-infection of SARS-CoV-2 with influenza A or B at this institution was 11.8%. The majority of individuals were infected with influenza A (84.4%), which is the strain that circulates worldwide, causing influenza pandemics. The researchers reported that there were no differences in symptoms between participants with both COVID-19 and the flu compared to those with only COVID-19. There was also a similar rate of hypertension, diabetes, and coronary heart disease between the two groups.

At the time of admission, participants were classified into three groups based on the severity of pneumonia symptoms: mild to moderate, severe, and critical. The researchers found that the proportion of participants in each category of severity was similar for those with influenza and those without.

Table 3. Classification of COVID-19 severity in participants with and without influenza.

Disease Severity	Participants with Influenza	Participants without Influenza
Mild to moderate	60.9%	60.9%
Severe	31.3%	29.7%
Critical	7.8%	9.4%

When the participants were assessed 28 days after the onset of symptoms, the researchers found there was no statistically significant difference between the groups in the proportion of participants whose infection had completely resolved, those who had had partial remission, participants who deteriorated, or those who had died. The only difference found between the two groups was that at the end of the study, 92.2% of people only infected with SARS-CoV-2 had tested negative for infection while a lower percentage (76.6%) of those with co-infections had tested negative.

Based on the data collected during the study, the researchers concluded that patients co-infected with influenza had prolonged viral shedding times, but coinfection with influenza was not associated with increased disease severity of COVID-19 pneumonia.

While it is difficult to predict due to uncertainties about the severity of the upcoming flu season, the odds of contracting both SARS-CoV-2 and influenza at the same time are considered small (Rubin, 2020). Michael T. Osterholm, the director of the Center for Infectious Disease Research and Policy at the University of Minnesota in Minneapolis, Minnesota estimates that only 3% or 4% of the population are infected with SARS-CoV-2 at a time, and 10% to 20% are infected with influenza virus during flu season. When the probabilities of exposure to both are combined, the chances are very small.

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