

Effects of non-pharmaceutical interventions for COVID-19 on influenza incidence: A systematic review

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ABSTRACT

Introduction

Since the outbreak of coronavirus disease 2019 (COVID-19), non-pharmaceutical interventions (NPIs) have been the primary preventative measure to mitigate the COVID-19 burden. However, these NPIs have also altered the pattern and incidence of other respiratory pathogens. This review aims to explore the effects of NPIs used against COVID-19, on influenza incidence.

Methods

A systematic literature search was conducted in selected databases (PubMed, Medline, Embase). Documents that highlighted a change in influenza epidemiology during the COVID-19 pandemic and were linked to NPIs were included.

The search covered articles from 1 January 2020 to 7 December 2022.

Results

This review included 13 studies reporting data from three different continents. A 14-100% decrease of influenza activity was observed since the enforcement of NPIs in early 2020.

Conclusion

This study suggests that the NPIs implemented during the COVID-19 pandemic have also significantly reduced influenza incidence. This is most likely because both coronavirus and influenza are transmitted through a similar route and the NPIs prevent this. The use of NPIs is suggested to overcome some burden of future influenza epidemics.

Type of NPI	Description	Objective
Face masks	Covering the nose and mouth using a mask	Prevent dispersal of respiratory droplets and aerosols
Cough etiquette	Covering coughs or sneezes – avoid using hands	Prevent suspension of respiratory droplets and aerosols
Hand hygiene	Washing and sanitising hands regularly	Reduce transmission through contact with surfaces
Social distancing	Avoiding crowds and maintain a distance of 2m	Reduces likelihood of droplet or aerosol transmission
Disinfecting surfaces	Frequent cleaning of high-touch objects	Reduce transmission through contact with surfaces or from fomites
Testing and isolation	Identifying infected individuals and separating them from the rest of the population	Prevent transmission from infected individuals to close contacts
Contact tracing and quarantine	Identifying exposed individuals and requesting them to isolate	Prevents transmission from exposed individuals
School closures	Temporarily closing schools or universities – distance learning	Stops spread among paediatric and young adult population, where mixing is more frequent and they can be vulnerable
Remote working	Limiting number of people in the offices	Allows social distancing to be maintained
Cancelling events	Limiting large gatherings	Reducing community transmission
Lockdown	Closing all non-essential business and implementing strict rules	Reducing population density in public spaces to prevent any transmission
Public health education	Keeping the public and scientists informed of any recommendation or changes – using social media, publications, news	Combat misinformation and encourage personal protective measures
Air quality improvement	Improving ventilation and air filtration	Reducing concentration of viral particles
Suspending international travel	Closing borders and having to quarantine or requiring negative tests when traveling	Prevents transmission between countries or geographical regions

Table 1: A list of widely used non-pharmaceutical interventions (NPI) and their mitigation objective.¹³

INTRODUCTION

Influenza is an acute respiratory infection caused by viruses of the Orthomyxoviridae family.^{1, 2} Influenza infects the respiratory tract, causing mild to severe morbidity or mortality in children and adults.³ These viruses are constantly changing, which means that influenza can emerge in new forms and has a typical seasonal epidemic pattern.⁴ On a global scale, it is estimated that these annual epidemics lead to between 3-5 million cases of severe illness and between 290,000 and 650,000 respiratory deaths.⁵ Apart from the healthcare burden, these epidemics also pose social and economic challenges.⁶ Vaccination is the most effective prevention strategy against influenza but this is undermined by the uncertainty of the epidemic stain and low vaccination uptake within the community.^{5,7} Therefore, it is helpful to explore alternative measures to prevent the spread of this common yet hazardous virus.

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) of the Coronaviridae family, was first reported in late December 2019.^{8,9} A virus sharing similar symptoms and clinical features to influenza, was declared a global pandemic by the World Health Organization (WHO) on 11 March 2020.¹⁰ In one year (end of 2020), global confirmed cases of coronavirus had surpassed 82.6 million, resulting in over 1.8 million deaths.^{11,12} As a significant health care burden with a lack of COVID-19 specific therapeutics or vaccines, the early public health response to the pandemic was the use of non-pharmaceutical interventions (NPIs).⁹ NPIs are actions that can be taken by individuals, communities, and governments to control the spread of an infectious disease without using medication. These measures include quarantine and isolation, social distancing, personal protective equipment (PPE), and hygiene and disinfection – Table 1 provides a list of commonly used NPIs during the coronavirus pandemic.¹³ NPIs are an important tool for mitigating the spread of infectious diseases and have played a key role in reducing the COVID-19 burden.

Data suggests that a combination of NPIs led to a 10-50% reduction in the weekly rate of COVID-19 transmission. Additionally, optimum implementation may have reduced peak healthcare demand by 2/3 and deaths by half.^{14, 15} Many researchers also observed a sudden decline of other respiratory viruses including influenza.¹⁶⁻¹⁸

This systematic review aims to summarise the effects of non-pharmaceutical interventions used against COVID-19, on influenza incidence.

METHODS

Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines were used for this review.¹⁹ Articles were sourced through online databases including PubMed, Embase and Medline.

Search strategy:

- A. [Influenza] (Title) OR [Flu] (Title) OR [Flu virus] (Title)
- B. [Coronavirus] (Title) OR [Covid-19] (Title) OR [2019-Ncov] (Title) OR [Covid19] (Title) OR [Covid-19] (Title) OR [Corona virus] (Title) OR [Sars-Cov-2] (Title) OR [Pandemic] (Title)

- C. [Management] (Title/Abstract) OR [Treatment] (Title/Abstract) OR [Intervention] (Title/Abstract) OR [Therapy] (Title/Abstract)
- D. [Incidence] (Title/Abstract) OR [Prevalence] (Title/Abstract) OR [Epidemiology] (Title/Abstract) OR [Frequency] (Title/Abstract) OR [Statistics] (Title/Abstract) OR [Numbers] (Title/Abstract) OR [Cases] (Title/Abstract) OR [Screening] (Title/Abstract)
- E. [A] AND [B] AND [C] AND [D].

The search was conducted on 7 December 2022 and the search entry [E] identified the final results.

Eligibility criteria:

Peer-reviewed English articles, published from 1 January 2020 to current (7 December 2022) and articles with full abstracts available were included.

- The exclusion criteria were as follows:
- Duplicated results
- Review article or any studies with no original data
- Literature not assessing effect of COVID-19 on influenza incidence
- Articles looking at the effect on influenza but not mentioning NPIs
- Articles exploring NPIs, not used during the COVID-19 pandemic
- Studies not looking at the effect on the whole population (only looking at armed forces or cancer patients)

RESULTS

In this study, 2149 documents were identified after applying the search strategy and two relevant studies were identified via other methods. After applying the eligibility criteria, 397 articles were eligible for screening. Removing duplicates (n=149) and after applying the exclusion criteria (n=235), 13 studies were included that investigated the effects of NPIs on influenza incidence during the COVID-19 period.

From these, ten studies looked at data from countries in Asia, three in North America and one in Africa. Furthermore, all the articles included had an observational study design, measuring influenza incidence using data on Influenza like illness (ILI) symptoms, influenza positivity, confirmed influenza cases or flu related hospitalisations. All the studies compared data over various influenza epidemic seasons/years and links to NPIs were made through highlighting when a certain measure was introduced by using phases of pre and post COVID-19 interventions or assessing adherence to personal protective measures or looking at hand hygiene sales and airport arrivals data. Table 2 shows a summary of all the findings.

In Lebanon, Youssef D and his colleagues, conducted a cross sectional observational study looking at the relationship between frequency of implementing personal protective measures (PPM) and likelihood of ILI symptoms. Conducted in April 2021, they used a convenience sampling method via an online survey asking participants if they experienced any ILI symptoms in the previous six months. An ILI symptom was well defined. A 5-Likert scale was used to determine adherence to

Author, Year and Location of study (Reference)	Study and Methods	Effect of NPIs on Influenza Incidence
Doroshenko A et al., 2021, Alberta (Canada) ²⁰	Observational study – using national influenza positivity surveillance data	94.3% in influenza positivity
Geng Y et al., 2021, Henan (China) ²¹	Observational study – using national influenza infection surveillance data	11.92% reduction in influenza A and a 2.15 % reduction in influenza B positivity
Huang Q-M et al., 2022, China, United States, Japan, Singapore ²²	Observational study – using national influenza infection and ILI surveillance data	61-99% decrease of influenza burden
Kim J-H et al., 2022, Korea ²³	Observational study – using national influenza positivity surveillance data	No positivity (0%) of influenza cases in the post-NPI period of 2021/2022 (100% reduction)
Kim S et al., 2022, Korea ²⁴	Observational study – using influenza cases reported from hospital ED departments	Cases fell from 101.6 per 1000 ED visits to 2 per 1000 (98% decrease) and remained substantially low till June 2021
Lee H et al., 2021, Korea ²⁵	Observational study – using national influenza infection, hospitalisation and ILI surveillance data	30.7% decrease in peak influenza activity and a 19.4-fold reduction in influenza hospitalisation
Shokri A et al., 2022, Iran ²⁶	Observational study – using national influenza infection surveillance data	From 51.1 cases per 100,000 in November 2019 to 0.1 per 100,000 (99.8% decrease)
Song S et al., 2022, Xi'an (China) ²⁷	Observational study – using national influenza infection surveillance data and 4 phases of NPI measures	97.68% decrease in influenza incidence
Tempia S et al., 2021, South Africa ²⁸	Observational study – using national influenza infection and ILI surveillance data	65.4% decrease of influenza cases
Wagatsuma K et al., 2022, Japan ²⁹	Observational study – using national influenza infection surveillance data alongside sales of hand hygiene products and passenger arrivals data	A sharp 66% decrease in influenza cases
Wang C et al., 2022, Beijing (China) ³⁰	Observational study – using national ILI surveillance data	76.2% decrease in ILI activity
Youssef D et al., 2022, Lebanon ³¹	Retrospective cross-sectional observational study – using a survey	Frequent adherence to personal protective measures such as face covering or hand hygiene, significantly reduces likelihood of ILI symptoms
Zhang K et al., 2021, Hamilton (Canada) ³²	Observational study – using influenza positive cases from a regional laboratory	0-0.1% positivity was detected (~100% decrease) and lasted till July 2021

Table 2: A summary of all studies included in this review and their relevant findings.

six PPMs. They found that the individuals who demonstrated a high level of adherence to COVID 19 PPMs were significantly less likely to have any ILI symptoms. Furthermore, regular implementation of each six PPMs – wearing face masks (aOR = 0.452, 95% CI = 0.349–0.693, p < 0.001); hand hygiene (aOR = 0.608, 95% CI = 0.524–0.922, p < 0.001); cough etiquette (aOR = 0.763, 95% CI = 0.598–0.918, p < 0.001); surface disinfection (aOR = 0.892, 95% CI = 0.632–0.911, p = 0.012); physical distancing (aOR = 0.646, 95% CI = 0.482–0.833, p = 0.031); avoiding crowded places (aOR = 0.739, 95% CI = 0.688–0.903, p = 0.049) – all highlighted a reduction in ILI symptoms.³¹

Another study in Beijing, looked at the impact of NPIs on ILI dynamics alongside urbanisation. They gathered and analysed ILI surveillance data from the Beijing Influenza Surveillance Network from January 2013 to March 2021. The data showed a steady increase in ILI cases until 2019, 3.9 per 100 person per year to 5.8, followed by a drastic decrease in 2020 to 2.2 per 100 person per year – this is when NPIs including travel restrictions and school closures were reinforced. Further analysis highlighted an overall 76.2% decrease in ILI activity. This period included the second half of the 2019-2020 influenza epidemic (reduced by 53.4%) and the 2020-2021 influenza season (reduced by 87%). The

authors also explored the effects of NPIs on different age groups and suggested the greatest ILL activity decline amongst school children (5-14 years) of 92.2%.^{26, 30}

Adherence to NPIs causing a reduction of influenza incidence during the COVID-19 period was also observed in Japan. Wagatsuma K et al. quantified the causal effect by comparing the average influenza cases per month from 2014 – 2020 obtained from the National Epidemiological Surveillance of Infectious Diseases. For NPI measurements, they obtained monthly retail sales of hand hygiene products and monthly airline passenger arrival data for the same period of 2014-2020. The results showed an abrupt decrease in influenza activity of 66% in 2020, compared to the preceding six years. The study also presented an increase of ¥3 billion (£47.6 million) per month spent on hand hygiene products in 2020 and a sharp decline of domestic and international travel, 82.4% and 52.5% decrease respectively. When compared with the influenza incidence, it was concluded that for every ¥1 billion spent there was a 5.8% decline in influenza burden and for every one million increase in domestic and international arrivals, the influenza cases increased by 7.1% and 24.9% respectively.²⁹

Similarly, Song S et al., with the objective to explore the long-term effects of NPIs against COVID-19 in Xi'an (China), conducted a time series analysis, using weekly reports of confirmed influenza cases from the Xi'an Centre for Disease Control and Prevention (CDC) from 28 March 2011 to 31 December 2021. To incorporate NPI data, four phases were used – Pre-COVID, Phase 1 – 3. Phase 1 (25 January 2020 – 8 June 2020) saw the highest emergency response with strict measures including lockdown, school closure and traffic restriction, Phase 3 (18 January 2021 – 31 December 2021) was minimum precautions such as wearing a mask. This study found a 97.68% reduction in incidence of influenza in 2020/2021 following Phase 1 in January, and an 87.22% reduction in 2021/2022 when phase 3 was implemented. During phase 1, weekly influenza incidence decreased by 95.45%. Furthermore, like the study in Beijing,³⁰ a significant reduction in influenza cases among 6-15 years olds was observed after the pandemic²⁷ Geng Y et al., in a surveillance study in Henan (China), depicted a 11.92% reduction in influenza A and a 2.15% reduction in influenza B positivity in 2020, when compared to 2019.²¹

In Korea, three separate studies, all concluded that the utilisation of NPIs as a public health measure against coronavirus resulted in reduced transmission and incidence of influenza. Kim S and his colleagues were interested in interpreting weekly influenza cases presenting in five urban emergency departments (ED) during the epidemic seasons of 2017/2018, 2018/2019 and 2019/2020. They split each season into three phases – phase 1 (weeks 40-52), phase 2 (weeks 1-9) and phase 3 (weeks 10-22). They found that the influenza cases per 1000 ED visits fell from 101.6 to 56.6 (44.3% decrease) between weeks four to five and from roughly 50 to two cases per 1000 after week nine (96% decrease). Simultaneously, during week four Korea detected its first coronavirus case and enforced “yellow” alert (hand hygiene, cough etiquette, wearing masks) and in week nine an outbreak occurred causing “red” alert (school closures, restricted movement, suspending mass gatherings).²⁴ Lee H et al. found that the 2019/2020 epidemic season was cut short by 6-12 weeks, with 30.7% decrease in peak influenza activity and a 19.4-fold reduction in influenza hospitalisation.

Interestingly, analysis of influenza stains for the past seven consecutive seasons showed a large decrease in influenza B circulation accounting for only 4%, in contrast to 26.6% to 54.9% in the past.²⁵ Finally, Kim J-H et al., focusing on 2021/2022, found no positivity (0%) of influenza cases, when compared with the pre-NPI period. Korea had started to ease its NPI measures in January 2022 but international travellers were still required to quarantine and their symptoms monitored. On the contrary, the results also showed a 1.8-fold increase in respiratory syncytial virus (RSV) positivity in 2021/2022, following the easing of NPIs.²³

Dorshenko A and his team in Alberta (Canada), conducted a time series analysis of surveillance data from 2017 to 2020. They suggested a significant reduction of 94.3% in influenza positivity in the postintervention period (-94.3%; 95% CI, -93.8 to 97.4%; P<.001). They also found a 76.5% reduction in other non-influenza respiratory viruses (-76.5%; 95% CI, -77.3 to -75.8%; P<.001).^{20, 32}

Huang Q-M et al. gathered influenza positivity and ILL surveillance data for China, United States, Japan and Singapore, covering a period from 2015 to 2020. They considered pre-COVID, early COVID, and a period of compulsory intervention. The study found that the influenza incidence peak for the 2019/2020 season was initially higher than previous seasons in China and the United States (pre-COVID), followed by a sharp decline of 94% and 99% respectively (period of compulsory NPIs). A 77% and 61% decrease of influenza burden was recorded for Japan and Singapore respectively (early COVID). Following the initial tumbling of cases, all four regions also observed an almost zero influenza incidence period for six months.²² Likewise, Tempia S. and his colleagues, described a decrease from 12.7% to 4.4% actual influenza cases in all ILL cases observed in 2020 (65.4% decrease). They also showed almost zero influenza activity even when schools, airports and business were fully reopened with no restrictions.²⁸

DISCUSSION

With the objective of exploring the effects of COVID-19 preventative NPIs on influenza incidence, all 13 studies suggested a substantial 14-100% decrease of influenza activity since the enforcement of NPIs in early 2020 in their respected regions.²¹⁻³³ The coronavirus pandemic disrupted the normal seasonal pattern of the influenza epidemic, with sporadic cases being detected outside the typical epidemic duration²⁸ and the number of cases being zero or undetected in some regions.^{23, 32} One explanation of this is that the NPIs used for COVID-19 (social distancing, face covering etc.) (Table 1) are general preventative measures against multiple pathogens. Mycobacterium tuberculosis or influenza, a bacterium or a virus respectively – are both transmitted through airborne droplets from an infected individual similar to COVID-19, therefore, measures such as wearing a face mask or maintaining a 2m distance are reducing the likelihood of spread of both pathogens and thus diseases. There are a plethora of airborne infections and NPIs are an excellent preventative measure.^{33, 34} This explanation is supported by two studies from the results that show a 76.5% reduction in non-influenza viruses and no positivity of RSV infections.^{20, 23}

Youssef D et al. providing a snapshot of the community ILL cases in Lebanon was good because they may have been able to account for individuals with poor health care seeking

behaviour due to the pandemic. The study demonstrated a significant reduction in ILI symptoms when individuals were regularly adhering to personal NPIs.³¹ Similarly, Wagastsuma et al. highlighted that for every ¥1 billion spent on hand hygiene products in 2020, there was a 5.8% decline in influenza burden.²⁹ This finding compliments the Lebanon study and emphasises the importance of hand hygiene in preventing influenza infections. All these PPMs are recommended by the WHO and various literatures have highlighted the benefits of these PPMs individually.³¹ For instance, there is mechanistic evidence that hand hygiene inactivates bacteria and viruses³⁵ and a meta-analysis reporting 16–21% decrease in respiratory infections.³⁶ Infectious airborne droplets can contaminate surfaces and if someone else comes in contact with the same surface, they are susceptible to infection. Measures such as good hand hygiene, cough etiquettes and surface disinfection reduce surface contamination and thus disease transmission.

The greatest ILI activity decline was outlined amongst school aged children in two studies.^{27, 30} Both of these regions, like many, implemented online learning or school closures as NPI measures against COVID-19. School children are exposed to more complex social networks and crowded places. Previous research has shown that the influenza virus spreads quickly when there is a high level of human contact, and schools can be particularly conducive to the rapid transmission of the virus due to the close proximity of students and the potential for touching contaminated surfaces.^{37, 38} Therefore, by stopping interaction between children in schools, influenza incidence within children is reduced and transmission from children to parents or grandparents is also terminated. However, it is important to consider the negative effects of closing schools such as declining academic performance, psychological distress in children and parents, economic burden on parents, lack of school meals and domestic violence.^{39, 40}

Data from Xi'an (China), Korea, United States, Japan and Singapore suggests a greater decline (94–99%) in influenza cases during the “strict” or “red” phase when compared to “early covid” or “yellow” phase (44–87%).^{21, 24, 28} The “strict” phase would include the highest emergency measures such as lockdown, school closures and restricted movement. These are drastic NPIs but are very effective because they prevent any non-essential or urgent interactions and individuals are more likely to follow instructions due to legal persecutions. Whereas, the “early covid” or relaxing phase would stress hand hygiene or mask recommendation. These NPIs are more focused on education and awareness of PPMs, which people tend to follow if they feel vulnerable or uncertain and are not as effective. While “strict” NPIs can be effective in controlling the spread of an influenza epidemic, they can also have unintended consequences in the long term. These effects may be more pronounced in low- and middle-income settings where public health resources are scarce. NPIs implemented over an extended period of time may contribute to health inequalities and negatively impact both physical and mental health, particularly in vulnerable communities. For example, quarantine and social distancing can lead to psychological stress and even post-traumatic stress symptoms, and may increase the risk of mortality due to social isolation.⁴¹ It is important to carefully consider the potential long-term effects of NPIs when implementing them.

A number of other findings from the results of this systematic review highlighted that the influenza cases remained to an almost zero level in early 2022, even after NPIs were lifted and most things were back to pre-pandemic

normal.^{22,23,28} This could be due to individuals continuing to practice PPMs such as hand hygiene and avoiding crowded places as they are now more aware and conscience of the benefits. However, the same studies also found that the RSV cases, following easing of NPIs, increased sharply to a greater burden than before COVID-19. One explanation by Kim J-H et al. was that the RSV spike began from an endemic source whilst influenza from international travel was still being strictly quarantined.²³ Further research and observation of epidemic patterns of influenza and other respiratory virus will help explain this finding. Another result was a 19.4-fold reduction in influenza hospitalisations emphasising the potential of NPIs against influenza epidemics and reducing the healthcare burden.²⁵

All the primary research articles in this review were able to explore the effects of NPIs used during COVID-19 on influenza but there were some limitations. In Lebanon, there is subjectivity and recall bias when using a questionnaire, also it is very difficult to get a truly random sample.³¹ Furthermore, the use of national surveillance data in multiple studies may have limited sensitivity to influenza infection detection, and the use of ILI as a measure of influenza burden is based on clinical presentation instead of laboratory confirmation, and ILI can encompass many different viruses including COVID-19. Therefore, it is difficult to get a true picture of influenza incidence. Finally, the decline in influenza could be due to reduced health care seeking behaviours or decreased testing as the focus shifted towards COVID-19.

This systematic review has some limitations. Firstly, research on COVID-19 is constantly evolving, with new findings being published globally on a regular basis and many aspects are still unknown. Despite a broad search strategy, most recent studies may not have been included. For example, two articles included in this review were identified from other sources as they were not found in the systematic search. This suggests that the search strategy was not appropriate and could cause bias. The use of MESH terms to include all relevant key terms would improve the search. Other limitations are the influenza vaccination rates of different regions, confounding factors such as viral interference and climate factors including temperature and humidity that effect seasonality of influenza, were not considered. Lastly, due to most studies being observational, effectiveness of individual NPI measures cannot be commented on and it is difficult to assess the long-term effects of NPIs because the topic is still current and ongoing.

CONCLUSION

In conclusion, regular influenza epidemics can be a major burden on the population and healthcare, however well planned NPIs as public health measures can combat this. This systematic review evaluated evidence accumulated between January 2020 and December 2022 to quantitatively highlight the impact of NPIs used to mitigate COVID-19 and their collateral effect on influenza incidence. All the studies suggested a decrease in influenza burden since the implementation of NPIs mainly due to reduced transmission however further research is recommended on the effectiveness of individual NPIs, effect of the pandemic on influenza lineage and other factors such as viral interactions.

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