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Role of Non-pharmaceutical Interventions (NPIs) During COVID-19 Pandemic: A Systematic Literature Review

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Abstract: Background: Non-pharmaceutical interventions (NPIs) as a means of prevention during the COVID-19 pandemic have gained increasing attention. NPIs are important to reduce infectious disease and flatten the curve of infection. However, data or literature on the effectiveness of NPIs is scarce. In this review, we aim to investigate the effectiveness of NPIs in the community based on previous literature. **Methods:** A literature search was conducted on seven databases (OVID, EBSCOHOST, WOS, SCOPUS, TRIP, JSTOR, and PUBMED) using the PICO method which yielded 208 articles. A PRISMA flow diagram and extraction tables were used to analyze the final 14 eligible articles spanning nine countries. **Results:** There were nine articles on human surveillance, two on patient and contact management, two on community restrictions, and one article discussing the combination of NPIs (quarantine, closure of facilities, and transit site surveillance). With the use of NPIs, there was a significant reduction of infection episodes among the target population. **Conclusions:** There has been an increasing demand for scientific evidence on NPIs during the COVID-19 pandemic, and present policy recommendations rely heavily on expert judgement. Randomized trials are required to obtain better evidence for these interventions. However, in the absence of definitive evidence, this review will help experts create feasible and widely acceptable policies and protocols for mitigation plans.

Keywords: COVID-19 pandemic; cough etiquette; hand hygiene; quarantine; closure of facilities; face mask; PPE

1. Introduction

As of June 4, 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or otherwise known as COVID-19, has affected more than 6.56 million individuals worldwide and caused more than 387,987 deaths[1]. The World Health Organization (WHO) has declared the pandemic as a Public Health Emergency of International Concern (PHEIC) on January 30, 2020[2]. Governments across the globe quickly implemented emergency lockdowns in their respective countries to help flatten the curve of infection. With the unavailability of effective vaccines, non-pharmaceutical interventions (NPIs) have been given serious attention to prevent and curb COVID-19 transmission. Numerous unknown factors, such as the distance of infective spread and the mode of transmission, have thrown a curveball to scientists. Some argue that the infection is spread via aerosolized droplets, whereas some state that it is airborne. Nevertheless, until an effective vaccine or treatment intervention becomes available, COVID-19 prevention will continuously rely on NPIs, including pandemic mitigation in the community[3]. To prevent the disease from spreading and to reduce morbidity and mortality among the public, policymakers have introduced conflicting advice on physical and social distancing. Besides, the use of N95 respirators and face masks have been controversial, especially when personal protective

equipment (PPE) shortages arose. Among the other implemented NPIs include self-quarantine, isolation of ill individuals, cough etiquette, hand hygiene, and the use of PPE[4]. NPIs are important to reduce infectious disease and flatten the curve of infection. However, data or literature on the effectiveness of NPIs is scarce. In this review, we aim to determine the effectiveness of NPIs in the community based on previous literature.

2. Methodology

A total of 208 scientific articles were identified after an extensive search on several databases (TRIP, OVID, EBSCOHOST, WOS, SCOPUS, JSTOR, and PUBMED) using NPIs search terms. Other search terms included people with WHO-defined confirmed or probable COVID-19, MERSCOV, SARS, or influenza-like illnesses (ILI). Close contacts to the index cases were also accounted for. NPIs such as one-meter social distancing, quarantine, use of a face mask or N95 respirators, proper hand hygiene and cough etiquette, and closure of facilities were also included. Various combinations of the Medical Subject Headings (MeSH) were searched for in the databases from the year 2000 [Supplementary File 1: S1] using the PICO method[5]. The inclusion criteria were the English language, peer-reviewed articles from the year 2000 to 2020. The exclusion criteria were animal studies and systematic reviews. A flow diagram of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Figure 1) was created[6]. From the search, we identified 208 titles, 14 (across nine countries) of which were eventually selected based on general relevance and compatibility [Supplementary File 2: S2]. Titles and abstracts were screened at the initial search. The full text of the articles was reviewed, and the data were extracted into pre-piloted forms in MS Excel. To avoid the risk of bias, two authors independently assessed the articles. Disagreements were resolved by discussion and consensus. Data were extracted by study identifier, study design, setting, population, intervention and comparator characteristics, main outcomes, and findings.

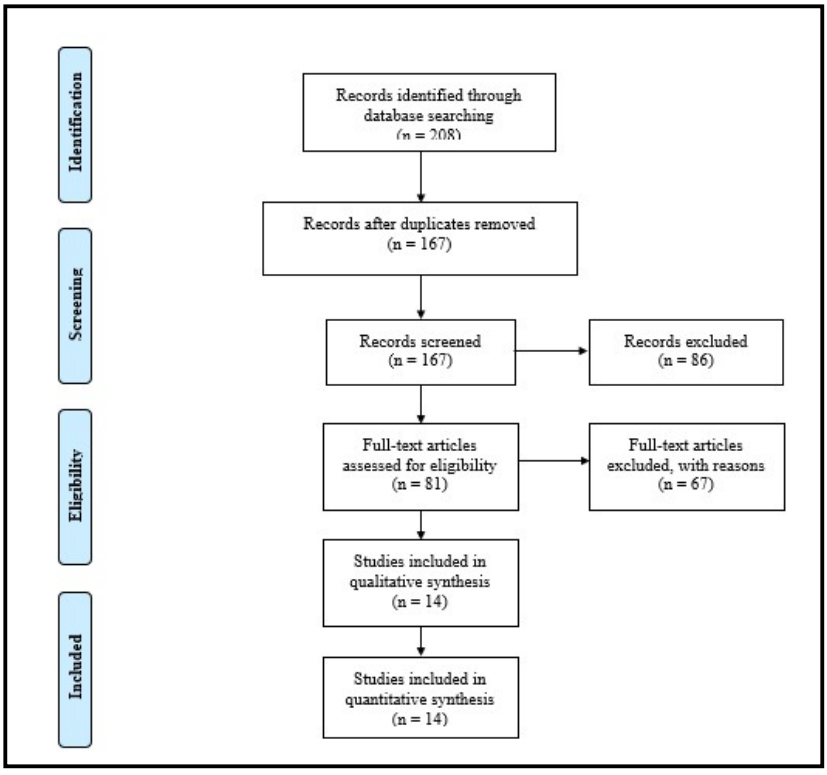

Figure 1. Prisma Diagram showing the results of the literature search[6].

The NPIs ascertained through our database search include (i) human surveillance, (ii) patient and contact management, and (iii) community restrictions (Table 1).

Table 1. Non-pharmaceutical interventions (NPIs) during influenza outbreaks[7].

Human Surveillance
• Case reporting
• Early rapid viral diagnosis
• Disinfection
• Hand hygiene
• Respiratory etiquette
• Surgical and N95 masks
• Other personal protective equipment*
Patient Management
• Isolation of sick individuals
• Provision of social support services to the isolated
Contact Management
• Quarantine**
• Voluntary sheltering***
• Contact tracing
Community Restrictions
• School closures
• Workplace closures
• Cancellation of group events
• International and domestic travel restrictions****
*Gowns, gloves, and protective eye covers
**Separation of exposed individuals from others
***Voluntary sequestration of healthy persons to avoid exposure
****Exit and entry screening, travel advisories

3. Results

3.1. Human Surveillance

A total of nine articles were identified, which involved hand hygiene, respiratory etiquette, and use of face mask in community settings [4, 8–16]. The studies are presented in Table 2 based on their results, applicability, and limitations as there were vast differences in the study design, participants, and interventions.

Of the nine studies, four were conducted in school settings, in which the outcome of the intervention was measured by the number of total absent days and numbers of secondary infections. A 3-year quasi-experimental study conducted by Apisarnthanarak et al. in Thailand found a significant reduction in laboratory-confirmed influenza infection which was associated with the practice of hand hygiene and cough etiquette among preschoolers, 60.8% in period 2 ($p = 0.008$) and 19% in period 3 ($p = 0.002$)[8]. A similar intervention performed by Stebbins et al. which measured a randomized controlled trial among elementary school students in the USA showed that there was no significant effect of the intervention on the primary study outcome of all laboratory-confirmed influenza cases (incidence rate ratio [IRR] 0.81; 95% confidence interval [CI] 0.54–1.23). However, the study revealed a statistically significant difference in protocol-specified ancillary outcomes in which a significant reduction in laboratory-confirmed influenza A infections was observed among children in intervention school compared with those in control schools, with an adjusted IRR of 0.48 (95% CI 0.26–0.87). Moreover, the study demonstrated a significant reduction in total absent days among the intervention group compared with the control group, with an adjusted IRR of 0.74 (95% CI 0.56–0.97)[14]. A few randomized controlled studies were conducted among households to assess the involvement of hand hygiene with the usage of face masks. The studies conducted by Cowling in Hong Kong

found no significant difference between the intervention group and the control group. Nevertheless, a reduced transmission among influenza confirmed cases to contacts in the intervention group was observed (adjusted OR, 0.33 [95% CI 0.13–0.87])[9].

Two other studies conducted by Aiello et al. and Seuss et al. also found a significant reduction in secondary infection in the intervention group compared with the control group[4, 13]. However, the study by Simmerman found no significant difference in terms of secondary infection in the hand hygiene group (OR = 1.20; 95% CI 0.76–1.88; p = 0.442) or the hand hygiene and face mask group (OR = 1.16; 95% CI 0.74–1.82; p = 0.525)[12].

Three studies were conducted to evaluate the effectiveness of hand hygiene. A randomized controlled trial conducted by Talaat et al. in Egypt included 20,882 school children who were divided into the intervention arm and control arm. In this trial, a significant decrease in the amount of absenteeism (reduced by 40%, $p < 0.0001$) and laboratory-confirmed influenza (reduced by 50%, $p < 0.0001$)[15] was found. Another study conducted by Lau et al. revealed that the percentages of total absent days and illness-related absent days were significantly lower in the intervention group during the flu season ($p = 0.002$, $p < 0.001$, respectively). The difference was significant during the influenza season but declined in the following months[11]. Finally, Savolainen-Kopra concluded that hand hygiene, with the use of water and soap, was associated with reduced influenza infection (reduced by 6.7%, $p = 0.04$)[16].

3.2. Patient and Contact Management

Two observational studies that evaluated the effectiveness of quarantine during the SARS outbreak in Taiwan in 2003 (Table 3) were identified. A study by Hsieh et al. found that quarantining contacts that were potentially exposed to suspected SARS patients (Level A quarantine) prevents approximately 461 additional cases of SARS and 62 additional deaths, as compared with quarantining travelers from SARS-infected areas (Level B quarantine)[17]. A study conducted by Wang supported Hsieh's findings. They both found that people who are potentially exposed to suspected SARS patients have a three times higher risk of developing SARS compared with travelers from SARS-infected areas. Wang also stated that only people with known exposure to persons infected with SARS could reduce the number of people that needed to be quarantined by 64%[18].

3.3. Community Restriction

Two observational studies on school closure during the influenza outbreak in Israel and Australia (Table 4) were conducted. A study by Heymann found a statistically significant difference in the weekly ratio of influenza-like diagnoses to non-respiratory diagnoses ($p = 0.0074$) during school closure compared with other years[19]. A survey on 233 parents in Perth, Australia, revealed that 47% thought the school closure was appropriate, 33% thought it was inappropriate, and 20% did not respond. During the school closure, only six cases reported that fulfillment of the case definition for ILI indicates the effectiveness of school closure during influenza outbreak[20].

3.4. Combination

Finally, Bartlett[21] investigated the effects of quarantine, closure of facilities, and transit site surveillance during the SARS outbreak in Beijing in 2003 (Table 5). An estimated number of around 2,610 public schools; public entertainment, such as theatres, bars, and libraries; and indoor sports facilities were closed from April 24, 2003, until early July 2003. From his observation, around 2,195 close contacts were quarantined. The attack rates were 6.3% (95% CI 5.3%–7.3%), with a range of 15.4% (95% CI 11.5%–19.2%) among spouses to 0.36% (95% CI 0%–0.77%) among work and school contacts. He found that the attack rate increased as the age of the group increased. The attack rates were 5.0% (95% CI 0%–10.5%) in children younger than 10 years and 27.6% (95% CI 18.2%–37.0%) in adults aged 60 to 69 years. Through transit site screening, only 12 out of 14 million individuals

who were screened for fever were found to have probable SARS. The time lag between illness onset and hospitalization decreased from a median of 5–6 days on or before April 20, 2003 (the day the outbreak was announced to the public), to 2 days after April 20 ($p < 0.001$)[21].

4. Discussion

In our review, there was limited evidence to support the effectiveness of NPIs in reducing the transmission of the influenza virus during outbreaks. It is important to determine which public health interventions would be effective as preventive measures to mitigate the influenza pandemic. NPIs such as hand hygiene, respiratory etiquette, face mask, and PPE could be most effective in short-distance transmission, either through direct or indirect contact. More comprehensive precautions are required to prevent the spread of disease in larger groups of people, such as isolation of sick people, quarantine of close contacts, closure of facilities, massive screening, restrictions of domestic and international travels, and cancellation of group events.

In a recent review by Bankston, it was concluded that influenza transmission among human beings occurs generally in short rather than long distances[22]. This emphasizes the importance of personal prevention in reducing the spread of infectious diseases within the community. Most of the infections that occurred caused an increase in absenteeism in schools and workplaces. Further evidence revealed that the substantial benefit of hand hygiene to prevent influenza transmission[11, 15, 16] is suggestive for direct or indirect contact as one of the most important modes of transmission. Furthermore, the effectiveness of combining personal prevention (hand hygiene, cough etiquette, and face mask) indicated[4, 8, 9, 13] that the interventions were able to reduce infections. However, there have been growing concerns about the implementation of the closure of facilities as it will negatively impact the socioeconomic status of the community[20]. Nevertheless, NPIs have resulted in major improvements in containing the spread of infectious diseases based on the available data and their outcomes.

The effectiveness of the NPIs was probably impacted by the compliance issues in the community[12, 20]. Various studies revealed low or non-compliance to NPIs[12, 20] or low acceptance among the communities. Thus, further research is required to investigate the influence of cultural and socio-behavioural factors on the levels of compliance to NPIs during a pandemic. For example, the use of face masks is more common during the SARS epidemic in Hong Kong than in Singapore[23]. This may be due to the differences in culture, which will also affect the implementation of NPI policies. Due to a lack of evidence of other forms of NPIs, such as cancellation of group events and restrictions of international and domestic travels, further research is needed to determine the effectiveness of NPIs as part of the mitigation strategy of public health. The use of disinfectants as personal prevention is also important, but due to lack of research or literature, it is less encouraged as part of the prevention method during a pandemic. Pandemic guidelines provided by the WHO and the US Centers for Disease Control and Prevention (CDC) have clearly outlined various methods for implementing NPIs to enhance its effectiveness in containing infectious diseases, especially during influenza outbreaks, such as COVID-19[24, 25]. The strengths of our review include a comprehensive literature search before the selection of articles and critical discussion of the findings which comprise wide coverage of NPIs that have been commonly used during the outbreak and related to the current situation. However, the primary limitation of our study is that during our review, articles related to the application of NPIs during the COVID-19 outbreak were lacking, which lead us to focused more on NPIs use during the influenza pandemic.

5. Conclusion

While waiting for new pharmacological treatment for COVID-19 and effective vaccines, this systematic review further reaffirms the need for NPIs to curb influenza transmission and to prevent further spread. Human surveillance, patient, and contact management as well as community restriction play significant roles in combating this pandemic. The demand for scientific evidence of NPIs during the influenza pandemic is imminent. Expert judgments on NPIs that are likely to be beneficial, feasible, and socially acceptable during outbreaks will guide policymakers in creating future guidelines and protocols. These findings should be considered while creating national, state, local, or facility epidemic mitigation plans. Further studies to evaluate the impact of NPIs to reduce the cases of ILI or Severe Acute Respiratory Infection (SARI) in the community will contribute to the promotion of public health and preparedness planning for emerging infectious diseases.

Table 2. Summary of the nine articles under human surveillance.

Study	Setting	Participants and follow-up	Study design	Interventions evaluated	Main outcomes	Findings
Aiello et al., 2012	5 university residence hall, Michigan University, USA	1178 individuals	Randomized intervention trial	Hand hygiene, face mask, and control group	Incidence of ILI cases	Significant reduction in the rate of ILI in the intervention group as compared with the control group
Apisarnthanarak et al., 2009	Private Thailand Kindergarten	240 children	Quasi-experimental study	Hand hygiene and cough etiquette	Incidence of ILI cases	Significant reduction of cases in period 2 and period 3
Cowling, 2009	45 outpatient clinics in the private and public sectors in Hong Kong	794 households	Cluster-randomized controlled trial	Hand hygiene, hand hygiene plus surgical face mask, and control group	rT-PCR-confirmed influenza infection	Significant fewer infection cases in the intervention arm compared with the control arm
Lau et al., 2012	2 Chicago Public Elementary Schools	981 students	Prospective cohort study	Hand hygiene and control group	The percentage of the total absent days and percentage of illness-related absent days	The low percentage of absenteeism could be associated with the use of hand hygiene
Salvolainen-Kopra et al., 2012	21 clusters in 6 companies in Helsinki, Finland	683 employees	Cluster-randomized intervention trial	Hand hygiene with soap and water, alcohol rub, and control group	Infection episodes	Significant reduction of infection episodes in hand hygiene with soap arm compared with alcohol rub and control group arm

Simmerman et al., 2011	The outpatient department of the Queen Sirikit National Institute of Child Health (QSNICH) in Bangkok	1589 households	Randomized controlled trial	Hand hygiene, hand hygiene plus surgical face mask, and control group	Secondary influenza infection cases	No significant difference between intervention groups
Stebbins et al., 2011	10 elementary schools in Pittsburgh, USA	3360 students	Randomized controlled trial	Hand hygiene, cough etiquette, and control group	Total absenteeism episodes and laboratory-confirmed cases of influenza	No significant differences in laboratory-confirmed cases, but there was a reduction in total absenteeism episodes
Suess et al., 2012	Recruited by the general practitioner and pediatrician in Berlin, Germany	84 households	Cluster-randomized controlled trial	Hand hygiene, face mask, and control group	Secondary infection cases	Significant reductions of infections in the intervention group compared with the control group
Talaat et al., 2011	60 elementary schools in Cairo, Egypt	20882 students	Randomized controlled trial	Hand hygiene and control group	Laboratory-confirmed influenza and the number of absenteeism caused by ILI	Significant decrease in the intervention group compared with the control group

Table 3. Summary of the two articles under patient and contact management.

Study	Setting	Participants and follow-up	Study design	Interventions evaluated	Main outcomes	Findings
Hsieh et al., 2007	SARS outbreak in Taiwan	Community	Observational study	Quarantine Level A: people with potential contacts with suspected SARS patients Quarantine Level B: people traveling from the SARS area	Number of SARS cases and mortality	Level A quarantine could be associated with the prevention of approximately 461 additional SARS cases and 62 additional deaths as compared with Level B quarantine

Wang et al., 2007	SARS outbreak in Taiwan	Community	Observational study	Quarantine Levels A & B (as above)	Identifying people who fit the criteria for quarantine	Quarantining people with known exposure to persons infected with SARS could have reduced the number of persons quarantined by approximately 64%

Table 4. Summary of the two articles under community restriction.

Study	Setting	Participants and follow-up	Study design	Interventions evaluated	Main outcomes	Findings
Effler et al., 2010	Elementary schools in Perth, Australia	233 parents	Observational study	School closure	Survey on family preparedness and impact during the closure of the school	47% thought the school closure was appropriate, 33% thought it was inappropriate, and 20% remain unknown
Heymann et al., 2009	Israel nationwide elementary schools	Children (6–12 years) Household members aged >12 years presumed to be living with these children and all other Maccabi members	Observational study	School closure	The weekly ratio of ILI diagnoses to non-respiratory diagnoses	The weekly ratio of ILI diagnoses to non-respiratory diagnoses was statistically significant for school children

Table 5. Summary of articles under the combined non-pharmaceutical intervention.

Study	Setting	Participants and follow-up	Study design	Interventions evaluated	Main outcomes	Findings
Bartlett, 2004	SARS outbreak in Beijing, China	2521 probable cases	Observational study	Quarantine, closure of facilities, and transit site screening	Attack rate and number of probable cases	The multiple control measures implemented in Beijing likely led to the rapid resolution of the SARS outbreak

List of Abbreviations

NPIs	Non-pharmaceutical interventions
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
WHO	World Health Organization
PHEIC	Public Health Emergency of International Concern
PPE	Personal Protective Equipment
ILI	Influenza-Like Illnesses
MeSH	Medical Subject Headings
CDC	Centers for Disease Control and Prevention
SARI	Severe Acute Respiratory Infection

Supplementary Materials: The following are available online at https://drive.google.com/drive/folders/1XuNBUqe8cJp77-lwG2vB7dGw72bGtWdh?usp=sharing, Table S1: PICO table, Table S2: List of final eligible articles.

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