

REVIEW ARTICLE

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

Su Peng Chua, Faiz Daud, Normaslina Mustaza

Department of Community Health, Faculty of Medicine, University Kebangsaan Malaysia, 56000, Cheras, Kuala Lumpur, Malaysia

ABSTRACT

Non-pharmaceutical interventions (NPIs) as a means of prevention during the COVID-19 pandemic have gained increasing attention. NPIs are important to reduce infectious diseases 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. A literature search was conducted on seven databases (OVID, EBSCOHOST, WOS, SCOPUS, TRIP, JSTOR, and PUBMED) using the PICO method which yielded 208 articles from 12th March to 1st April 2020. A PRISMA flow diagram and extraction tables were used to analyze the final 14 eligible articles spanning nine countries. 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. 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, this review will help experts create feasible and widely acceptable policies and protocols for mitigation plans in the absence of definitive evidence.

Keywords: COVID-19 pandemic, Cough etiquette, Hand hygiene, Quarantine, face mask

Corresponding Author:

Faiz Daud, MPH

Email: faizdaud@ppukm.ukm.edu.my

Tel: +6019-2712008

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.

METHODOLOGY

The review protocol – PRISMA

The study was guided by the PRISMA review protocol. PRISMA or otherwise known as Preferred Reporting Items for Systematic Reviews and Meta-Analyses is designed specifically for systematic reviews and meta-analyses (5). PRISMA aims to prompt researchers so that they will source the right information with an accurate level of detail. Based on this review protocol, the researchers started their systematic literature review by formulating

appropriate research questions. The researchers started the systematic search that consists of three main sub-processes: identification, screening (inclusion and exclusion criteria), and eligibility. Next, the researchers proceeded to appraise the quality of the selected articles using the Mixed Methods Appraisal Tool (MMAT) Version 2018 (6) to ensure the quality of the articles for reviewing. Finally, the researchers explore in detail the data that were extracted for analysis and validation.

Formulation of research questions

The formulation of the research question for this study was based on PICO from 12th March to 1st April 2020. PICO is a tool that assists authors to develop a suitable research question for the review. It is based on three main concepts namely Population or Problem, Interest, and Context (7). Based on these concepts, the researchers have included the three main aspects in the review namely community (Population), non-pharmaceutical interventions (Interest), and flattening the curve, reducing morbidity and mortality of COVID-19 pandemic (Context) which guided the researchers to formulate its main research question “What are the non-pharmaceutical interventions (NPIs) effective in combating COVID-19 pandemic in the community?”.

Systematic searching strategies

There are three main processes in the systematic searching strategies process namely identification, screening, and eligibility (Fig. 1).

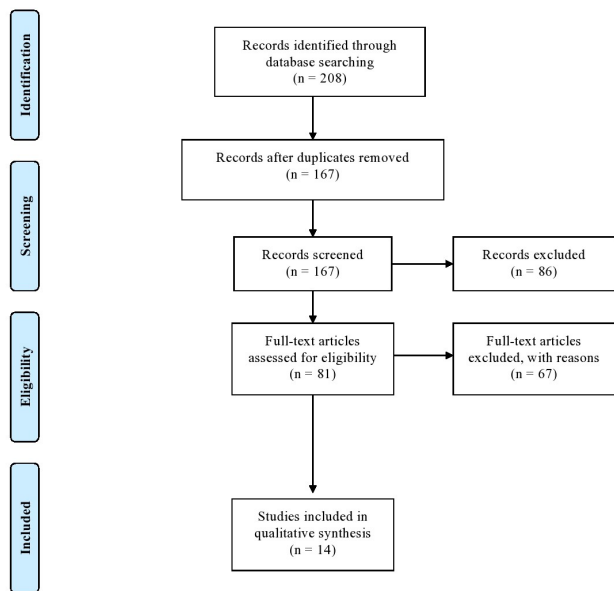


Figure 1: Prisma diagram showing the results of the literature search

Identification

Identification is the first stage involved for systematic searching strategies in this current review, whereby the identification of the synonym, related MeSH terms, and variation for the main keywords for the study are

made. This process will allow more options for the selected databases to search for more relevant articles. 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 using the PICO method (7). Seven primary databases were used for literature search namely TRIP, OVID, EBSCOHOST, WoS, Scopus, PubMed, and JSTOR. The search was also enriched by using Boolean operators and phrase searching technique; resulted in a total of 208 articles from all the included databases. The found articles were then exported from the databases and arranged for the screening process in the excel sheet.

Screening

Screening is a stage in which articles will be screened and chosen by the researchers based on specific criteria. Firstly, the titles for all articles were screened to look for duplicates. Duplicates may occur as the search was done from multiple databases. Out of 208 articles, 41 duplicate articles were removed and the balance of 167 articles was then filtered using title screening. Title screening was done based on the inclusion and exclusion criteria that have been discussed and agreed upon by all the researchers of this review. The inclusion criteria were: (1) articles that were published from 2000 to 2020, (2) full original articles, (3) articles written in the English language, and (4) observational and interventional studies related to the current study. Meanwhile, exclusion criteria were: (1) animal studies, (2) in vivo/in vitro studies, and (3) systematic reviews. Articles that were not original articles such as conference abstracts, book chapters, reports, systematic reviews, and meta-analysis were also omitted. Based on these inclusion and exclusion criteria, title screening was done and if the title seemed uncertain, the researcher would read the abstract to decide if it should be included or excluded. From this screening stage, a total of 86 articles were removed. The remaining 81 articles then proceeded with full-text articles assessments and eligibility.

Eligibility

The third stage is the eligibility process which was manually monitored by the researchers for eligibility. Full articles were retrieved and were divided among the researchers. Articles that focus on NPIs during epidemics were all included for data synthesis. This stage excluded 67 articles due to various reasons such as not focusing on NPIs during epidemics and the main outcome was not on reducing mortality or morbidity or flattening the curve of infections. Therefore, 11 eligible articles then proceeded with the quality appraisal.

Quality appraisal

The final list of studies was ranked for quality according to the MMAT which is a valid tool proven to be effective and practical for the quality assessment of a mixed-methods review (6). Narrative analysis and appraisal of selected articles were done using standardized predesigned data extraction form to ensure all related information was extracted accurately (6). Two reviewers are needed to appraise these articles. Both reviewers must accept the articles to be included in the systematic review. Any disagreement will be discussed among them and a final decision will be made. In the end, 14 articles were selected for the review.

Data extraction and analysis

Thematic analysis was used in this systematic review (8). The thematic analysis is a descriptive analysis that allows data to be merged with other data analysis techniques (9). The researchers went through all selected articles comprehensively where findings were extracted and presented in a table. The thematic analysis then began where the researchers identified patterns of extracted data of reviewed articles and gathered them in a group before successfully categorized them into three different themes. The themes developed were then discussed with a group of panel experts in public health-related research. The panel expert group subsequently approved the themes generated as being appropriate to the results of the review. 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. The NPIs ascertained through our database search included (i) human surveillance, (ii) patient and contact management, and (iii) community restrictions (Table I).

Table I: Non-pharmaceutical interventions (NPIs) during influenza outbreaks.

Human Surveillance
<ul style="list-style-type: none"> • Case reporting • Early rapid viral diagnosis • Disinfection • Hand hygiene • Respiratory etiquette • Surgical & N95 masks • Other personal protective equipment*
Patient Management
<ul style="list-style-type: none"> • Isolation of sick individuals • Provision of social support services to the isolated
Contact Management
<ul style="list-style-type: none"> • Quarantine** • Voluntary sheltering*** • Contact tracing
Community Restrictions
<ul style="list-style-type: none"> • School closures • Workplace closures • Cancellation of group events • International and domestic travel restrictions****

*Gowns, gloves and protective eye covers **Separating exposed individuals from others
 ***Voluntary sequestration of healthy persons to avoid exposure
 ****Exit and entry screening, travel advisories

RESULTS

Human Surveillance

A total of nine articles were identified, which involved hand hygiene, respiratory etiquette, and use of face mask in community settings (4, 10-18). The studies are presented in Table II 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 Apisarntharak 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 ($p = 0.002$)(10). 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% 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)(16). 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]) (11).

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, 15). 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; $p = 0.525$) (14).

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

Table II: 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 (4)	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
Apisamtharak et al., 2009 (10)	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 (11)	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 (13)	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 (18)	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 (14)	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 (16)	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 (15)	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 (17)	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

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%, $p < 0.0001$) (17) 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 (13). Finally, Savolainen-Kopra concluded that hand hygiene, with the use of water and soap, was associated with reduced influenza infection (reduced by 6.7%, $p = 0.04$) (18).

Patient and Contact Management

Two observational studies that evaluated the effectiveness of quarantine during the SARS outbreak in Taiwan in 2003 (Table III) 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 travellers from SARS-infected areas (Level B quarantine) (19). 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 travellers 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% (20).

Community Restriction

Two observational studies on school closure during the influenza outbreak in Israel and Australia (Table IV) 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 (21). 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 fulfilment of the case definition for ILI indicates the effectiveness of school closure during influenza outbreak (22).

Combination

Finally, Bartlett (23) investigated the effects of quarantine,

Table III: 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 (19)	SARS outbreak in Taiwan	Community	Observational study	Quarantine Level A: people with potential contacts with suspected SARS patients Quarantine Level B: people traveling from 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 (20)	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 IV: 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 (22)	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 (21)	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

closure of facilities, and transit site surveillance during the SARS outbreak in Beijing in 2003 (Table V). 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 ($p < 0.001$) (23).

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 (24). This emphasizes the importance of personal prevention in

Table V: Summary of articles under the combined non-pharmaceutical intervention

Study	Setting	Participants and follow-up	Study design	Interventions evaluated	Main outcomes	Findings
Bartlett, 2004 (23)	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

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 (13, 17, 18) 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, 10, 11, 15) 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 (22). 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 (14, 22). Various studies revealed low or non-compliance to NPIs (14, 22) 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 (25). 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 (26, 27). 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.

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.

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