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An Overview of Existing Evidence for Non-Pharmacological Interventions against COVID-19 Transmission

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Abstract

Background: Non-pharmaceutical interventions (NPIs) are public health measures that aim to prevent and control COVID-19 transmission in the community. This overview aimed to summarize the most commonly available options of NPIs for reducing COVID-19 transmission implemented globally.

Materials and Methods: In this overview, eight databases: Medline, EMBASE, PsycINFO, Cochrane Library, EMBASE, CINAHL, Web of Science, Scopus, and WHO database of publications on COVID-19 for peer-reviewed studies that reported on potential non-pharmacological interventions for COVID-19 were searched from 1 December 2019 through 10 January 2023. Systematic review studies proposing NPIs for reducing COVID-19 transmission were included. Two authors independently undertook screening selection, data extraction, and quality assessment (using AMSTAR 2 and SANRA).

Results: Fifteen related studies were selected. The findings suggested that the continued use of NPIs was the best containment strategy until achieving 'herd immunity' to reduce disease severity and mortality. There are three main categories of NPIs: individual (personal hygiene, hand washing, face masks), environmental (cleaning and ventilation of indoor spaces), and communal (social distancing, isolation, and quarantine). According to CDC recommendations, early response and a combination of NPIs should be implemented simultaneously to maximize effectiveness. However, most NPIs can be detrimental to the economy and physical, mental, and social well-being of the population. Therefore, their use should be guided by data on the local epidemiological situations, with the overall goal of protecting the most vulnerable individuals in society.

Conclusion: Early response and a combination of individual (hand hygiene and use of facemasks), environmental (cleaning and ventilation of indoor spaces), and communal NPLs (social distancing, isolation, and quarantine) are effective at reducing COVID-19 cases and deaths.

Key Words: COVID-19, Interventions, Non-Pharmacological, Prevention.

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1- INTRODUCTION

Throughout history, humans have witnessed various natural and anthropological disasters that disrupted the normal routine of life and caused human, financial, economic, and social losses, so the usual resources failed to meet these needs (1, 2). The World Health Organization (WHO) considers disasters as sudden ecological phenomena that require extra-organizational assistance. From the perspective of medical knowledge, an extraordinary situation occurs when the number of patients at a time is so high that additional workforce and resources are needed for treatment and care (3). Unexpected events could turn into small or large disasters based on population size and density, and restoring the conditions to the original state may be difficult and exhausting (4).

A recent crisis that has afflicted human society is the disease caused by the disease known as COVID-19. The cause was a new type of genetically modified virus from the family of coronaviruses called SARS-CoV-2,which was first detected in Wuhan, China in December 2019, and called COVID-19 soon after (5, 6). The extreme contagiosity of the virus resulted in a rapid spread throughout the world, infecting almost all countries in a short time (6-10).

After the first positive case of the new coronavirus was confirmed by the South Korean Center for Disease Control and Prevention on January 20, 2020, and following the global spread of cases, the WHO issued a statement on the outbreak of the new coronavirus on January 30, 2020, and declared it the sixth cause of global public health emergency, and a threat not only to China but to all countries (11, 12). Before the new coronavirus, public health emergency was declared due to the outbreak of the Spanish flu (H1N1) (2009), poliovirus (2014), Ebola virus in West Africa (2014), Zika virus (2016), and Ebola virus in the Democratic Republic of Congo (2019) (13, 14). The rapid global spread of the disease led the World Health Organization to declare COVID-19 a pandemic and worldwide threat (15, 16). Consequently, governments around the world implemented multiple non-pharmaceutical interventions (NPIs) to prevent or control COVID-19 infections (17-21).

Non-pharmacological interventions (NPI) or therapies (NPT) are non-chemical interventions that are theoretically supported, targeted, and replicable, performed on a patient or caregiver, and capable of obtaining a relevant benefit. NPIs are also known as community mitigation strategies (22). A large number of techniques in physiotherapy (e.g., massage, kinesitherapy), manual techniques (joint manipulations, chiropractic), psychotherapy, yoga, meditation, and other methods framed under the term non-conventional medical therapies (NCMT) (such as acupuncture, moxibustion, homeopathy) belong to the NPT realm (23).

Previous studies have found evidence for and against the effectiveness of NPIs (24-27). A recent review suggests that most studies have reported the effectiveness of NPIs (28). Still, there is varying evidence for the effectiveness of NPIs worldwide, emphasizing the importance of assessing the impact of NPIs on the transmission of COVID-19 to justify and validate their implementation. A better understanding of the effectiveness of NPIs supports future public health decisions on their use to counter potential successive waves of COVID-19. The present overview of systematic reviews and reviews summarizing the commonly available options of NPIs for reducing COVID-19 transmission aims to provide a comprehensive approach to safe and effective interventions.

2- MATERIALS AND METHODS

2-1. Study design

An overview was conducted of systematic, rapid, narrative, and scoping reviews. The Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) checklist was used as a template (29). The overview of systematic reviews followed the methodological guidance on the conduct of overviews of reviews published by the Cochrane collaboration (30).

2-2. Included studies

Systematic (preprint or published, with or without meta-analysis), scoping, narrative, and rapid reviews that summarized and synthesized primary studies on the effectiveness of non-pharmacological treatments/interventions for cases with a confirmed COVID-19 diagnosis were included in this overview. Studies were not excluded based on language, and records published in languages other than English were assessed for eligibility using machine translation (Google Translate).

2-3. Exclusion criteria

Letters, commentaries, expert opinions, theoretical and unstructured reviews, and protocols did not meet the mentioned eligibility criteria and were excluded.

2-4. Information sources

A systemic search of electronic databases Medline (via PubMed), Cochrane Library, EMBASE- Ovid, PyscINFO, CINAHL, Web of Science, Scopus, the WHO database of publications on COVID-19, and Google Scholar search engine was performed for peer-reviewed studies on potential non-pharmacological treatments/interventions for COVID-19 from 1 December 2019 through 10 January 2023. The search was done independently and in duplication by two reviewers, and any disagreement between the reviews was resolved by the supervisor.

2-5. Search

Search words were a combination of appropriate Boolean operators and included subject heading terms and keywords relevant to COVID-19 and various treatments/intervention approaches.

2-6. Study selection

Database search was done for possible studies, abstracts of the studies were screened for identification of eligible studies, full text articles were obtained and assessed and a final list of included studies was made. This process was done independently and in duplication by two reviewers and any disagreement was resolved by the superior reviewer. References were organized and managed using EndNote software (version X8).

2-7. Data collection process

A form was developed based on the data extraction template from the Cochrane Consumers and Communication Review Group and was followed for each study. Two reviewers collected the data independently. The collected data were combined and compared for accuracy, and a superior reviewer solved any discrepancies.

2-8. Data items

A data collection form was designed and piloted by two independent authors. The data collected from the selected studies included authors' names, study type (e.g., systematic or rapid review), publication date, study population or settings, number of included studies in each systematic review, the applied intervention (e.g., facemask, hand washing), journal name and impact factor, and main findings.

2-9. Risk of bias in individual studies

Two independent reviewers evaluated the methodological quality of the included reviews using A Measurement Tool to

Assess Systematic Reviews-2 (AMSTAR-2) (31). This 16-item tool appraises the methodological aspects of systematic reviews that include randomized or non-randomized primary studies. The methodological quality for each review was rated as critically low (i.e., more than one critical flaw with/without non-critical weaknesses), low (i.e., one critical flaw with/without non-critical weaknesses), moderate (i.e., more than one non-critical weakness), and high (i.e., no weakness or one non-critical weakness). Scores on the AMSTAR-2 tool range from zero to 16, and higher scores correspond to a higher quality of systematic reviews (31).

Narrative reviews were evaluated with the modified SANRA scale with six items. Each item has a score from 0 to 2, with 0 being a low and 2 a high standard score. The scale covers the following topics: explanation of (1) the importance and (2) the aims of the review, (3) literature search, and (4) referencing and presentation of (5) evidence level and (6) relevant endpoint data. The maximum possible score of a narrative review is 12 (32). Two reviewers performed the quality assessment independently and in duplication, and the third reviewer resolved any discrepancies.

2-10. Synthesis of results

A meta-analysis was not conducted due to the difference in the included studies, study designs, sample size, type of interventions used, and duration of interventions. Studies were summarized narratively, and an overview of their methods and main findings were presented.

2-11. Ethics

Approval by the research ethics committee was not necessary as the study analyzed only publicly available articles.

3- RESULTS

A total of 15 related studies (four systematic reviews and ten review articles) were included (**Figure 1**). The combined results of included studies indicated that three different non-pharmacological approaches, namely individual, environmental, and community NPIs, have been suggested for reducing COVID-19 transmission. Personal NPIs (e.g., facemasks and hand hygiene) are everyday preventive actions apart from pharmaceutical interventions such as vaccination and medicines that prevent the infection and spread of respiratory illnesses. Environmental NPIs (e.g., cleaning and ventilation of indoor spaces) are simple everyday preventive actions that help lower the risk of contact with COVID-19. Community NPIs (e.g., social distancing, isolation, and quarantine) are other critical measures to address the pandemic.

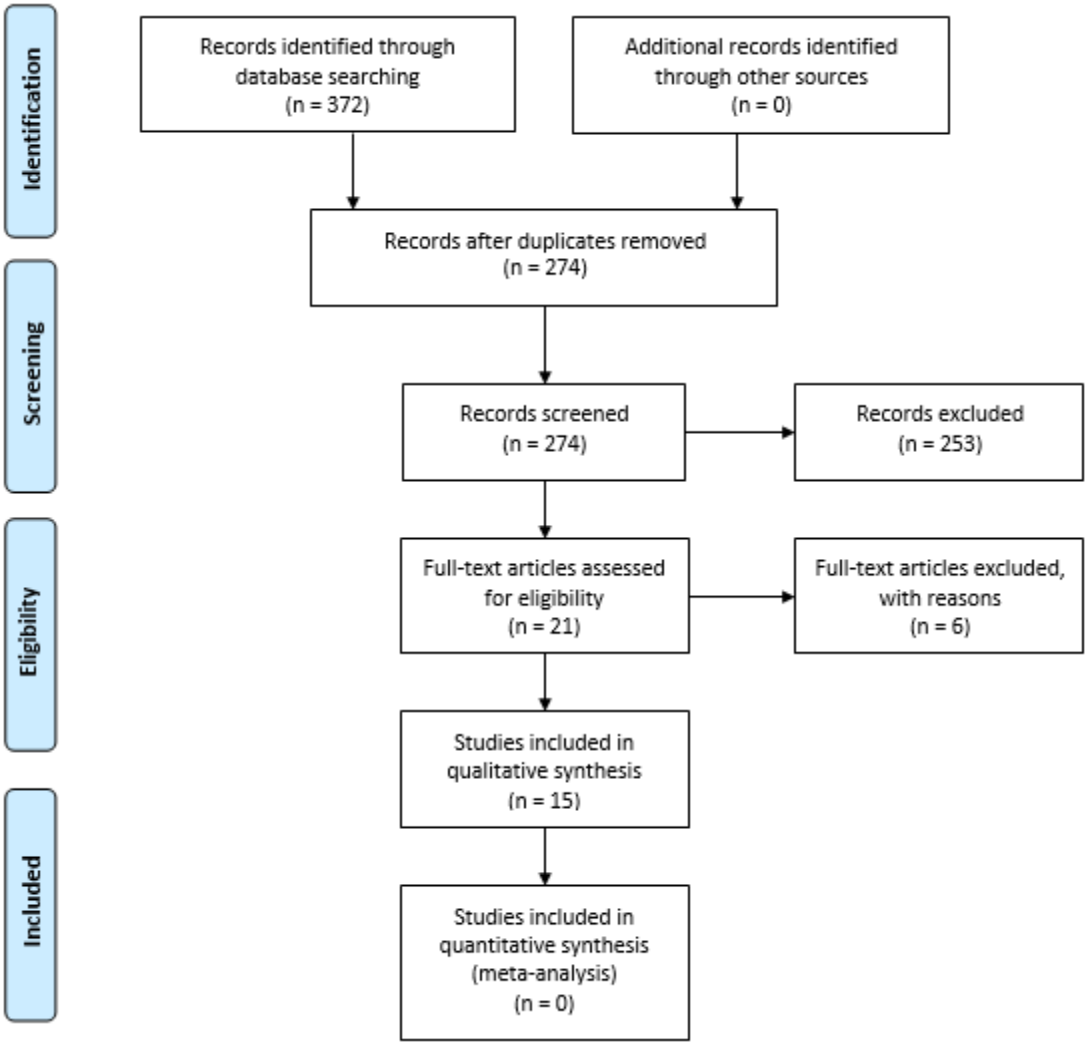

Fig.1: PRISMA flowchart.

3-1. Quality of evidence in individual systematic reviews

Table 1 shows the detailed results of the quality assessment of four systematic reviews, including the assessment of individual items and its summary. The AMSTAR-2 score had a mean of 9.2 (range 0–16). The criteria indicated that two systematic reviews had critically low quality, and two systematic reviews were of low quality. Systematic reviews require a risk of bias assessment of included primary studies, and four (100%) of the included systematic reviews presented a table summarizing bias.

Table 2 shows the detailed results of the quality assessment of 11 reviews, including the assessment of individual items and its summary. The mean sum score across all 11 reviews was 8.4 out of the 12-point SANRA scale.

Table-1: Quality assessment of systematic reviews included in overview (n=4).

Author, Year, Reference	AMSTAR 2 assessment for individual items (31)																Quality assessment (AMSTAR-2)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Mendez-Brito et al., (28)	N	PY	N	PY	Y	Y	N	PY	N	N	NA	NA	Y	Y	NA	Y	critically low
Chandan et al., (33)	Y	PY	Y	PY	Y	Y	N	PY	N	N	NA	NA	Y	Y	NA	Y	low
Talic et al., (34)	Y	PY	Y	PY	Y	Y	N	PY	N	N	NA	NA	Y	Y	NA	Y	low
Pereira et al., (35)	N	PY	Y	PY	Y	Y	N	PY	N	N	NA	NA	Y	Y	NA	Y	critically low

Y: Yes, N: No, NA: Not applicable or not available, PY: Partial Yes.

High - Zero or one non-critical weakness: The systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest. **Moderate** - More than one non-critical weakness*: The systematic review has more than one weakness, but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review. **Low** - One critical flaw with or without non-critical weaknesses: The review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest. **Critically low** - More than one critical flaw with or without non-critical weaknesses: The review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies (31).

Table-2: Quality assessment of reviews included in overview (n=11).

Author, Year, Reference	SANRA assessment for individual items (32)						Quality assessment (SANRA), ranged: (0-12)
	1	2	3	4	5	6	
Khalili et al., 36	2	1	2	1	1	1	8
Bin Arif et al., 37	2	1	2	1	1	2	9
Clemente-Suárez et al., 38	2	2	2	2	1	2	11
Shankar et al., 39	2	1	2	1	1	2	9
Tafreshi, 40	2	1	2	1	1	2	9
Goswami et al., 41	2	1	1	1	1	1	7
Zildzic et al., 42	2	2	2	1	1	2	10
Odusanya et al., 43	2	1	2	1	1	1	8
Chowdhury et al., 44	2	1	2	2	1	1	9
Gialama et al., 45	2	1	1	0	1	1	6
Atef et al., 46	2	1	1	1	1	1	7

The modified SANRA scale with 6-item version. Each item has a score from 0 to 2, 0 being the low standard while 2 is a high standard score, and covers the following topics: explanation of (1) the importance and (2) the aims of the review, (3) literature search and (4) referencing and presentation of (5) evidence level and (6) relevant endpoint data. The maximum score a narrative review can achieve is 12 (32).

3-2. Characteristics of included reviews

A total of 15 studies were included in the review, from which 14 have been published, and one was a preprint. Their combined results indicated the different non-pharmacological approaches to improving symptomatology, contagion, and the spread of COVID-19. The study selection process is shown in **Figure 1**.

Four systematic reviews and 11 reviews were included. One of the reviews was in the pediatric field and examined the food biochemistry in children infected with COVID-19. All studies were published in English between August 2020 and December 2022 in 14 different journals. Systematic literature searches were performed from 2019 (the entire year) up to January 9, 2023. One of the systematic reviews included a meta-analysis in their statistical analysis. The main characteristics of the included systematic reviews are summarized in the following and in **Table 3**.

1. A systematic review (five clinical trials) aimed to identify the existing evidence for non-pharmacological treatments to support patients with post-viral syndromes (PVS), including long COVID-19. The results showed that four non-pharmacological interventions (Pilates, tele-rehabilitation, resistance exercises, and neuromodulation) exhibited statistically significant benefits in patients experiencing signs and symptoms of PVS. The extensive public health burden of long COVID-19 has created an urgent need for further trials of supportive interventions for chronic symptoms following SARS-CoV-2 exposure (33).

2. A systematic review aimed to evaluate the evidence on the effectiveness of public health measures in reducing the incidence and mortality of COVID-19 and SARS-CoV-2 transmission. The findings suggested that personal and social protective measures, such as washing hands, wearing masks, and physical distancing, were associated with reductions in the incidence of COVID-19 (34).

3. A systematic review aimed to summarize the current evidence from empirical studies on the comparative effectiveness of NPIs implemented worldwide to control the COVID-19 pandemic. The results showed that closing the schools, followed by closing workplaces, businesses, and venues, and bans on public events were the most effective NPIs in controlling the spread of COVID-19. Early response and a combination of specific social distancing measures were effective in reducing COVID-19 cases and deaths. Public information campaigns and mask requirements had a significant role in controlling the pandemic while being less disruptive for the population than other NPIs. There was no evidence of the effectiveness of public transport closure, testing, contact tracing strategies, and quarantining or isolation of individuals (28).

4. A systematic review (of 28 studies) aimed to investigate the non-pharmacological treatments of patients with COVID-19. The results showed that no specific treatment was approved for patients with COVID-19, and the available evidence could not indicate the benefits or harms of non-pharmacological treatments yet. However, several studies showed that some treatments (including oxygen therapy, prone position, inhaled nitric oxide, intravenous infusion, passive immunotherapy, and mesenchymal stem cells (MSC)) could have a significant effect on COVID-19 (35).

5. An overview aimed to summarize the findings of systematic reviews on the pharmacological and non-pharmacological therapeutic interventions for COVID-19. The results showed that oxygen therapy and invasive or non-invasive mechanical ventilation were the most common non-pharmacological supportive care. Also, the quality of most included reviews was rated as low or critically low (36).

6. A review aimed to discuss the potential pharmacological and non-pharmacological treatment modalities for COVID-19. The results revealed that non-pharmacological

measures, including the usage of personal protective equipment, proper hand hygiene, and social distancing, were effective in curbing the spread of the infection (37).

7. A review aimed to highlight the principal non-pharmacological interventions in COVID-19. The results showed that interventions based on physical activity, nutritional, psychological, and physical therapy, and lifestyle changes could be effective in treating the disease (38).

8. A review aimed to summarize the available evidence on the impact of NPIs on COVID-19 containment. The results showed that hygiene measures (such as using facemasks) were more effective in preventing the transmission of infection at the individual level. Also, current evidence from modeling studies, natural before/after studies, and anecdotal evidence from the strategies adopted by 'role model' countries suggested that the continued use of NPIs could be the only containment strategy until achieving 'herd immunity' to reduce the disease severity and mortality. In addition, wearing facemasks should be continued for personal protection from COVID-19, even after vaccination (39).

9. A review aimed to evaluate the efficacy of the most common PI and NPI measures in controlling the COVID-19 pandemic control. The results showed that pharmacological and non-pharmacological interventions had no superiority over each other, and implementing a logical and feasible combination of both was required for the effective control and successful eradication of the disease according to the pandemic characteristics and country situations (40).

10. A review aimed to summarize the pharmacological and non-pharmacological therapeutic approaches used as prophylactic measures during the COVID-19 pandemic. The results indicated that prevention was a better option than treatment. Social distancing (a minimum distance of two meters), self-quarantine (using disposable tissues), good eating habits, and a healthy lifestyle are the best measures for preventing this global pandemic disease and can boost the immune system to keep it fighting fit. In addition, regular yogic breathing practices can prolong inhalation and exhalation, allowing more oxygen into the blood and expelling toxins and vitiated air out of the body (41).

11. A review aimed to evaluate the impact of non-pharmacological measures such as stress and sleep control (with different measures against the negative effects of anxiety and depression on the mental state), and the possible positive impacts of "forest bathing" on improving the immune response to the virus and its consequences. The results showed that the chronic course and complications of COVID-19 significantly affected the physical, mental, and emotional state of patients. Non-pharmacological measures, such as stress and sleep control, spending time in nature, a healthy diet, and physical activity, may improve the immune response to COVID-19. These measures and their positive effects on all aspects of health can make a major contribution to controlling and improving the quality of life during the COVID-19 pandemic (42).

12. A review aimed to identify the effective NPIs found that isolation, quarantine, physical distancing, use of facemasks, and hand hygiene were the most effective and best used in combination and simultaneously. The evidence showed that these measures should be instituted early on and for sustained periods. Also, they should be implemented in the context of the cultural and socioeconomic conditions of the population (43).

13. In low and middle-income countries (LMICs), strict social distancing measures (e.g., nationwide lockdown) in response to the COVID-19 pandemic were unsustainable in the long term due to knock-on socioeconomic and psychological effects. A review aimed to summarize the appraisal of available non-pharmacological interventions to lift lockdowns safely. The results proposed three non-pharmacological strategies: (1) sustained mitigation, (2) zonal lockdown, and (3) rolling lockdown (dynamic measures). However, these strategies should not be considered mutually exclusive and could be further adapted and combined depending on local disease epidemiology and socioeconomic circumstances (44).

14. An overview aimed to discuss important barriers and facilitators to adherence with NPIs based on existing knowledge and recent local literature. The results proposed three approaches/strategies that improved adherence, as follows.

(i) Individual-level barriers (improving the knowledge and understanding of risk through timely and high-quality information);

(ii) Structural and societal factors (helping tackle inequalities through the provision of psychosocial and practical support for socially vulnerable populations); and

(iii) Facilitating positive social norms and 'social emotions,' increasing the sense of collective responsibility by fostering empathy, altruism, and solidarity (45).

15. A review aimed to explore the effect of nutrition (in particular, the fat component) on the COVID-19 course in pediatric patients. The results showed that the modification of the dietary fat (as a non-pharmacological approach) could prevent or decrease the severity of COVID-19 in pediatrics. Obesity has comorbid risk factors, so a diet that could decrease the possibility of obesity would reduce the susceptibility to severe COVID-19. In addition, raising the amount of dietary fat in relation to other macronutrients (as in the ketogenic diet) could yield anti-inflammatory signals such as OHB that reduce the severity of cytokine storms. Furthermore, fat-soluble vitamins and supplements (such as omega-3) had significant roles in boosting immunity against COVID-19 (46).

Table 3: Characteristics of included systematic reviews (n=4).

Authors, Reference	Journal name	IF	Publication date	Study type	Study population/ setting	Number of included studies	Intervention applied	Main findings
Chandan et al., 33	Preprint	-	2020	Systematic review	Adults and children with a PVS including long COVID-19	five clinical trials	Pilates, telerehabilitation, resistance exercises and neuromodulation	Four NPIs (Pilates, tele-rehabilitation, resistance exercises and neuromodulation) reported statistically significant benefits in those who have experienced signs and symptoms related to PVS.
Talic et al., 34	The BMJ	96.2	2021	Systematic review	Worldwide	72 studies	Hand washing, mask wearing, chlorine or ethanol based disinfectant, physical distancing, staying at home, lockdown, quarantine, school closure, business closure, border closure, interstate travel, restrictions, and screening for fever.	The findings suggest that personal and social measures, including hand washing, mask wearing, and physical distancing are effective at reducing the incidence of COVID-19.
Mendez-Brito et al., 28	J of Infection	38.6	2021	Systematic review	Worldwide	34 studies	NPIs such as: school closing, workplace closing, public event cancelation, social gathering restrictions, public transport closure, stay-at-home requirements, internal movement restrictions, international travel restrictions, public information campaigns, testing policies, contact tracing policies and facial covering policies.	The results showed that school closing, followed by workplace closing, business and venue closing and public event bans were the most effective NPIs in controlling the spread of COVID-19.
Pereira et al., 35	Research on Biomedical Engineering	1.8	2021	Systematic review	Patients with COVID-19	28 studies	Inclusion of non-pharmacological treatments, specific to treatments on COVID-19.	Some studies show that some treatments (i.e., oxygen therapy, prone position, inhaling nitric oxide, intravenous infusion, passive immunotherapy, mesenchymal stem cells (MSC), can play an important role in relation to COVID-19.

PVS: Post-viral syndromes, NPIs: Non-pharmaceutical interventions.

4- DISCUSSION

This overview aimed to summarize the most commonly available NPIs for reducing COVID-19 transmission. The combined results of included studies indicated that prevention is superior to cure, and vaccination is the best way to prevent COVID-19. Evidence suggests that the continued use of NPIs is the best containment strategy until achieving 'herd immunity' to reduce the severity and mortality of the disease. There are three main categories of NPIs: individual (i.e., hand hygiene, healthy lifestyle, and facemasks), environmental (i.e., cleaning and ventilation of indoor spaces), and communal (i.e., isolation, quarantine, and social distancing). However, NPIs have exhibited negative impacts on economies and the physical, mental, and social well-being of the underlying population (47-49).

The COVID-19 pandemic has imposed substantial pressure on healthcare systems worldwide, and there remains an urgent need for effective strategies for the prevention and treatment of COVID-19 (50-54). With the development of COVID-19 vaccines with high but not absolute efficacy and the possibility of new virus variants limiting the efficacy of vaccination, it is necessary to turn to preventive strategies (such as NPIs) instead of therapeutic measures. The overwhelming majority of people would require a long time to achieve immunization, and overcoming the disease takes much time, especially in developing countries (55).

Non-pharmaceutical interventions were used before vaccines became widely available and continue to complement vaccination effects. Implementing these strategies could contribute to reducing the adverse effects of medication, decreasing healthcare expenditure, and improving environmental sustainability. Therefore, NPIs are recommended as a first-line measure for reducing COVID-19 transmission (23). In this context, governments worldwide have implemented several NPIs to mitigate or suppress COVID-19 infections. However, these measures require the compliance of the entire population to be effective (17-21). Evidence shows that the combined use of three NPIs levels (communal, environmental, and individual) is a relatively simple intervention to keep people safe and break the cycle of COVID-19 transmission (56-61).

4-1. Community level

The communal NPIs, such as isolation, quarantine, and social distancing, are critical ways to address the pandemic. These measures include the isolation of confirmed or suspected cases of COVID-19, managed in dedicated isolation facilities or at home (for mild cases) for a definite period. Community NPIs are policies and strategies apart from pharmaceutical interventions (such as vaccination and medical treatment delivery methods) placed by organizations and communities to help slow the spread of disease during an infectious disease outbreak, such as the COVID-19 pandemic. Two of the most commonly used community NPIs include:

- **Social distancing**: Proposing ways to increase the distance between people in places where people commonly come into close contact with one another. Priority settings include schools, workplaces, events, meetings, and similar places where people gather.
- **Closures**: Temporarily closing schools, places of worship, sporting events, concerts, festivals, conferences, and similar settings where people gather.

It should be noted that community NPIs, such as social distancing and closure, require careful planning and coordination. Public health professionals, planners, and leaders must work together to reduce the

risk of respiratory illnesses such as the COVID-19 pandemic in organizations and communities (56-73).

4-2. Environmental level

Evidence indicates that SARS-CoV-2 can survive for some time and has been detected on frequently-touched surfaces in healthcare facilities. As with other respiratory viruses, touching contaminated surfaces and thus transferring the virus to the nose, mouth, or eyes through the hands is believed to be a route of transmission. Therefore, environmental cleaning is recommended to decrease the spread of the virus through this route (56-60, 74, 75). Environmental NPIs include routine surface cleaning to eliminate the coronavirus from frequently touched surfaces and objects, such as desks and doorknobs in homes, childcare facilities, schools, workplaces, and other settings where people regularly gather (56-59). While a COVID-19 vaccination is the best way to prevent COVID-19, environmental NPIs are simple everyday preventive actions that help lower their risk of coming in contact with COVID-19 and other similar viruses on surfaces. Routine surface cleaning acts as an extra layer of protection even after people are vaccinated (56-61).

SARS-CoV-2 is an enveloped virus and, therefore, sensitive to common vermicide detergents and disinfectants. In cases of widespread community transmission, regular cleaning and disinfecting of surfaces in public spaces are recommended (58, 60, 76, 77). Other methods of surface disinfection, such as spraying disinfectants (also known as fumigation) outdoors or on large indoor surfaces (rooms, classrooms, or buildings) or using UV light radiation, are not recommended due to low effectiveness, possible damage to the environment, and the potential exposure of humans to irritant chemicals (58, 60, 78).

Heating, ventilation, and air-conditioning systems may play a complementary role in decreasing transmission in indoor spaces (including means of transportation) by increasing air exchange, decreasing air recirculation, and increasing the use of outdoor air. Increasing the rate of air exchanges per hour reduces transmission risk in closed spaces. This may be achieved by natural or mechanical ventilation, depending on the setting. The use of air recirculation without filtration should be avoided as much as possible (57-59). Educating and informing people on cleaning frequently touched surfaces and objects at home, school, work, and large gatherings are effective strategies for minimizing the risks of respiratory illnesses (58, 59, 70).

4-3. Individual level

Personal NPIs are everyday preventive actions other than pharmaceutical interventions (getting vaccinated and taking medicine) that can help prevent the infection and spread of respiratory illnesses. They include:

- Staying home during sickness
- Covering coughs and sneezes with a tissue
- Washing hands with soap and water
- Adherence to a healthy lifestyle and healthy diet, and
- Physical distance.

Factors influencing the risk of COVID-19 transmission include the setting (indoors or outdoors), whether the infectious individual is coughing, sneezing, or talking at the time of contact, the duration of exposure, and environmental conditions, such as temperature, humidity, and airflow. Transmission risk is also related to factors such as the concentration of viral particles in respiratory droplets and the

number of droplets produced (63, 70, 79, 80).

In a systematic review and meta-analysis, the physical distancing of one meter or more was linked to an approximate five-fold reduction in COVID-19 transmission risk (81). Avoiding physical contact and keeping a physical distance of 1 to 2 meters is considered a significant preventive measure and has been widely promoted worldwide (57, 58, 82).

Adherence to respiratory hygiene measures (e.g., wearing facemasks, using face shields, using a paper tissue or cloth handkerchief, cough etiquette) is strongly recommended during the COVID-19 pandemic and considered an overall good practice for preventing all diseases transmitted by direct contact through respiratory secretions (83-88). Hand hygiene (washing hands regularly with soap and water for 20-40 seconds) is recommended by WHO as a crucial preventative measure in various environments (healthcare and community settings) based on evidence from studies on influenza and other respiratory viral infections and the capacity of SARS-CoV-2 to survive on surfaces and objects (88, 89).

The effectiveness may increase in combination with other measures (e.g., the use of facemasks) (585, 60, 88). Proper hand hygiene measures are strongly recommended for the prevention of COVID-19 and all diseases transmissible by direct contact through respiratory secretions or the fecal-oral route. Likewise, the widespread availability of hand-washing facilities, water, soap, and hand hygiene solutions is crucial and must be ensured (58-61). Using facemasks is strongly recommended when physical distancing cannot be guaranteed in the community, both indoors (e.g., supermarkets, shops, and public transport) and in crowded outdoor settings with community transmission of COVID-19. In addition, the use of facemasks is essential for groups at risk of developing severe complications following infection (e.g., elderly individuals or those with underlying conditions), and people whose occupations involve extensive face-to-face contact with the public in areas with ongoing transmission. Evidence shows that facemasks are not only effective in reducing the release of respiratory secretions (source control), but also in protecting individuals (who wear them correctly) from infection (self-protection) (58, 60, 89-91).

Also, the use of face masks in the community should be considered a complementary measure and not a replacement for other preventive measures to reduce community transmission (92, 93). In addition, the potential environmental implications of the widespread use of facemasks should be considered when developing a facemask policy. The production and disposal of large amounts of facemasks from synthetic materials, if not appropriately managed, may harm the environment (91, 94). Based on the evidence, face shields have been promoted for use in the community due to several advantages over facemasks, such as ease of decontamination, not hindering communication, and being better tolerated (58, 95, 96).

Educating and reminding people about taking these everyday preventive actions consistently at home, school, work, and gatherings are an essential part of NPL strategies for minimizing the risks of the coronavirus and other respiratory illnesses. CDC recommends that countries incorporate a combination of personal, community, and environmental NPIs into their COVID-19 pandemic plans to achieve the maximum effect (61). Policymakers should expect a delay of up to 40 days from the introduction of NPI and an observed effect on the trajectory of the epidemic, which is longer than the

incubation period of the infection. This may be related to the time it takes for people to change their behavior and for the change in behavior to have an effect (97). In addition, the successful and sustained implementation of measures is a direct function of the social, economic, and cultural status of different population groups and territories (56).

At the same time, it is necessary to address the adverse effects and consequences of implementing these measures, whether social, economic, or health-related (e.g., by extending social protection to informal workers and people who have lost their income) (57- 59). Further studies on NPIs are recommended to improve their safety and efficacy after adequate vaccination coverage. Although herbal medicine or treatments with medicinal plants are part of the treatments in non-conventional medical therapies (NCMT), they are not included in this review as they deal with chemical substances. This is no implication against their use; rather, it would be desirable to supplement NPTs with medicinal plants of proven efficacy and safety.

5- CONCLUSION

The combined results of included studies indicated that prevention is a better option than cure, and vaccination is the best way to prevent COVID-19. Non-pharmaceutical interventions were used before vaccines became widely available and continue to complement vaccination efforts. Current evidence suggests that the continued use of NPIs is the best containment strategy until achieving 'herd immunity' by vaccination to reduce the severity and mortality of the disease. Based on the results, there are three different non-pharmacological interventions: individual (hand hygiene, healthy lifestyle, and using facemasks), environmental (cleaning and ventilation of indoor spaces), and community NPIs (isolation, quarantine, and social distancing), which can be effective strategies to reduce the infection. Educating and reminding people to observe these everyday preventive actions consistently at home, school, work, and gatherings are an important part of NPL strategies for minimizing the risks of the coronavirus and other respiratory illnesses. However, using NPIs has been shown to negatively influence economies and the physical, mental, and social well-being of the underlying population. Therefore, any decision on the optimal strategy for the implementation of NPIs should consider the epidemiological situation and the characteristics of the targeted population.

6- AUTHORS' CONTRIBUTIONS

Study conception or design: SMH, and FS; Data analyzing and draft manuscript preparation: SS, MN, NM, and SM; Critical revision of the paper: SMH, and SS; Supervision of the research: SMH and FS; Final approval of the version to be published: SMH, SS, MN, NM, SM, and FS.

7- CONFLICT OF INTEREST: None.

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