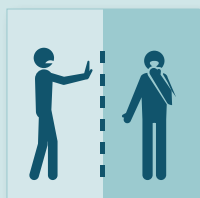# Non-pharmaceutical public health measures for mitigating the risk and impact of **epidemic** and **pandemic** influenza

World Health Organization

Contents

Non-pharmaceutical public health measures for mitigating the risk and impact of epidemic and pandemic influenza

Acknowledgements

Abbreviations and acronyms

ACH	air changes per hour
CI	confidence interval
COMBI	communication for behavioural impact
GDP	gross domestic product
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IHR	International Health Regulations
NPI	non-pharmaceutical intervention
OR	odds ratio
PISA	pandemic influenza severity assessment
RCT	randomized controlled trial
RNA	ribonucleic acid
RR	rate ratio
SAR	Special Administrative Region
USA	United States of America
UV	ultraviolet
WHO	World Health Organization

Glossary

Contact tracing   Identification and follow-up of persons who may have come into contact with an infected person.

Closure   Halting the operation of an institution or business.

Entry and exit screening   Screening travellers for influenza virus infection at their arrival in and departure from border crossings, ports and airports.

Isolation   Separation or confinement of a person who has or is suspected of having influenza virus infection, to prevent further infections.

Movement restriction   Limitation on the movements of a person who has or is suspected of having influenza virus infection.

Personal protective measures   Measures to reduce personal risk of infection, such as hand washing and face masks.

Quarantine   Separation or restriction of the movement of persons who may be infected, based either on exposure to other infected people or on a history of travel to affected areas.

R_0   Basic reproductive number, a measure of transmissibility. This number represents the average number of people infected by one infectious case in a completely susceptible population.

Respiratory etiquette   Simple hygiene practices taken by people who are coughing or sneezing to prevent person-to-person transmission of respiratory infections.

Symptomatic influenza   Influenza virus infection causing an acute illness, most commonly with rapid onset of fever and other respiratory symptoms, although a proportion of illnesses are afebrile.

Travel Advice   Health advice to travellers provided by national or international health agencies to help travellers understand the risks involved during the travel and take the necessary preventive measures or precautions to protect their health while travelling.

EXECUTIVE SUMMARY

Introduction

Influenza pandemics occur at unpredictable intervals, and cause considerable morbidity and mortality. Influenza virus is readily transmissible from person to person, mainly during close contact, and is challenging to control. In the early stage of influenza epidemics and pandemics, there may be delay in the availability of specific vaccines and limited supply of antiviral drugs. Non-pharmaceutical interventions (NPIs) are the only set of pandemic countermeasures that are readily available at all times and in all countries. The potential impacts of NPIs on an influenza epidemic or pandemic are to delay the introduction of the pandemic virus into a population; delay the height and peak of the epidemic if the epidemic has started; reduce transmission by personal protective or environmental measures; and reduce the total number of infections and hence the total number of severe cases.

Scope and purpose

This document provides recommendations for the use of NPIs in future influenza epidemics and pandemics based on existing guidance documents and the latest scientific literature. The specific recommendations are based on a systematic review of the evidence on the effectiveness of NPIs, including personal protective measures, environmental measures, social distancing measures and travel-related measures. The information provided here will be useful for national authorities that are developing or updating their plans for mitigating the impact of influenza epidemics and pandemics.

Target audience

This guideline is intended to support the development and updating of national plans for mitigating influenza epidemics and pandemics in community settings. The recommendations included in this guideline will also be of interest to individuals, organizations, institutions and local health authorities.

Methods

The guideline development process included the following stages:

1. Identify a list of NPIs that have the potential to contribute to pandemic mitigation for further review and evaluation.

2. Identify and evaluate existing systematic reviews of the NPIs listed in Step 1, and perform new systematic reviews for each NPI if recently published reviews were not available.

3. Assess the body of evidence on the effectiveness of each of the NPIs.

4. Determine the direction and strength of recommendations.

5. Draft the guideline document based on evidence and planning for strategy implementation.

The guideline development process included the formation of four main groups: a World Health Organization (WHO) guideline steering group, a systematic review team from the University of Hong Kong, a guideline development group and an external review group. The primary responsibilities of these four groups are, respectively, to oversee the process of the guideline development, to review the evidence base for each NPI, to formulate recommendations based on scientific evidence and other considerations, and to review the guidelines.

Available evidence

The evidence base for this guideline included systematic reviews of 18 NPIs, covering:

- personal protective measures (e.g. hand hygiene, respiratory etiquette and face masks);

- environmental measures (e.g. surface and object cleaning, and other environmental measures);

- social distancing measures (e.g. contact tracing, isolation of sick individuals, quarantine of exposed individuals, school measures and closures, workplace measures and closures, and avoiding crowding); and

- travel-related measures (e.g. travel advice, entry and exit screening, internal travel restrictions and border closure).

The evidence base on the effectiveness of NPIs in community settings is limited, and the overall quality of evidence was very low for most interventions. There have been a number of high-quality randomized controlled trials (RCTs) demonstrating that personal protective measures such as hand hygiene and face masks have, at best, a small effect on influenza transmission, although higher compliance in a severe pandemic might improve effectiveness. However, there are few RCTs for other NPIs, and much of the evidence base is from observational studies and computer simulations. School closures can reduce influenza transmission but would need to be carefully timed in order to achieve mitigation objectives. Travel-related measures are unlikely to be successful in most locations because current screening tools such as thermal scanners cannot identify pre-symptomatic infections and afebrile infections, and travel restrictions and travel bans are likely to have prohibitive economic consequences.

Recommendations

Eighteen recommendations are provided in this guideline (Table 1). The recommendations take into account the quality of the supporting evidence, the strength of each recommendation and other considerations. In taking decisions on interventions, each WHO Member State and each local area will need to take into account the feasibility and acceptability of proposed interventions, in addition to their anticipated effectiveness and impact. This guideline provides an overview of relevant considerations.

Table 1. Recommendations on the use of NPIs by severity level

SEVERITY	PANDEMIC[a]	EPIDEMIC
Any	Hand hygiene Respiratory etiquette Face masks for symptomatic individuals Surface and object cleaning Increased ventilation Isolation of sick individuals Travel advice	Hand hygiene Respiratory etiquette Face masks for symptomatic individuals Surface and object cleaning Increased ventilation Isolation of sick individuals Travel advice
Moderate	*As above, plus* Avoiding crowding	*As above, plus* Avoiding crowding
High	*As above, plus* Face masks for public School measures and closures	*As above, plus* Face masks for public School measures and closures
Extraordinary	*As above, plus* Workplace measures and closures Internal travel restrictions	*As above, plus* Workplace measures and closures
Not recommended in any circumstances	UV light Modifying humidity Contact tracing Quarantine of exposed individuals Entry and exit screening Border closure	UV light Modifying humidity Contact tracing Quarantine of exposed individuals Entry and exit screening Internal travel restrictions Border closure

NPI: non-pharmaceutical intervention; UV: ultraviolet.

[a] A pandemic is defined as a global epidemic caused by a new influenza virus to which there is little or no pre-existing immunity in the human population (*1*).

The most effective strategy to mitigate the impact of a pandemic is to reduce contacts between infected and uninfected persons, thereby reducing the spread of infection, the peak demand for hospital beds, and the total number of infections, hospitalizations and deaths. However, social distancing measures (e.g. contact tracing, isolation, quarantine, school and workplace measures and closures, and avoiding crowding) can be highly disruptive, and the cost of these measures must be weighed against their potential impact. Early assessments of the severity and likely impact of the pandemic strain will help public health authorities to determine the strength of intervention. In all influenza epidemics and pandemics, recommending that those who are ill isolate themselves at home should reduce transmission. Facilitating this should be a particular priority. In more severe pandemics, measures to increase social distancing in schools, workplaces and public areas would further reduce transmission.

Experimental studies suggest that hand hygiene can reduce virus on the hands. However, there is insufficient scientific evidence from RCTs to support the efficacy of hand hygiene alone to reduce influenza transmission in influenza epidemics and pandemics. Hand hygiene is an important intervention to reduce the risk of other common infectious diseases; therefore, it *should be recommended at all times*, regardless of the lack of efficacy against confirmed influenza reported in a number of RCTs. There is also a lack of evidence for the effectiveness of improved respiratory etiquette and the use of face masks in community settings during influenza epidemics and pandemics. Nevertheless, these NPIs may be conditionally recommended for ill persons because of other considerations (e.g. the high cost of face masks), and they are generally feasible and acceptable. It is likely that these personal interventions could be effective if implemented in combination.

There is sufficient evidence on the lack of effectiveness of entry and exit screening to justify not recommending these measures in influenza pandemics and epidemics. There is weak evidence, mainly from simulation studies, that travel restrictions may only delay the introduction of infections for a short period, and this measure may affect mitigation programmes, be disruptive of supply chains or be unacceptable to communities for various reasons. There is no evidence on the effectiveness of travel advice; however, given the potential benefits. it is recommended that health authorities provide advice for travellers. Border closures may be considered only by small island nations in severe pandemics and epidemics, but must be weighed against potentially serious economic consequences.

This document will serve as a core component of WHO's influenza prevention and control programme in community settings. The successful implementation of this guideline depends on the inclusion of NPIs as a robust strategic plan at national and local levels, as well as the appropriate application of its recommendations.

1. INTRODUCTION

1.1. Introduction

1.1.1. Human influenza virus transmission

Influenza virus infection causes acute respiratory illness that is usually self-limiting but can be severe in some cases. Influenza virus infects the upper and lower respiratory tract, and spreads between people, mainly during close contact. The routes of transmission are often categorized into three specific modes – contact, aerosols and (large) respiratory droplets (2) – as outlined below.

Contact transmission

Contact transmission is either direct or indirect. Transmission via direct physical contact can occur between an infected individual and a susceptible individual (e.g. through kissing or shaking hands). Transmission via indirect contact occurs through an intermediate object (e.g. touching contaminated surfaces or objects, and then touching nose or eyes) (2). Several studies have shown that influenza virus can survive for prolonged periods on certain types of surfaces, and can survive on hands for a short time (3).

Aerosol transmission

Influenza virus can be detected in fine particle aerosols with an aerodynamic diameter of less than 5 μm, emitted by infected individuals in exhalations, coughs and sneezes (4). These tiny particles (<5 μm) can reach the membrane surfaces of the upper respiratory tract and the epithelial cells of the lower respiratory tract (2). Although most aerosol transmission is likely to occur at close range because of dilution and inactivation over distance and time, these particles can remain suspended in the air for extended periods and may be responsible for higher rates of transmission, particularly in crowded areas (5).

Respiratory droplet transmission

Droplet transmission is typically defined as transmission via droplets that follow a ballistic trajectory after emission and do not remain airborne; these particles have an aerodynamic diameter of 5–10 μm (6). Virus-laden droplets are expelled into the environment by breathing, coughing and sneezing. These droplets generally travel short distances (1–2 m from the source) (5). Respiratory droplets are often thought to be the most common route of influenza transmission, although there is limited evidence to support this view.

Impacts of modes of transmission

The various modes of transmission have implications for the effectiveness of personal protective measures against influenza transmission. Also, uncertainty over the specific role of contact and aerosol transmission has hindered the optimization of control strategies. In settings where multiple exposures occur, removing one mode of transmission (e.g. by intense hand hygiene) may not be sufficient to reduce overall transmission (7). Isolating infected individuals – that is, keeping them away from others – is likely to reduce transmission by all modes.

1.1.2. Public health importance

Influenza epidemics cause considerable impact each year, and influenza pandemics occur from time to time with potentially devastating health and economic effects. Because of the delay in the availability of specific vaccines and the limited stockpiles of antiviral drugs, non-pharmaceutical interventions (NPIs) are often the only available intervention when a new pandemic influenza virus emerges and begins to spread (8). The implementation of community mitigation measures may help to reduce the impact of influenza epidemics and pandemics.

Seasonal and pandemic influenza

Seasonal epidemics of human influenza A and B virus infections occur in the winter months almost every year in temperate locations (*9*), leading to the commonly used term "seasonal" influenza. In tropical and subtropical locations, influenza A and B epidemics occur with weaker seasonality (10) or with year-round circulation (*11*).

Influenza viruses rapidly evolve to escape the immunity that results from prior infections, allowing continued circulation. The virus strains included in influenza vaccines are reviewed twice each year and are updated if necessary, to maintain higher effectiveness against prevalent circulating strains. Segments of the population at higher risk of severe outcomes from seasonal influenza infections include young children, older adults, adults with underlying medical conditions and pregnant women (*9*).

Influenza pandemics occur when a new influenza A virus emerges to which the population has little or no immunity. Before the 2009–2010 pandemic, it was believed that pandemics occurred when new influenza A subtypes emerged in the human population and replaced the previously circulating subtypes, as occurred in 1918–1919 with A(H1N1), in 1957–1958 with A(H2N2) and in 1968–1969 with A(H3N2). When influenza A(H1N1) re-emerged in 1977 after a 20-year absence (*12*), and co-circulated with A(H3N2) rather than replacing it, the re-emergence was not declared a pandemic. However, when the A(H1N1)pdm09 strain emerged in 2009, it was declared a pandemic after it spread globally, demonstrating that pandemic strains do not need to be a new subtype, but with shifted antigenicity from same sub type of seasonal influenza viruses circulating previously.(*13*). Influenza pandemics are associated with higher attack rates because of the lack of population immunity, and they can have a substantial health impact. Some of the differences between seasonal and pandemic influenza are shown in Table 2 (*9, 14-16*).

Table 2. Comparison of interpandemic ("seasonal") influenza epidemics and pandemic influenza

	INTERPANDEMIC INFLUENZA	PANDEMIC INFLUENZA
Frequency	Common: every year or almost every year	Irregular: perhaps a few times each century
Viruses involved	Influenza A and B[a]	Influenza A
Antigenic characteristics	Relatively small antigenic changes every year	Major antigenic change in surface proteins
Immunity	Some population immunity from previous infections and from vaccination	Low levels of population immunity
Vaccines	Specific vaccines available, with strains reviewed twice per year and updated as appropriate	Specific vaccines may not be available for the first 6 months
Antivirals	Antiviral drugs available in some locations, and used for the treatment of severe influenza or as clinically appropriate	Large stockpiles of antiviral drugs available in some locations

[b] Influenza C virus infections are sporadically detected, but this type has not been linked to large epidemics or major disease burden.

	INTERPANDEMIC INFLUENZA	PANDEMIC INFLUENZA
Vulnerable population	Groups with weaker immunity at highest risk of severe disease (e.g. young children, older adults, adults with underlying medical conditions and pregnant women)	Attack rates may be highest in children and young adults; pregnant women are often at higher risk, as documented in several previous pandemics; the population segments at highest risk of severe influenza are unpredictable
Impact	Perhaps 500 000 respiratory deaths on average each year	Potentially millions of deaths

There were three major pandemics in the 20th century, commonly referred to as the "Spanish flu" in 1918–1919, the "Asian flu" in 1957–1958 and the "Hong Kong flu" in 1968–1969 (Table 3). The most serious of these was the pandemic caused by the A(H1N1) virus in 1918–1919, which resulted in 20–50 million deaths, and had a particularly notable impact on mortality in young adults (17). The A(H2N2) pandemic in 1957–1958 and the A(H3N2) pandemic in 1968–1969 each caused around 1 million deaths worldwide, with the greatest impact on mortality being in older adults (18).

The first influenza pandemic in the 21st century, which occurred in 2009–2010, was caused by a new strain of influenza A(H1N1) virus that was antigenically shifted from the seasonal influenza A(H1N1) strains circulating at the time, but antigenically similar to A(H1N1) strains that had circulated before 1950 (19). The virus is thought to have emerged in central America shortly before it was first detected in North America in April 2009, and subsequently spread rapidly to other parts of the world (20). Because of the similarity with older A(H1N1) viruses, older adults had some immunity, reducing the impact of A(H1N1)pdm09 in this age group (21). Globally, the pandemic was estimated to have caused 123 000–203 000 respiratory deaths in 2009 (22).

Table 3. Influenza pandemics in the 20th and 21st century

PANDEMIC	INFLUENZA A SUBTYPE	MORTALITY IMPACT
1918–1919 "Spanish flu"	H1N1	20–50 million deaths (17)
1957–1958 "Asian flu"	H2N2	1.1 million deaths (23)
1968–1969 "Hong Kong flu"	H3N2	1 million deaths (23)
2009–2010 H1N1pdm09	H1N1	123 000–203 000 respiratory deaths (22)

Influenza pandemics typically occur in epidemic waves. For example, in 2009 the United States of America (USA) experienced a spring epidemic of A(H1N1)pdm09 that had a limited impact; the spring epidemic was followed by a much larger autumn epidemic that had a major health impact (24). Subsequent epidemics of A(H1N1)pdm09 have occurred every 2–3 years since 2009, with similar epidemiological characteristics to other seasonal influenza epidemics.

The origin of pandemics

A much greater range of influenza A subtypes of viruses circulates in animals, particularly in wild aquatic birds. Although human infections with avian influenza A subtypes are sporadic, there is a risk that these viruses will develop the capacity for effective transmission among humans, leading to the next pandemic. The emergence of highly pathogenic A(H5N1) in 1997 raised the significant concern because of the severity of laboratory-confirmed human infections (*25*). More than 1000 laboratory-confirmed human infections with avian influenza A(H7N9) virus occurred in China in the period 2013–2018 (*26*), with no sustained human-to-human transmission (*27*). Several other avian influenza A subtypes (e.g. H9N2, H6N1 and H7N7) have caused sporadic human infections (*28*). As demonstrated in 2009, influenza pandemics can also emerge from swine influenza viruses.

Non-pharmaceutical interventions

NPIs (also known as non-pharmacological interventions) include all measures or actions, other than the use of vaccines or medicines, that can be implemented to slow the spread of influenza in a population. In the early stage of influenza epidemics and pandemics, NPIs are often the most accessible interventions, because of the time it takes to make specific vaccines available and because most locations do not have large stockpiles of antiviral drugs (*8*). Therefore, these mitigation measures will play a major role in reducing transmission in community settings. There are several objectives of NPIs in an epidemic that is the first wave or subsequent wave of a pandemic or a seasonal influenza epidemic (*29, 30*).

Some NPIs may be able to delay the start of an epidemic, which could be particularly important if the resulting delay is long enough to allow specific vaccines to be distributed and reduce the impact of the epidemic. Once an epidemic has started, NPIs may also be used to delay the peak of the epidemic, again allowing time for vaccines to be distributed, or for health care providers to better prepare for a surge in cases.

By reducing transmission in the community, the epidemic may be spread out over a longer period, with a reduced epidemic peak. This can be particularly important if the health system has limited resources or capacity (e.g. in terms of hospital beds and ventilators). Also, overall morbidity and mortality can be reduced even if the total number of infections across the epidemic is not reduced.

Some interventions may aim to reduce the total number of infections, and therefore also reduce the total number of severe cases, hospitalizations and deaths.

Each of these consequences should contribute to reducing the overall impact of the epidemic or pandemic. NPIs outside of health care settings usually focus on reducing transmission by personal protective or environmental measures (e.g. hand hygiene); reducing the spread in the community (e.g. isolating and treating patients, closing schools and cancelling mass gatherings); limiting the international spread (e.g. traveller screening); and improving risk communication with the public (*31*).

Fig. 1. Intended impact of NPIs on an influenza epidemic or pandemic by reducing person-to-person transmission.
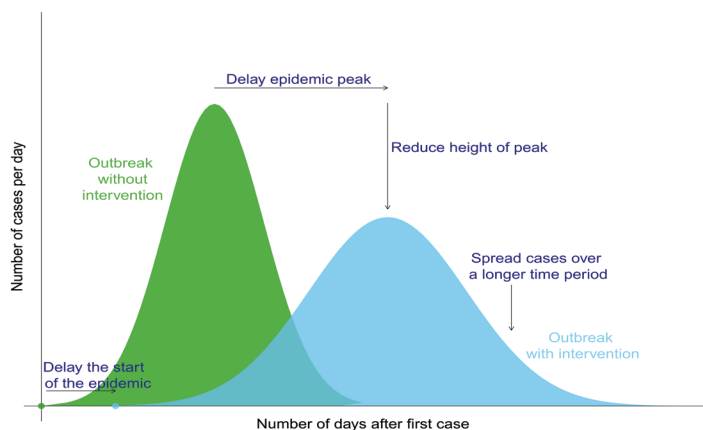
NPI: non-pharmaceutical intervention.
*Sources: US Centers for Disease Control and Prevention and
European Centre for Disease Prevention and Control guidelines (29, 30).*

1.1.3. History of the guidelines for NPIs in influenza pandemics

WHO published guidance on NPIs in 2009 in response to the emergence of influenza A(H1N1)pdm09 (32-35). That guidance provided recommendations on the measures that can be used to reduce influenza transmission and mitigate the impact of epidemics and pandemics. The present update is the first since the 2009–2010 pandemic, and it takes into account both the experiences during that pandemic and the research on NPIs done during the pandemic and since then. This guideline includes an updated review of all available evidence on the effectiveness of NPIs in mitigating the risk and impact of influenza epidemics and pandemics, and will contribute to preparations for the next pandemic.

1.2.   Scope, purpose and target audience

The overarching question posed in this guideline is "*What are the effective non-pharmaceutical public health measures for mitigating the risk and impact of influenza epidemics and pandemics in community settings?*"

Target audience
This guideline aims to support the development and updating of national plans for mitigating influenza epidemics and pandemics in community settings. The advice will also be of interest to individuals, organizations, institutions and local health authorities.

Scope and purpose
This guideline was developed from the existing guidance documents and the scientific literature. It examines evidence on the effectiveness of each of the NPIs in community settings, and provides recommendations for dealing with future influenza epidemics and pandemics. The recommendations given here may help national or local health authorities to plan and make decisions for individuals or institutions outside of health care settings. The essential elements of these decisions are personal protective measures, environmental measures, social distancing measures, travel-related measures and risk communication. In addition, countries, localities, communities, schools, families and individuals can use this NPI guideline to determine the most appropriate measures to use, to mitigate the spread and minimize the adverse consequences of influenza epidemics and pandemics. Specific targets for the early implementation of NPIs include slowing the transmission of infections in the community, spreading cases out over a longer period and reducing peak demand for medical services. Health system preparedness measures (e.g. ensuring adequate hospital beds, essential medicines and medical equipment) were outside the scope of this guideline.

The systematic review had some limitations, including publication bias and difficulties in addressing generalisability owing to the countries and regions where the studies selected were performed. Social and cultural differences between different countries and regions will influence the overall effectiveness of the NPI in different countries, and this needs to be emphasized, to moderate expectations. Implementation of NPIs should be flexible depending on the local or national situation (or both).

1.3. International Health Regulations

The International Health Regulations (IHR) (2005) (*36*) entered into force in 2007 and have two overarching objectives (Article 2):

- to set out obligations and mechanisms for "a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade"; and

- to strengthen the preparedness and capacities of countries so they can proactively detect, assess, report and address acute public health threats early.

The IHR (2005) seek to balance the sovereignty of individual States Parties with the common good of the international community, and take account of economic and social interests as well as the protection of health. Under the IHR (2005), governments are entitled to implement public health measures to protect the health of their populations during public health events respecting three golden rules, which are that such measures must be based on scientific principles, respect human rights, and not be more onerous or intrusive than reasonably available alternatives. When measures exceed these parameters, countries are obliged to provide the public health rationale to WHO within 48 hours of implementation, and to rescind the measures if they are deemed unjustified.

1.4. Pandemic influenza severity assessment framework

The pandemic influenza severity assessment (PISA) framework was introduced by WHO in 2017 (*37*). The severity of an influenza epidemic or pandemic is evaluated and monitored through three specific indicators: transmissibility (referring to incidence), seriousness of disease, and impact on health care system and society. The severity is categorized into five levels: no activity or below seasonal threshold, low, moderate, high or extraordinary (*37*). The PISA framework is being tested and improved during seasonal influenza epidemics; the aim is to help public health authorities to monitor and assess the severity of influenza, and to inform appropriate decisions and recommendations on interventions. Of particular relevance to these guidelines on NPI use, the PISA evaluation of severity may inform the choice of which interventions to use and when to use them (e.g. some interventions may only be recommended in severe epidemics or pandemics).

1.5. Guideline development process

1.5.1. Contributors to the process

This guidance document was developed with contributions from the systematic review team, guideline development and review groups and WHO Secretariat (the steering group) in accordance with the requirements of the *WHO handbook for guideline development* (*38*). The details of the contributors can be found in the Acknowledgements.

1.5.2. Guideline development steps

Systematic review
Following the process outlined in the *WHO handbook for guideline development* (*38*), evidence was identified, synthesized and presented in a comprehensive and unbiased manner. Based on the list of specific NPIs provided by the steering group, a systematic review was conducted for each NPI using four databases (MEDLINE, PubMed, EMBASE and Cochrane Library) and the Cochrane Central Register of Controlled Trials (CENTRAL).

The review steps were as follows:
1.   Developing research questions, and inclusion or exclusion criteria.
2.   Searching for any systematic review published within 5 years (i.e. since January 2014), and updating that existing review if a recently published review was found.
3.   Conducting a full systematic review if a recent review could not be identified.
4.   Selecting articles and extracting data. Two independent reviewers screened all titles and abstracts of the potentially relevant studies; if the studies described the effectiveness of NPIs in reducing influenza virus transmission, the reviewers read the full-length text and extracted relevant data.

No language restriction was applied in the search. The specific search terms and criteria can be found in the Annex. Two reviewers independently screened titles, abstracts and full texts, and two reviewers independently conducted the data extraction for each study. If a consensus could not be reached, further discussion was held or an opinion was obtained from a third independent reviewer.

The systematic review explored the evidence base on the effectiveness of each NPI. The specific targets of the evidence included reducing transmission, delaying the start of the epidemic, delaying the peak of the epidemic, spreading out infections over a longer period, and reducing the total number of infections.

Evaluation of the evidence
For each included study the risk of bias was assessed as part of the quality of evidence evaluation. In general, randomized controlled trials (RCTs) provided the strongest evidence, followed by observational studies and then computer simulations. The strength of individual studies could also be modified based on the risk of bias. The main types of bias in the systematic review of interventions are discussed below (*39*).

Potential limitations in RCTs include:
•   lack of allocation concealment;
•   lack of blinding;
•   loss to follow-up and failure to adhere to the intention-to-treat principle;
•   reporting bias; and
•   lack of generalizability due to strict inclusion criteria.

*Potential limitations in observational studies in*clude:
•   failure to describe the eligibility criteria;
•   flaws in the measurement of exposure or outcome (or both);
•   potential for bias due to confounding; and
•   incomplete or inadequate follow-up.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) (*40*) approach was used to rate the quality of evidence for each NPI, based on the question of whether NPIs can reduce influenza transmission in the community. The quality of evidence was ranked as high, moderate, low or very low, based on each study's risk of bias (including publication bias), consistency, directness and precision of results (*40*). Two reviewers independently assessed the risk of bias and the quality of evidence. Disagreements were resolved by a third reviewer if consensus could not be reached.

Development of recommendations

A technical consultation meeting for the development of this guidance was held in Hong Kong Special Administrative Region (SAR), China, on 26–28 March 2019. The systematic review team presented the outcomes of the systematic review. Recommendations were formulated by the guideline development group to determine the direction and strength of a recommendation by six indicators according to the WHO handbook for guideline development (*38*); the indicators are quality of the evidence, values and preferences, balance of benefits and harms, resource implications, acceptability and feasibility. In addition, ethical issues were taken into consideration. The strength of recommendations expressed the confidence of the guideline development group members in balancing desirable and undesirable consequences, which were classified as:

- "recommended" – the group is confident that the desirable effects outweigh the undesirable results;
- "conditionally recommended" – the group believes that the balance between benefits and harms is uncertain, and some conditions should apply when implementing the recommendation; or
- "not recommended" – the group is confident that the disadvantages outweigh the advantages.

2. SUMMARY OF RECOMMENDATIONS

The eighteen recommendations, which fall under 15 measures, are summarized in Table 4. The recommendations are based on the quality of evidence, which is indicated within the table, and on the other indicators (i.e. values and preferences, balance of benefits and harms, resource implications, acceptability, feasibility and ethical considerations).

Table 4. Summary of recommendations for each NPI

MEASURES	RECOMMENDATIONS	QUALITY OF EVIDENCE	STRENGTH OF RECOMMENDATION	WHEN TO APPLY
Hand hygiene	Hand hygiene is recommended as part of general hygiene and infection prevention, including during periods of seasonal or pandemic influenza. Although RCTs have not found that hand hygiene is effective in reducing transmission of laboratory-confirmed influenza specifically, mechanistic studies have shown that hand hygiene can remove influenza virus from the hands, and hand hygiene has been shown to reduce the risk of respiratory infections in general.	Moderate (lack of effectiveness in reducing influenza transmission)	Recommended	At all times
Respiratory etiquette	Respiratory etiquette is recommended at all times during influenza epidemics and pandemics. Although there is no evidence that this is effective in reducing influenza transmission, there is mechanistic plausibility for the potential effectiveness of this measure.	None	Recommended	At all times

MEASURES	RECOMMENDATIONS	QUALITY OF EVIDENCE	STRENGTH OF RECOMMENDATION	WHEN TO APPLY
Face masks	Face masks worn by asymptomatic people are conditionally recommended in severe epidemics or pandemics, to reduce transmission in the community. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.	Moderate (lack of effectiveness in reducing influenza transmission)	Conditionally recommended	In severe epidemics or pandemics
	A disposable surgical mask is recommended to be worn at all times by symptomatic individuals when in contact with other individuals. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.	Moderate (lack of effectiveness in reducing influenza transmission)	Recommended	At all times for symptomatic individuals
Surface and object cleaning	Surface and object cleaning measures with safe cleaning products are recommended as a public health intervention in all settings in order to reduce influenza transmission. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.	Low (lack of effectiveness in reducing influenza transmission)	Recommended	At all times

MEASURES	RECOMMENDATIONS	QUALITY OF EVIDENCE	STRENGTH OF RECOMMENDATION	WHEN TO APPLY
Other environmental measures	Installing UV light in enclosed and crowded places (e.g. educational institutions and workplaces) is not recommended for reasons of feasibility and safety.	None	Not recommended	N/A
	Increasing ventilation is recommended in all settings to reduce the transmission of influenza virus. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.	Very low (effective)	Recommended	At all times
	There is no evidence that modifying humidity (either increasing humidity in dry climates, or reducing humidity in hot and humid climates) is an effective intervention, and this is not recommended because of concerns about cost, feasibility and safety.	None	Not recommended	N/A
Contact tracing	Active contact tracing is not recommended in general because there is no obvious rationale for it in most Member States. This intervention could be considered in some locations and circumstances to collect information on the characteristics of the disease and to identify cases, or to delay widespread transmission in the very early stages of a pandemic in isolated communities.	Very low (unknown)	Not recommended	N/A

MEASURES	RECOMMENDATIONS	QUALITY OF EVIDENCE	STRENGTH OF RECOMMENDATION	WHEN TO APPLY
Isolation of sick individuals	Voluntary isolation at home of sick individuals with uncomplicated illness is recommended during all influenza epidemics and pandemics, with the exception of the individuals who need to seek medical attention. The duration of isolation depends on the severity of illness (usually 5–7 days) until major symptoms disappear.	Very low (effective)	Recommended	At all times
Quarantine of exposed individuals	Home quarantine of exposed individuals to reduce transmission is not recommended because there is no obvious rationale for this measure, and there would be considerable difficulties in implementing it.	Very low (variable effectiveness)	Not recommended	N/A
School measures and closures	School measures (e.g. stricter exclusion policies for ill children, increasing desk spacing, reducing mixing between classes, and staggering recesses and lunchbreaks) are conditionally recommended, with gradation of interventions based on severity. Coordinated proactive school closures or class dismissals are suggested during a severe epidemic or pandemic. In such cases, the adverse effects on the community should be fully considered (e.g. family burden and economic considerations), and the timing and duration should be limited to a period that is judged to be optimal.	Very low (variable effectiveness)	Conditionally recommended	Gradation of interventions based on severity; school closure can be considered in severe epidemics and pandemics

MEASURES	RECOMMENDATIONS	QUALITY OF EVIDENCE	STRENGTH OF RECOMMENDATION	WHEN TO APPLY
Workplace measures and closures	Workplace measures (e.g. encouraging teleworking from home, staggering shifts, and loosening policies for sick leave and paid leave) are conditionally recommended, with gradation of interventions based on severity. Extreme measures such as workplace closures can be considered in extraordinarily severe pandemics in order to reduce transmission.	Very low (effective)	Conditionally recommended	Gradation of interventions based on severity; workplace closure should be a last step only considered in extraordinarily severe epidemics and pandemics
Avoiding crowding	Avoiding crowding during moderate and severe epidemics and pandemics is conditionally recommended, with gradation of strategies linked with severity in order to increase the distance and reduce the density among populations.	Very low (unknown)	Conditionally recommended	Moderate and severe epidemics and pandemics
Travel advice	Travel advice is recommended for citizens before their travel as a public health intervention in order to avoid potential exposure to influenza and to reduce the spread of influenza.	None	Recommended	Early phase of pandemics
Entry and exit screening	Entry and exit screening for infection in travellers is not recommended, because of the lack of sensitivity of these measures in identifying infected but asymptomatic (i.e. pre-symptomatic) travellers.	Very low (lack of effectiveness in reducing influenza transmission)	Not Recommended	N/A

MEASURES	RECOMMENDATIONS	QUALITY OF EVIDENCE	STRENGTH OF RECOMMENDATION	WHEN TO APPLY
Internal travel restrictions	Internal travel restrictions are conditionally recommended during an early stage of a localized and extraordinarily severe pandemic for a limited period of time. Before implementation, it is important to consider cost–effectiveness, acceptability and feasibility, as well as ethical and legal considerations in relation to this measure.	Very low (effective)	Conditionally recommended	Early phase of extraordinarily severe pandemics
Border closure	Border closure is generally not recommended unless required by national law in extraordinary circumstances during a severe pandemic, and countries implementing this measure should notify WHO as required by the IHR (2005).	Very low (variable effectiveness)	Not recommended	N/A

IHR: International Health Regulations; N/A: not applicable; NPI: non-pharmaceutical intervention; RCT: randomized controlled trial; UV: ultraviolet; WHO: World Health Organization.

3. COMMUNICATION FOR BEHAVIOURAL IMPACT

Communication for behavioural impact (COMBI) (*41*) is a planning framework and an implementation method for using communication strategically to achieve positive behavioural and social results. It involves health education, health literacy, health promotion, risk communication and social mobilization, and it plays a critical role in the implementation of the NPI measures by modifying behaviour. COMBI identifies the barriers and constraints that prevent people from choosing to adopt healthy behaviour, and ensures that communication is appropriately applied and can contribute to achieving expected behavioural impact.

In the implementation of the recommended NPI measures, COMBI should be used to:
* share the rationale;
* encourage active engagement;
* empower people with information;
* adapt recommendations to the local context; and
* quickly develop effective communication strategies, messages and materials, using existing resources and partnerships.

The rest of this section discusses each of these points.

Share the rationale
This involves explaining to people why certain behaviour is important. Transparency in sharing information and its rationale helps to build trust and increases the likelihood of cooperation.

Encourage active engagement
This involves:
* encouraging people to seek information from credible sources; and
* ensuring that neighbours, communities and networks receive and understand accurate information, report possible influenza cases and help communities in managing ill people.

In this approach, people are viewed as "partners in prevention", rather than simply as recipients of information. The approach is therefore likely to create ownership, resulting in better adoption of recommended behaviours and more proactive communities. Such partners in prevention are also more likely to find creative ways to mobilize community resources and help build capacity that might be useful in the future.

Empower people with information
People and communities will take their own decisions on the basis of the balance of forces of their own circumstances. The communication approach should emphasize information sharing and community problem solving as ways of helping people to find a set of doable actions, so that they ask "How can we effectively prevent infection and protect ourselves, our families and our community?"

Adapt recommendations to the local context
It is important to take into account people's capacity to act on the advice being given. The recommended behaviour must be doable and be adapted to people's lifestyle; otherwise, it will not be widely adopted. For example, there is a need to ensure that marginalized groups (e.g. those living in inadequate or overcrowded housing, religious minorities and people beyond the reach of

the mass media) are also engaged in prevention and protection, have access to information and have the capacity to act upon it.

Use existing resources and partnerships to quickly develop effective communication strategies, messages and materials
Working through existing communication and coordination bodies makes it easier to harmonize messages, approaches and use of channels. It is important to invest resources in understanding the current knowledge, attitude and practices on the implementation of NPIs – this can help to reduce the impact of pandemic and thus craft policy and workflow to more effectively manage the public's concerns, compliance and expectations. In turn, this may help Member States to achieve a higher effectiveness for these NPIs. Training on crisis communication for selected community leaders and key national stakeholders as part of pandemic preparedness is also important.

4. PERSONAL PROTECTIVE MEASURES

This section covers three types of personal protective measures: hand hygiene, respiratory etiquette and face masks.

4.1. Hand hygiene

Summary of evidence
Twelve articles describing 11 RCTs (two studies were the same project during the same period but studied different questions) of hand hygiene were included in a systematic review, and a meta-analysis was undertaken of 10 studies including more than 11 000 participants in total (*42-53*). It was not possible to make a pooled estimate of the effectiveness of hand hygiene with or without face masks because of the high heterogeneity (see Annex). In the pooled analysis of six studies that examined hand hygiene together with face masks, there was no statistically significant protective effect when all settings outside of health care were combined (rate ratio [RR]: 0.91, 95% confidence interval [CI]: 0.73–1.13, P=0.39, I2=35%) (*42-47*). Two studies were conducted in an elementary school setting but had very different findings: one study conducted in the USA found no significant effect of hand hygiene, with a precise estimate of the risk ratio close to 1; in contrast, a large trial in Egypt reported a statistically significant reduction of more than 50% in laboratory-confirmed influenza cases in the intervention group (RR: 0.47, 95% CI: 0.39–0.56, P<0.01) (*48, 49*). Two studies in university halls of residence found no statistically significant effect of hand hygiene with face masks (RR: 0.48, 95% CI: 0.21–1.08, P=0.08, I2=0%) (*42, 43*). In addition, in household settings the efficacy of hand hygiene with or without a face mask was not significant (RR: 1.05, 95% CI=0.86–1.27, P=0.65, I2=57%) (*44-47, 50, 51*). Several trials reported that poor adherence to hand hygiene may contribute to the low efficacy observed (*44-46*).

Influenza virus can survive for a short time on human hands and transmit from contaminated surfaces to hands, supporting the potential for contact transmission to occur (*54-56*). Hand hygiene is effective to inactivate or reduce viable influenza virus on human hands (*57-59*). In theory, hand hygiene could prevent indirect contact transmission of influenza; however, hand hygiene adherence is often suboptimal, even in intervention studies.

Testing the efficacy of hand hygiene in RCTs is complicated by the fact that the comparison groups cannot be asked to stop washing their hands. Thus, evidence from RCTs is typically based on either an increase in the quantity of hand hygiene episodes or non-inferiority trials focusing on certain products (e.g. hand sanitizer in combination with hand washing versus hand washing alone), making it difficult to estimate the efficacy of hand hygiene alone. Within this context, existing

hand hygiene studies are of a moderate overall quality, and they do not provide strong evidence that increased hand hygiene or different hand hygiene modalities are highly effective at reducing influenza. However, there are several experimental studies (*57-60*) that provide evidence that hand hygiene can inactivate or remove influenza and therefore reduce transmission.

OVERALL RESULT OF EVIDENCE ON HAND HYGIENE

1. Eleven RCTs were included in this review. Although hand hygiene was not effective against laboratory-confirmed influenza in a meta-analysis in community settings and university halls, it was effective in one of two trials conducted in schools.

2. Although compliance with optimal (intense) hand hygiene practices was imperfect in these RCTs, compliance with proper hand hygiene might not be substantially higher in community settings, even in severe influenza epidemics and pandemics.

3. Experimental studies suggested that hand hygiene could effectively inactivate or reduce influenza virus on hands; hence, theoretically, hand hygiene could prevent influenza transmission.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations

The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence

There is a moderate overall quality of evidence that hand hygiene does not have a substantial effect on transmission of laboratory-confirmed influenza.

Values and preferences

It is well-established that hand hygiene can substantially reduce many important infectious diseases, particularly diarrhoeal diseases, and there is good evidence that hand hygiene can also reduce respiratory illnesses, although not laboratory-confirmed influenza. Hand hygiene is most often performed with water and soap; alcohol-based hand sanitizers are another option for waterless hand disinfection in some locations. Most communities would understand the importance and effectiveness of hand hygiene in preventing common infections, and would agree with the concept of encouraging hand hygiene to prevent infection, although education campaigns might be needed in some communities.

Balance of benefits and harms

Hand hygiene had no significant effect on transmission of laboratory-confirmed influenza, other than in the RCT in schools in Egypt. The guideline development group concluded that, in general, the evidence from controlled trials indicates that hand hygiene is not effective in preventing laboratory-confirmed influenza, but it is possible that a major change in hand hygiene from a very low level to a very high level might reduce influenza transmission. Hand hygiene does prevent transmission of other infections, including diarrhoeal and respiratory diseases, and can substantially improve public health (61). There are no adverse effects of hand hygiene, other than possible soap or alcohol allergies (62).

Resource implications

Hand hygiene is one of the most cost-effective measures for preventing infections in health care settings (*63*). It is an important component of general hygiene campaigns in communities, and can reduce the incidence of a variety of infections and associated morbidity and mortality. Clean running water is not available in some communities and would be a barrier. Alcohol hand-rub may be too expensive in some settings.

Ethical considerations

There are no major ethical issues regarding hand hygiene with soap and water. Alcohol-based hand-rub might not be permitted in some locations due to religious objections (*64*).

Acceptability

More than half of published national pandemic plans have included hand hygiene as a prevention measure (*65*). Given the low cost and broad impact on infections, it is a very acceptable intervention. However, the guideline development group considered that compliance and adherence is low (especially compliance to proper hand hygiene practice) because it is hard to make substantial behavioural changes.

Feasibility

Many countries have already conducted public hand hygiene campaigns to reduce communicable diseases (*65*). This intervention is considered to be very feasible.

RECOMMENDATION:

Hand hygiene is recommended as part of general hygiene and infection prevention, including during periods of seasonal or pandemic influenza. Although RCTs have not found that hand hygiene is effective in reducing transmission of laboratory-confirmed influenza specifically, mechanistic studies have shown that hand hygiene can remove influenza virus from the hands, and hand hygiene has been shown to reduce the risk of respiratory infections in general.

Population: General public

When to apply: At all times

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Moderate (lack of effectiveness in reducing influenza transmission)	Moderate quality of evidence from 10 RCTs in a meta-analysis involving >11 000 participants that hand hygiene is ineffective in reducing influenza transmission in the community, although experimental studies suggested that hand hygiene could theoretically prevent influenza transmission.
Values and preferences	Favourable Favourable	Hand hygiene has an established effect on common diarrhoeal infections and can also reduce some respiratory infections and other infections.

FACTORS	ASSESSMENT	RATIONALE
Balance of benefits and harms	Favourable	No important adverse effects of hand hygiene with water and soap, other than possible soap or alcohol allergies.
Resource implications	Favourable	Hand hygiene with soap and water is generally very cost-effective given the reduction in common infections and no additional equipment is needed.
Ethical considerations	Conditional	No major ethical issues. There may be religious objections to alcohol hand-rub.
Acceptability	Favourable	No major concerns with acceptability, but the compliance and adherence of this intervention may be difficult to change substantially.
Feasibility	Favourable	Very feasible because it is normal practice.

Overall strength of recommendation	**Recommended**	**Although hand hygiene does not have proven efficacy against laboratory-confirmed influenza in RCTs, it is recommended because it has been shown to deactivate or remove influenza virus from the hands in experimental studies, and can reduce the burden of those other infections on the health system during influenza epidemics and pandemics.**

Knowledge gaps: There are important gaps in our knowledge of the mechanisms of person-to-person transmission of influenza, including the importance of direct and indirect contact, the degree of viral contamination on hands and various types of surfaces in different settings, and the potential for contact transmission to occur in different locations and under different environmental conditions. Additional research on increasing hand hygiene compliance would also be valuable. There is little information on whether greater reductions in transmission could be possible with combinations of personal interventions (e.g. isolation away from family members as much as possible, plus using face masks and enhancing hand hygiene).

RCT: randomized controlled trial.

4.2. Respiratory etiquette

Summary of evidence
Respiratory etiquette refers to the actions used when people cough or sneeze *(66)*; it is a simple hygiene practice to prevent person-to-person transmission of respiratory infections. Measures include *(67)* covering the mouth and nose with a hand, sleeve or tissue when coughing or sneezing; finding the nearest waste basket to dispose of the used tissue immediately; and washing hands after touching respiratory secretions or contaminated objects (or both). A total of 80 articles were retrieved from four electronic databases, and no scientific studies were identified for inclusion in this review.

Respiratory etiquette is a common and acceptable practice in relation to personal hygiene; however, there is no research on the effectiveness of respiratory etiquette on the reduction of laboratory-confirmed influenza virus infection.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
The quality of evidence could not be judged because no study was identified.

Values and preferences
Respiratory etiquette and hygiene is recognized as important in many communities. Improvements in respiratory etiquette in communities could prevent the spread of a variety of infections.

Balance of benefits and harms
There are no anticipated harms of improved respiratory etiquette.

Resource implications
Efforts to improve respiratory etiquette in communities would not be expensive and could be included as part of broader public health campaigns.

Ethical considerations
There are no major ethical considerations in relation to respiratory etiquette. Cultural contexts may be considered when recommending specific actions such as covering coughs with hands or tissues.

Acceptability
Improved respiratory etiquette should be acceptable in most locations.

Feasibility
This is a feasible intervention, and respiratory etiquette campaigns have been successful for acute respiratory infections *(66)*. Furthermore, 32 Member States have included respiratory etiquette in their national pandemic preparedness plans *(65)*.

RECOMMENDATION:

Respiratory etiquette is recommended at all times during influenza epidemics and pandemics. Although there is no evidence that this is effective in reducing influenza transmission, there is mechanistic plausibility for the potential effectiveness of this measure.

Population: General public

When to apply: At all times

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	None	No scientific evidence on the effectiveness of respiratory etiquette.
Values and preferences	Conditional	Respiratory etiquette is a simple personal protective measure to prevent infection, but may not always be recognized as important in some cultures and locations.
Balance of benefits and harms	Favourable	No anticipated harms.
Resource implications	Favourable	No significant costs for the general public.
Ethical considerations	Favourable	There are no major ethical considerations. Cultural contexts and norms may be considered when recommending specific actions such as covering coughs with hands or tissues.
Acceptability	Favourable	No major concerns with acceptability.
Feasibility	Favourable	Highly feasible.

Overall strength of recommendation	**Recommended**	**Although there is no research on the impact of respiratory etiquette on laboratory-confirmed influenza infection, this is a simple, feasible and acceptable intervention that may reduce transmission and reduce the impact of epidemics and pandemics.**

> **Knowledge gaps:** There is still no evidence about the quantitative effectiveness of respiratory etiquette against influenza virus. RCTs of interventions to improve respiratory etiquette would be valuable.

RCT: randomized controlled trial.

4.3.   Face masks

Summary of evidence
Ten relevant RCTs were identified for this review and meta-analysis to quantify the efficacy of community-based use of face masks, including more than 6000 participants in total (*42-47, 50, 68-70*). Most trials combined face masks with improved hand hygiene, and examined the use of face masks in infected individuals (source control) and in susceptible individuals. In the pooled analysis, although the point estimates suggested a relative risk reduction in laboratory-confirmed influenza of 22% (RR: 0.78, 95% CI: 0.51–1.20, I2=30%, P=0.25) in the face mask group, and a reduction of 8% in the face mask group regardless of whether or not hand hygiene was also enhanced (RR: 0.92, 95% CI=0.75–1.12, I2=30%, P=0.40), the evidence was insufficient to exclude chance as an explanation for the reduced risk of transmission. Some studies reported that low compliance in face mask use could reduce their effectiveness. A study suggested that surgical and N95 (respirator) masks were effective in preventing the spread of influenza (*71*).

> **OVERALL RESULT OF EVIDENCE ON FACE MASKS**
>
> 1.   Ten RCTs were included in the meta-analysis, and there was no evidence that face masks are effective in reducing transmission of laboratory-confirmed influenza.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a moderate overall quality of evidence that face masks do not have a substantial effect on transmission of influenza.

Values and preferences
Face mask use is common to prevent transmission of infections in health care settings around the world, and a widely used measure in some communities, particularly in South-East Asia.

Balance of benefits and harms
There are no major adverse effects of face mask use. There might be issues with allergies in some individuals, and prolonged use of face masks can be uncomfortable or inconvenient.

Resource implications
Reusable cloth face masks are not recommended. Medical face masks are generally not reusable, and an adequate supply would be essential if the use of face masks was recommended. If worn by a symptomatic case, that person might require multiple masks per day for multiple days of illness.

Ethical considerations
There are no major ethical considerations in the use of face masks. Masks may be more culturally acceptable in some locations, and other health behaviours may affect compliance (*72*).

Acceptability
Face masks are widely used in health care settings to prevent transmission of infections, and are used in the community in some parts of the world (*65*). They are likely to be acceptable if recommended, particularly in more severe epidemics and pandemics. However, face masks are not appropriate under some circumstances (e.g. during sleep). The guideline development group also considered that compliance may not be high in some areas and populations.

Feasibility
Twenty-eight Member States have included the use of face masks in their national influenza preparedness plan (*65*). Feasibility can be enhanced by education campaigns to improve usage and compliance. The guideline development group believed that this intervention is feasible, especially for symptomatic individuals.

RECOMMENDATION:

Face masks worn by asymptomatic people are conditionally recommended in severe epidemics or pandemics, to reduce transmission in the community. Disposable, surgical masks are recommended to be worn at all times by symptomatic individuals when in contact with other individuals. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.

Population: Population with symptomatic individuals; and general public for protection

When to apply: At all times for symptomatic individuals (disposable surgical mask), and in severe epidemics or pandemics for public protection (face masks)

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Moderate (lack of effectiveness in reducing influenza transmission)	According to the GRADE approach, there was moderate quality of evidence involving >6000 participants that face masks are ineffective in reducing influenza transmission in the community.
Values and preferences	Favourable	Masks can be worn by symptomatic or exposed persons to reduce transmission (source control), or by uninfected persons in the community to reduce their risk of infection.
Balance of benefits and harms	Favourable	No significant harms anticipated.
Resource implications	Conditional	Costly in some settings, and supplies may be limited.

FACTORS	ASSESSMENT	RATIONALE
Ethical considerations	Favourable	No major ethical considerations.
Acceptability	Conditional	Likely to be acceptable, but not appropriate in some circumstances and the adherence and compliance is low.
Feasibility	Conditional	Dependent on availability, but more feasible for symptomatic individuals.

Overall strength of recommendation	**Recommended for symptomatic individuals, and conditionally recommended for public protection**	**Given the costs and the uncertain effectiveness, face masks are conditionally recommended only in severe influenza epidemics or pandemics for the protection of the general population, but are recommended for symptomatic individuals at all times.**

Knowledge gaps: There are important gaps in our knowledge of the mechanisms of person-to-person transmission of influenza, including the importance of transmission through droplets of different sizes including small particle aerosols, and the potential for droplet and aerosol transmission to occur in different locations and with different environmental conditions. Additional high-quality RCTs of the efficacy of face masks against laboratory-confirmed influenza would be valuable.

GRADE: Grading of Recommendations Assessment, Development and Evaluation; RCT: randomized controlled trial.

5. ENVIRONMENTAL MEASURES

5.1. Surface and object cleaning

Summary of evidence

Three studies were included in the systematic review to study the effectiveness of surface and object cleaning in reducing influenza transmission (*73-75*). An RCT with disinfection of toys and linen in day care facilities found a reduction in the detection of viruses in the environment, but no significant effect on laboratory-confirmed influenza or acute respiratory illnesses among children (*74*). Another RCT conducted in elementary schools reported that surface disinfection combined with hand hygiene could reduce absenteeism due to gastrointestinal illness, but not absenteeism due to respiratory illness (*75*). A cross-sectional study showed that passive contact with sodium hypochlorite (bleach) in households was significantly associated with an increase in the rate of self-reported influenza, which the authors of the article hypothesized had occurred due to the immunosuppressive properties of bleach (*73*).

Influenza virus can survive on surfaces and objects for a few hours and up to 1 week (*54, 55, 76-78*). Influenza virus RNA has been detected in various settings outside of health care settings, but little of the RNA was found to be viable (*74, 79-83*). Surface and object cleaning is effective at inactivating or reducing viable influenza virus on surfaces (*84-86*). In theory, surface and object cleaning could prevent indirect contact transmission of influenza.

OVERALL RESULT OF EVIDENCE ON SURFACE AND OBJECT CLEANING

1. Two RCTs and one cross-sectional study were included in the systematic review.

2. There was evidence that surface and object cleaning could reduce detections of virus in the environment, but there was no evidence of effectiveness against laboratory-confirmed influenza virus infection.

3. Experimental studies suggested that surface and object cleaning could effectively inactivate or reduce viable influenza virus on surfaces; theoretically, this intervention could prevent influenza transmission.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a low overall quality of evidence that cleaning of surfaces and objects does not have a substantial effect on transmission of respiratory disease.

Values and preferences
A telephone survey in Europe found that most (*82%*) participants believed that cleaning or disinfecting objects might reduce the risk of influenza (*87*). Environmental cleaning is a common strategy to reduce a variety of infections.

Balance of benefits and harms
Cleaning using detergent-based cleaners or bleach can inactivate or remove influenza viruses from surfaces and objects, and in theory could reduce influenza transmission. However, most disinfectants (e.g. bleach) require a pre-cleaning step before the disinfectant is applied, and it is not safe to add water to chlorine solutions (*88, 89*). Incorrect use of disinfectants and poor ventilation when using the disinfectant can be harmful (*29*).

Resource implications
The implementation of surface and object cleaning would involve relatively minor resources. The cost of disinfectants is relatively low.

Ethical considerations
Cleaning product selection is a major issue. Some disinfectants are irritants and may lead to adverse effects in sensitive populations (*73*); also, they may not be applicable in some countries or regions due to the prohibition of alcohol (*64*). However, most countries have no legislation restricting the use of alcohol in household cleaning agents, and even in Muslim tradition, alcohol is permitted as a cleansing ingredient (*64*). In addition, the safety of cleaning personnel should also be considered.

Acceptability

This intervention is highly accepted by policy-makers and health workers worldwide. However, the acceptability may vary among different countries.

Feasibility

This intervention is highly feasible. Disinfectants are available from a variety of sources, such as general supermarkets or convenience stores.

RECOMMENDATION:

Surface and object cleaning measures with safe cleaning products are recommended as a public health intervention in all settings in order to reduce influenza transmission. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.

Population: General population

When to apply: At all times

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Low (lack of effectiveness in reducing influenza transmission)	Very limited evidence on the effectiveness or lack of effectiveness of environmental cleaning. Surface and object cleaning is ineffective in reducing respiratory disease transmission in the community, although experimental studies suggest that theoretically surface and object cleaning could prevent influenza transmission.
Values and preferences	Favourable	Likely to be perceived as a simple but important measure, if recommended.
Balance of benefits and harms	Conditional	Safety concerns with some cleaning products.
Resource implications	Favourable	The cost of disinfectants is low.
Ethical considerations	Conditional	In some locations, cleaning with alcohol may not be allowed, but other chemicals can be used.
Acceptability	Favourable	Likely to be acceptable if recommended.
Feasibility	Favourable	Disinfectants can be obtained from various sources.

Overall strength of recommendation	Recommended	There are no major disadvantages of surface and object cleaning, so this measure is recommended despite the lack of evidence on effectiveness.

Knowledge gaps: Only three studies were included in our systematic review and only two of them were RCTs. More trials are needed to study the effect of surface and object cleaning on influenza prevention. The best evidence of pandemic preparedness would be provided by studies in which the outcome is laboratory-confirmed influenza, rather than acute respiratory infections. Studies are needed in various settings (e.g. household, school, workplace and public place). The effectiveness of different cleaning products in preventing influenza transmission – in terms of cleaning frequency, cleaning dosage, cleaning time point, and cleaning targeted surface and object material – remains unknown.

RCT: randomized controlled trial.

5.2. Other environmental measures

5.2.1. Ultraviolet light
Summary of evidence
The systematic review did not identify any studies that quantified the effectiveness of ultraviolet (UV) light in reducing influenza transmission. UV light is a means of disinfection; it breaks down microorganisms and can be used to prevent the spread of certain infectious diseases (*90*).

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
The quality of evidence could not be judged because no study was identified.

Values and preferences
The guideline development group noted that UV light intervention would not be useful if the surface is covered, and would probably have a limited impact on transmission given the likely modes of influenza transmission.

Balance of benefits and harms
The effectiveness of UV light against influenza transmission is uncertain. Exposure to UV light may increase the risk of skin cancers and eye problems (91). The guideline development group considered UV light intervention to be harmful in some circumstances.

Resource implications
Installing and maintaining UV light fixtures is expensive. However, the guideline development group believed that costs in settings with a large number of people (e.g. public transport) may be reasonable given the potential impact.

Ethical considerations
No major ethical concerns were identified in relation to the use of UV light.

Acceptability
The use of UV light to reduce influenza transmission by disinfection of the environment is likely to have limited acceptability, because of the costs and complexity of installation and maintenance. The guideline development group believed it would be unlikely that these fixtures could be installed at short notice, such as in the early stages of an influenza pandemic.

Feasibility
The use of UV disinfection is hindered by safety concerns.

RECOMMENDATION:

Installing UV light in enclosed and crowded places (e.g. educational institutions and workplaces) is not recommended for reasons of feasibility and safety.

Population: People exposed to risk in closed and crowded places

When to apply: N/A

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	None	No study was identified in the review.
Values and preferences	Conditional	Uncertain.
Balance of benefits and harms	Conditional	Safety concerns.
Resource implications	Conditional	Substantial costs associated with installing and maintaining UV light fixtures.
Ethical considerations	Conditional	No major ethical concerns.
Acceptability	Conditional	Uncertain acceptability given costs and complexity of installation and maintenance.
Feasibility	Conditional	UV light may not be feasible because of high costs and safety concerns.

Overall strength of recommendation	Not Recommended	The use of UV light is hindered by feasibility and safety concerns.

Knowledge gaps: The effectiveness of UV light in reducing influenza transmission still requires more evidence. Potential safety issues are also an important consideration and more scientific evidence is needed to confirm effectiveness and feasibility as a community mitigation measure for influenza epidemics and pandemics.

N/A: not applicable; UV: ultraviolet.

5.2.2. Increased ventilation

Summary of evidence

A simulation study predicted a reduction of transmission among kindergarten students by enhancing the air changes per hour (ACH) (*92*). Two simulation studies evaluated the effectiveness of increasing ventilation in reducing influenza transmission in community settings (*93, 94*). One of these two studies suggested a reduction of daily peak infections by increasing ACH under the baseline scenario (*93*), and the other predicted that the peak infection rate could be reduced by more than 60% by doubling or tripling the ventilation rate (*94*).

OVERALL RESULT OF EVIDENCE ON INCREASED VENTILATION

1. In simulation studies, increasing the ventilation rate reduced influenza transmission.

2. There is mechanistic plausibility for increased ventilation to reduce transmission – specifically aerosol transmission and perhaps to a lesser extent large respiratory droplet transmission or indirect contact transmission.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations

The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence

There is a very low overall quality of evidence that increasing ventilation has an effect on transmission of influenza.

Values and preferences

Increasing ventilation is a common practice in many locations, for a multitude of reasons.

Balance of benefits and harms

There is no major harm associated with increased ventilation. Airflow pattern and flow direction are important considerations (*95*). If the outdoor temperature is very low, thermal comfort may be an issue. Exposure to air pollution and allergens may trigger asthmatic attacks.

Resource implications

The cost of opening windows is likely to be low. There may be costs associated with increasing ventilation for buildings or homes with mechanical ventilation (e.g. increased electricity costs). In cold climates, increased natural or mechanical ventilation could also increase heating costs.

Ethical considerations

There are no major ethical considerations associated with the use of increased ventilation.

Acceptability

The acceptability of increased ventilation is likely to be high.

Feasibility

Increased ventilation is likely to be feasible in most settings.

RECOMMENDATION:

Increasing ventilation is recommended in all settings to reduce the transmission of influenza virus. Although there is no evidence that this is effective in reducing transmission, there is mechanistic plausibility for the potential effectiveness of this measure.

Population: General Population

When to apply: At all times

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (effective)	The only evidence was provided by simulation studies. In those studies, increased ventilation was predicted to be effective in reducing influenza transmission in the community.
Values and preferences	Favourable	Commonly used intervention.
Balance of benefits and harms	Conditional	Exposure to air pollution and allergens may trigger asthmatic attacks.
Resource implications	Conditional	May lead to increased heating costs or increased electricity costs.
Ethical considerations	Favourable	No major ethical considerations.
Acceptability	Favourable	Increased ventilation is highly accepted.
Feasibility	Conditional	Increased ventilation is feasible in most locations.

Overall strength of recommendation	Recommended	Effectiveness is uncertain, but increased ventilation is simple and feasible in most locations.

Knowledge gaps: Simulation models provide a weak level of evidence. RCTs would provide more compelling evidence on the efficacy of increasing ventilation in reducing influenza transmission.

RCT: randomized controlled trial.

5.2.3. Modifying humidity
Summary of evidence
Increased humidity has been correlated with reduced influenza transmission in cold and dry climates (*96, 97*), and very high humidity has been associated with increased transmission in hot and humid climates (*11*). Nevertheless, no study was identified in the review that quantified the effectiveness of modifying humidity (as an intervention) in reducing influenza transmission.

Elevated humidification (absolute humidity at 9 millibars) was shown to reduce influenza A virus detections in the air and on fomite (markers and wooden toys) in a preschool classroom (97). A simulation study also predicted a 17.5–31.6% reduction of influenza virus survival in rooms with a humidifier operating in a residential setting (98). Another simulation study predicted that nearly five times more influenza virus from stimulated coughs would remain infectious at 7–23% relative humidity (RH) than at an RH of more than 43% in a 1-hour collection (*99*).

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
The quality of evidence cannot be judged because no study was identified in the review.

Values and preferences
Uncertain.

Balance of benefits and harms
Humidification may increase the growth of mould and mildew, harming health (*100*). According to WHO, indoor dampness or mould creates a considerable health burden (e.g. asthma) in children (*101*).

Resource implications
Humidifiers are expensive to purchase and maintain.

Ethical considerations
There are no major ethical considerations in relation to modifying humidity.

Acceptability

Modifying humidity is likely to be acceptable.

Feasibility

There may be insufficient availability of humidifiers at short notice, and it may not be feasible to humidify buildings across a community.

RECOMMENDATION:

There is no evidence that modifying humidity (either increasing humidity in dry climates, or reducing humidity in hot and humid climates) is an effective intervention, and this is not recommended because of concerns about cost, feasibility and safety.

Population: N/A

When to apply: N/A

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	None	No study was identified in the review.
Values and preferences	Conditional	Uncertain.
Balance of benefits and harms	Conditional	Higher humidity may increase the growth of mould and mildew, causing harm.
Resource implications	Conditional	Costly to purchase and maintain.
Ethical considerations	Favourable	There are no major ethical considerations.
Acceptability	Favourable	Likely to be acceptable.
Feasibility	Conditional	Humidity may not be feasible as a population-level intervention.

Overall strength of recommendation	Not Recommended	**The use of mechanical humidity is hindered by feasibility and safety reasons.**

Knowledge gaps: The exact biological mechanism of how humidity affects the survival of the influenza virus is unclear (96, 97). Many studies have looked at the effect under laboratory conditions, but very few have tested these effects in natural settings. It would be informative to conduct RCTs of humidification as an intervention to reduce influenza transmission.

N/A: not applicable; RCT: randomized controlled trial.

6. SOCIAL DISTANCING MEASURES

6.1. Contact tracing

Summary of evidence

Four simulation studies were included in the systematic review (*102-105*), none of which studied contact tracing as a single intervention. Contact tracing was studied in combination with other interventions such as quarantine, isolation and provision of antiviral drugs. Evidence for the overall effectiveness of contact tracing varied. A simulation model with R0=1.8 reported that the combination of contact tracing, quarantine, isolation and antiviral drugs could reduce the infection attack rate by 40% (*102*), while another study predicted that it would be difficult to control influenza even with 90% contact tracing and quarantine because of the presumed high level of pre-symptomatic or asymptomatic transmission (*104*). A combination of isolation, treatment of cases, contact tracing, quarantine and post-exposure prophylaxis was estimated to delay the epidemic peak for 6 weeks, assuming a case detection rate of 30% (*105*). In addition, the combination of contact tracing with quarantine has been suggested to be more effective than when combined with symptom monitoring (*103*).

OVERALL RESULT OF EVIDENCE ON CONTACT TRACING

1. Evidence for overall effectiveness of contact tracing was limited. All included studies were simulation models.

2. Only one study reported on the effect of adding contact tracing to isolation and quarantine. Such addition was estimated to provide at most a modest benefit, but at the same time would increase considerably the number of quarantined individuals.

Summary of considerations of members of the guideline development group
for determining the direction and strength of the recommendations

The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence

There is a very low overall quality of evidence that contact tracing has an unknown effect on the transmission of influenza.

Values and preferences

There is uncertainty about the values and preferences of contact tracing among the community for control of influenza. Mandatory contact tracing may cause concerns and uneasiness to some cases and their contacts; however, voluntary reporting of contacts can prevent such concerns.

Balance of benefits and harms

Contact tracing allows the rapid identification of at-risk individuals once a case has been detected. This intervention reduces the delay between symptom onset and treatment, as well as implementation of preventive measures for onward transmission (*106*). The guideline development group considered contact tracing to be a potentially important measure in reducing cross-border transmission. However, contact tracing on a large scale can lead to ethical issues such as leakage of information, and inefficient usage of resources, including human resources (*107*).

Resource implications

Following up contacts of an infected individual who may have been exposed often has low cost–effectiveness in the control of influenza, resulting in high direct costs. Considerable amounts of human resources are also needed for contact tracing.

Ethical considerations

There are a few ethical issues surrounding the implementation of contact tracing as an intervention. Also, contact identification of infected individuals brings about privacy concerns (*107*). Some individuals may perceive stigma and refuse to be contact traced. Nevertheless, contact tracing may be justified, given that it allows the identification of persons at risk, and the timely provision of treatment and care (*106, 107*). There may be more ethical concerns when contact tracing is coupled with measures such as household quarantine. Contact tracing can substantially increase the proportion of people quarantined, but may not offer much additional benefit to existing interventions (*102*). In addition, contact tracing may not be an equitable intervention, because its successful implementation relies on availability of resources and technology.

Acceptability

The evidence is limited and the acceptability of contact tracing among the public is uncertain.

Feasibility

Contact tracing requires a large amount of trained personnel and resources (e.g. telecommunications); hence, it may be less feasible in low- to middle-income countries where resources are limited. In addition, the implementation and effectiveness of contact tracing rely on the capacity to detect cases, and contact tracing efforts are likely to be hampered by the short incubation and infectious periods of influenza (*104*). The triggers to activate and de-activate contact tracing for optimal effect in controlling influenza remain unknown.

RECOMMENDATION:

Active contact tracing is not recommended in general because there is no obvious rationale for it in most Member States. This intervention could be considered in some locations and circumstances to collect information on the characteristics of the disease and to identify cases, or to delay widespread transmission in the very early stages of a pandemic in isolated communities.

Population: Individuals who have come into contact with an infected person

When to apply: N/A

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (unknown)	All included articles are simulation models and the inherent limitations lead to a very low quality of evidence. Contact tracing combined with other interventions is effective in reducing influenza transmission in the community, but the effect of contact tracing alone is unknown.
Values and preferences	Conditional	There is uncertainty or variability in the values and preferences among different interest groups.

FACTORS	ASSESSMENT	RATIONALE
Balance of benefits and harms	Conditional	Contact tracing can reduce onward transmission; however, the relevant ethical issues and inefficient usage of resources mean that the balance of benefits and harms is uncertain.
Resource implications	Conditional	Contact tracing requires a large amount of resources, including human resources.
Ethical considerations	Conditional	Privacy and equity concerns may exist for the implementation of contact tracing.
Acceptability	Conditional	The acceptability of contact tracing among stakeholders is uncertain because of limited evidence.
Feasibility	Conditional	Feasibility of contact tracing may be low when resources are limited; also, it is affected by the short incubation period of influenza.

Overall strength of recommendation	Not Recommended	There is no obvious rationale in most Member States.

Knowledge gaps: There are few studies on the effectiveness of contact tracing on influenza in the community, and none that have studied contact tracing as a single intervention. Some epidemiological studies have documented contact tracing of air passengers and crew; however, the risk for influenza transmission onboard aircraft is still uncertain (*108*). Therefore, the effectiveness of contact tracing cannot be assessed from these studies. Moreover, currently available studies for community settings are all simulation studies – evidence of greater strength is needed to provide a more robust understanding of the effectiveness and value of contact tracing. Still unclear are the impacts of different intensities of contact tracing, and the optimal time frame, feasibility and cost–benefit.

N/A: not applicable.

6.2. Isolation of sick individuals

Summary of evidence
Terms relevant to isolation are defined below (Table 5).

Table 5. Definition of terms relevant to isolation

TERM	DEFINITION
Isolation	Separation or restriction of movement of ill persons with an infectious disease to prevent transmission to others (*109*).
Case isolation	Separation or restriction of movement of ill persons with an infectious disease at home or in a health care facility, to prevent transmission to others (*29, 109*).
Patient isolation	Isolation of ill persons with an infectious disease in a health care facility, to prevent transmission to others (*29*).
Home isolation	Home confinement of ill persons with an infectious disease (often not needing hospitalization), to prevent transmission to others (*29, 109*).
Voluntary isolation	Voluntary separation or restriction of movement of ill persons in a designated room to prevent transmission to others. This is usually in their own homes, but could be elsewhere (*109*).
Self-isolation	See '*Voluntary isolation*'.

The systematic review identified four epidemiological studies (*110-113*) and 11 simulation studies that were eligible for inclusion in our review (*102, 104, 114-122*).

Among the four epidemiological studies, a reduction in the cumulative incidence of infections and reproduction number due to an isolation policy was recorded during an influenza A(H1N1)pdm09 outbreak on a navy ship (*110*). Two studies suggested a reduction in attack rate in a physical training camp and a residential home for older adults (*110, 111*). In the 1918–1919 pandemic, excess death rates due to pneumonia and influenza decreased in New York City and Denver after isolation and quarantine were implemented (*113*).

Eleven simulation studies were conducted based on a wide range of assumptions, studying isolation as a single intervention or combined with other interventions. Six of the 11 studies predicted that implementation of case isolation would decrease the number of infections (*102, 114-117, 119*). In contrast, one study showed the difficulty in controlling influenza because of a potentially high proportion of asymptomatic transmission (*104*). Some studies predicted that isolation of sick individuals could delay the peak of an epidemic (*116-118*). One study predicted that isolation of 40% of cases would delay the epidemic peak by 83 days (*116*), while another predicted a similar effect, in which isolation of a reasonable proportion of cases would delay the arrival of the pandemic in countries globally (*118*). Although isolation alone was suggested to have a greater impact than other interventions, a combination of isolation and other interventions could further improve the effectiveness (*102, 115, 117, 119*).

> **OVERALL RESULT OF EVIDENCE ON ISOLATION OF SICK INDIVIDUALS**
>
> 1. Epidemiological and simulation studies suggested that isolation of sick individuals could reduce transmission in epidemics and pandemics. There is mechanistic plausibility for this intervention to be effective in reducing transmission.
>
> 2. The overall effectiveness of isolation is moderate, and combination with other interventions may improve the effectiveness.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence that isolation of sick individuals has a substantial effect on transmission of influenza except in closed settings.

Values and preferences
There could be variability in values and preferences among groups of people assigned to undergo isolation. Isolation can cause distress through fear and risk perceptions, especially when people face unclear information and communication during a disease outbreak (*123*). Many staff and contacts related to isolated patients may report social stigma and emotional strain due to loss of anonymity (*124*). Those who are not intimate with the patients, however, could consider isolation to be an effective intervention in reducing their own chances of being infected (*123*).

Balance of benefits and harms
The objective of case isolation is to reduce transmission by reducing contact between ill persons and those who are susceptible (109). The overall effectiveness of isolation is moderate, and is greater when combined with other NPIs. However, individuals who share a room with an isolated case (e.g. a family member or roommate) may be at a higher risk of infection, owing to increased contact (*125*).

Resource implications
The evidence for cost–benefit and cost–effectiveness of case isolation is limited across settings and all evaluation was qualitative rather than quantitative. A stochastic simulation model showed that encouraging voluntary isolation of patients is a more effective strategy than school closure. Case isolation is also relatively inexpensive compared with school closure (*126*). A model based on the population of Canada reported high cost–effectiveness with a combination of community-contact reduction measures including personal protective measures, voluntary isolation and antiviral therapy (*117*). However, the cost–effectiveness of isolation alone was unclear. Direct costs might have a disproportionate impact on low-income groups, although the impact was considered moderate, and was mainly related to employment losses through people staying at home for 7–10 days (*125, 127*). Isolating patients may also increase the workload of health care workers or family members. The implementation of case isolation would involve a relatively large amount of resources.

Ethical considerations

Implementation of isolation in general does not bring about many ethical concerns, because home isolation is often adopted voluntarily by individuals who do not feel well enough to work or engage in other daily activities (*116, 119*). Some ethical concerns may arise when isolation interventions are mandatory; the main concerns being freedom of movement (*128*) and social stigma (*124*). Although isolation is an important intervention, some individuals may face economic pressure to go to work rather than stay at home (*129*). Home isolation may also bring about increased risks of infection among household members. Older adults who live alone may not receive sufficient care and support when home isolation is implemented (*88*). Finally, although the evidence related to equity is limited, isolation could reduce the rate of infection in areas with poor sanitation and vulnerability, thereby increasing equity.

Acceptability

Isolation of sick individuals is generally widely accepted by policy-makers and health workers, whereas the acceptability and compliance of case isolation among the public varies. A survey conducted among university students in the USA showed that at least 75% of people would like to isolate themselves from others when they are ill (130); however, only 6.4% of the cases remained at home (home isolation) (*131*). In a review, five studies reported that 50–96% of respondents intend to stay home rather than go to work when they are symptomatic; however, in another six studies the values reported were significantly lower (1–26%) (*132*). Family structure or the presumed infection status of family members can affect whether people accept isolation plans (*102*); for example, young children are less likely to be isolated alone at any stage of an epidemic (*102*).

Feasibility

Isolation of sick individuals may not be feasible in certain circumstances, and there are some obstacles to isolation. Infected individuals who do not know of their infection status (e.g. pre-symptomatic or asymptomatic) could perpetuate transmission in the community (29). The effectiveness of case isolation is sensitive to the timing of response; however, such delay may be inevitable in some situations and will greatly reduce the effectiveness of this measure (*118*). In addition, ethical and social issues related to case isolation may contribute to the variable acceptability and compliance among the community.

RECOMMENDATION:

Voluntary isolation at home of sick individuals with uncomplicated illness is recommended during all influenza epidemics and pandemics, with the exception of the individuals who need to seek medical attention. The duration of isolation depends on the severity of illness (usually 5–7 days) until major symptoms disappear.

Population: Infected cases

When to apply: At all times

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (effective)	Most evidence was from simulation studies; four epidemiological studies are all considered as providing very low quality evidence. There is theoretical plausibility for isolation to be effective in reducing influenza transmission in the community.

FACTORS	ASSESSMENT	RATIONALE
Values and preferences	Conditional	Values and preferences vary substantially among the community. Fear and social stigma are commonly experienced by patients and health care workers, while individuals who are not related to the isolated patients may consider case isolation to be an effective intervention in reducing their chances of being infected.
Balance of benefits and harms	Conditional	Home isolation could increase the risk of infection among family members.
Resource implications	Conditional	Home isolation should not incur resources from the public sector but may be costly at a societal level. Isolation outside the home could be very costly.
Ethical considerations	Conditional	Some ethical concerns arise when isolation measures are mandated, such as restriction of freedom of movement, lack of support for older adults who do not have a carer and economic pressure from work absenteeism.
Acceptability	Favourable	Acceptability and compliance of isolation are variable, but generally at a moderate level.
Feasibility	Conditional	This intervention may not be feasible because of many obstacles.

Overall strength of recommendation	Recommended	**Home isolation of ill individuals is simple, feasible and likely to be acceptable in all influenza epidemics and pandemics. Isolation of ill individuals outside the home is unlikely to be feasible in most locations**

Knowledge gaps: Most currently available studies on the effectiveness of isolation are simulation studies, which have a low strength of evidence. Available epidemiological studies looked at isolation combined with other interventions, or did not use laboratory-confirmed influenza as the outcome of interest. Although it is difficult to study isolation using RCTs, such studies would be very valuable. Understanding of transmission dynamics is incomplete, including the importance of pre-symptomatic contagiousness (*133*) and the fraction of infections that are asymptomatic (*134*). The optimum strategy for symptomatic persons is still uncertain.

RCT: randomized controlled trial.

6.3. Quarantine of exposed individuals

Summary of evidence
Terms relevant to isolation are defined below (Table 6).

Table 6. Definition of terms relevant to quarantine

TERM	DEFINITION
Quarantine	Imposed separation or restriction of movement of persons who are exposed, who may or may not be infected but are not ill, and who may become infectious to others (*109*).
Household quarantine	Confinement (commonly at home) of non-ill household contacts of a person with proven or suspected influenza (*29, 109*).
Home quarantine	Home confinement of non-ill contacts of a person with proven or suspected influenza.
Self-quarantine	Voluntary confinement of non-ill contacts of a person with proven or suspected influenza.
Work quarantine	1) Measures taken by workers who have been exposed and who work in a setting where the disease is especially likely to transmit (or where there are people at higher risk from infection); for example, people working in homes for the elderly, and nurses in high-risk units (*109*). 2) Measures taken by health care workers who choose to stay away from their families when off duty, to avoid carrying the infection home (*109*).
Maritime quarantine	Monitoring of all ship's passengers and crew for a defined period before permission is given to disembark(*135*).
Onboard quarantine	Monitoring of all flight's passengers and crew for a defined period before permission is given to disembark (*136*); this is also known as "airport quarantine" (*136*).

Six epidemiological studies (*112, 135-139*) and 10 simulation studies (*102, 105, 114, 115, 117, 140-144*) were eligible for inclusion in the review. Quarantine measures studied included household quarantine, border quarantine and maritime quarantine. Quarantine was studied as a single intervention or in combination with other interventions, generally with isolation and antiviral prophylaxis.

A quasi-RCT in Japan illustrated that voluntary waiting at home reduced risk of infection and number of infections (137). When a combination of isolation and quarantine was implemented in 1918–1919, excess death rates due to pneumonia and influenza were shown to decrease in New York City and Denver (112). Mandatory quarantine has also been shown to reduce the number of cases at the peak of epidemic fivefold, and it delayed the epidemic peak during the pandemic (H1N1) 2009 in Beijing (139). Maritime quarantine in small island nations was reported to have delayed or prevented the arrival of the 1918–1919 pandemic, indirectly reducing mortality in the region (135). One study assessed onboard quarantine inspection and found a minimal

impact in detecting and preventing the entry of cases; however, following up with passengers thereafter was found to be effective in preventing secondary infection from travellers (*136*). An epidemiological study in Australia in 2009 found that the odds of a household contact who was currently quarantined with the index case-patient becoming a secondary case-patient increased for each additional day (adjusted odds ratio [OR]: 1.25, 95% CI: 1.06–1.47) (*138*).

Among the simulation studies reviewed, four studies predicted a reduction in attack rate and cumulated incidence when quarantine of exposed individuals is implemented (*102, 114, 115, 117*). Combining quarantine with other interventions (e.g. household isolation with prophylaxis, school closure and workplace distancing) was suggested to further reduce influenza transmission (*102, 114, 115*). In addition, household quarantine has been suggested to be highly effective in reducing peak size and the total number of cases in a pandemic (*144*), whereas border quarantine had a minimal impact on reducing the number of cases (1*43*). Three studies reported the effectiveness of household quarantine and border quarantine in delaying the epidemic peak (*105, 117, 143*). The combination with other interventions further improved the effectiveness of quarantine in delaying the epidemic peak (*117*).

If quarantine were to be implemented, a reasonable period of time would be 4 days after exposure, which covers two incubation periods of seasonal influenza. If data were available on the incubation period of a new pandemic strain, then the quarantine period could be adjusted accordingly.

OVERALL RESULT OF EVIDENCE ON QUARANTINE OF EXPOSED INDIVIDUALS

1. The review identified six epidemiological studies and 10 simulation studies eligible for inclusion.

2. Quarantine is generally effective in reducing burden of disease and transmissibility, and in delaying the peak of the epidemic.

3. Some studies suggested a significant improvement in effectiveness of quarantine when combined with other interventions such as case isolation, antiviral prophylaxis or school closure.

Summary of considerations of members of the guideline development group
for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence that quarantine of exposed individuals has an effect on transmission of influenza; the studies identified in the review reported or predicted variable effectiveness.

Values and preferences
Values and preferences among quarantined populations are uncertain and variable. A survey in Turkey showed that a moderate percentage of students (69.4%) believed that quarantine was an effective intervention in reducing the transmission of influenza (*145*). The public expressed serious concerns for the potential outcomes of mandatory quarantine, such as overcrowding, exposure to infection, and inability to work, shop or contact family members (*146, 147*). Fear and a sense of

shame were also experienced by a proportion of the community, and many thought it impolite to maintain a distance from a sick acquaintance or relative (*148*). Health care workers were adversely affected due to the fear of acquiring infection (*123*). However, a study reported that 86.9% of the respondents held an optimistic attitude towards the effectiveness of quarantine (*149*).

Balance of benefits and harms

The overall effectiveness of quarantine in reducing the burden of disease and delaying the peak of an epidemic is moderate. Quarantine may be particularly useful when antiviral drug resources are limited (*125*). However, the location of quarantine is an important factor in deciding whether the intervention will bring about any harm. During the influenza A(H1N1)pdm09 pandemic, a study from China reported that university students who were quarantined in the room with a confirmed case were at higher risk of illness (*150*). A quasi-cluster RCT reported similar results, finding that more home-quarantined individuals fell ill when there was a sick family member (*137*). The likelihood of a household contact who is concurrently quarantined with an isolated individual becoming a second case has been estimated to increase with each day of quarantine (*138*). Thus, family members who share the same room or facilities with the infected case may have an increased risk of acquiring influenza.

Resource implications

Large-scale quarantine could be resource intensive. Household quarantine may be more cost-effective in locations with limited capacity; however, enforcing quarantine or monitoring compliance could still be a challenge because of resource constraints.

Ethical considerations

As with isolation, the main ethical concern of quarantine is freedom of movement of individuals (*139*). However, such concern is more significant for quarantine, because current evidence on the effectiveness of quarantine varies, and the measure involves restriction of movement of asymptomatic and mostly uninfected individuals. Mandatory quarantine increases such ethical concern considerably compared with voluntary quarantine (*128*). In addition, household quarantine can increase the risks of household members becoming infected (*114, 137, 138*). It has been suggested that a combined policy of household quarantine with antiviral prophylaxis can alleviate such concerns (*114*), but large stockpiles of antiviral drugs may not always be available for prophylactic use. Maritime quarantine and border quarantine are subject to similar concerns. On the other hand, onboard quarantine involves a shorter duration of restriction of movement, but current evidence suggests that this intervention has low cost–effectiveness and minimal impact on influenza control.

Acceptability

Acceptability and compliance of quarantine are variable, but are generally at a moderate level (*125*). In a telephone survey conducted in Australia, more than 90% of respondents reported being willing to stay at home, especially after being given brief information about pandemic influenza (94.1% before and 97.5% after) (151). Two other studies had a similar conclusion, with 94% (*152*) and 92.8% (*149*) of respondents reported to adhere to a quarantine recommendation. However, a cross-sectional survey in Australia reported different results, with only 53% of households being fully compliant with quarantine. The compliance was better among individuals who had more understanding about quarantine (OR: 2.27) (*153*). Similar to the isolation of sick individuals, family structure or infection status of family members affects an individual's decision about whether to accept quarantine plans (*102*).

Feasibility

There are some barriers and obstacles to the successful implementation of quarantine of exposed individuals. Home quarantine with infected cases can significantly increase the risk of acquiring infection (*125*). In addition, because the incubation period of a novel pandemic influenza strain may be uncertain, home quarantine may at times be implemented for an extended period, which will cause financial burden on families due to work absenteeism (*154*). There have been programmes of quarantine in 61% of national pandemic plans, but detailed strategies of quarantine implementation were not provided and existing infrastructure may vary by country (*65*).

RECOMMENDATION:

Home quarantine of exposed individuals to reduce transmission is not recommended because there is no obvious rationale for this measure, and there would be considerable difficulties in implementing it.

Population: People who have had contact with infected cases

When to apply: N/A

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (variable effectiveness)	The quality of evidence across all included articles, with the exception of a quasi-cluster RCT, is very low. The effect of quarantine in reducing influenza transmission varied.
Values and preferences	Conditional	There are likely to be concerns about issues such as overcrowding, exposure to infection and inability to contact family members when quarantine measures are implemented. However, most people should consider quarantine as a justifiable intervention.
Balance of benefits and harms	Conditional	The overall effectiveness in control of influenza is moderate; however, individuals subjected to quarantine with an infected case could be at higher risk of acquiring infection.
Resource implications	Conditional	The evidence of cost–benefit or cost–effectiveness of quarantine measures is limited, but the guideline development group believed that resources could be better used in other mitigation measures.
Ethical considerations	Conditional	Individual freedom of movement and the increased risk of infection among individuals subjected to home quarantine with an infected case are essential ethical issues.

FACTORS	ASSESSMENT	RATIONALE
Acceptability	Favourable	Acceptability and compliance of quarantine varies, but are generally at a moderate level.
Feasibility	Conditional	The feasibility of quarantine measures may not be high owing to the possible increase in secondary cases, and the financial burden due to work absenteeism.

Overall strength of recommendation	Not Recommended	Not recommended due to feasibility concerns with very low quality of evidence.

Knowledge gaps: Most of the currently available evidence on the effectiveness of quarantine on influenza control was drawn from simulation studies, which have a low strength of evidence. Available epidemiological studies did not rely fully on laboratory-confirmed influenza as the outcome of interest. Although it is difficult to study quarantine using RCTs, robust data from experimental studies would be valuable. In addition, as part of simulation studies, assumptions have been made in various aspects of model construction, many of which still require more robust evidence; for example, the asymptomatic fraction among all infections, the possibility of "superspreaders" and the nature of compliance behaviour (*102, 141*). There was limited information in the literature on the ideal or optimum timing of quarantine.

N/A: not applicable; RCT: randomized controlled trial.

6.4. School measures and closures

Summary of evidence

School-age children are particularly important in influenza transmission in the community, and attack rates are typically highest in this age group in epidemics and pandemics. School measures to reduce influenza transmission vary in scope from very simple measures (e.g. increasing distancing between desks) through to drastic measures (e.g. completely closing all schools). The systematic review team focused on school closures because this is the most well-studied measure; the team also examined evidence on other measures.

One published review examined school measures other than school closures, including increasing desk distance between students, cancelling or postponing after-school activities, restricting access to common areas, staggering the school schedule, reducing mixing during transport to and from school, dividing classes into smaller groups, and cancelling classes that bring students together from multiple classrooms (*155*). Another potentially important measure could be increasing attention to influenza-like symptoms in children, and either ensuring that ill children do not attend school or segregating them from other students.

These measures could promote social distancing and decrease density among students, but there was limited evidence on the effectiveness of these measures (*155*).

Closure of schools can be reactive or proactive (Table 7) (*156*). Reactive closures occur when schools are closed after the occurrence of influenza outbreaks in those schools. Proactive closures occur when schools or groups of schools are closed as a deliberate measure to reduce transmission in the community, whether or not there have been influenza outbreaks in those schools. Class dismissal refers to the scenario where schools remain open but classes are not held; this can serve the purpose of continuing to provide school meals and childcare to some children (e.g. those from lower income families).

Table 7. Definition of terms relevant to school closures

TERM	DEFINITION
School closure	School is closed to all children and staff.
Class dismissal	School campus remains open with administrative staff, but most children stay home.
Reactive closure or dismissal	School is closed after a substantial incidence of ILI is reported among children or staff (or both) in that school.
Proactive closure or dismissal	School is closed before a substantial transmission among children and staff is reported.

ILI: influenza-like illness.

A systematic review published in 2013 identified 79 epidemiological studies on school closures, and summarized the evidence as demonstrating that this intervention could reduce the transmission of pandemic and seasonal influenza among school children; however, the optimum strategy (e.g. length of closure, and whether it should be reactive or proactive) remained unclear, owing to heterogeneity of the data (*157*). The current systematic review updated the 2013 review, identifying 22 additional epidemiological studies that met the inclusion criteria, giving a total evidence base of 101 studies (Annex).

Included studies fell into a number of types. The first type of study involved the analysis of proactive school closures implemented in seasonal epidemics or in pandemics. A comprehensive analysis of interventions conducted in the USA in the 1918–1919 pandemic estimated that early and sustained interventions, including school closures, reduced overall mortality by up to 25% in some cities (*158*). Two other studies examined NPIs in the 1918–1919 pandemic, and reported that the combined use of NPIs (including school closures) was able to delay the time to peak mortality, and to reduce peak mortality and overall mortality (*112, 159*). Two studies conducted in Hong Kong SAR during the 2009 pandemic reported that a proactive 4-week school closure followed by scheduled school summer holidays reduced transmission in the community (*160, 161*), with one study estimating that the reproductive number was reduced from 1.7 to 1.5 during the proactive closures, and to 1.1 during the rest of the summer holidays (*161*). A study of school closures in Mongolia estimated a reduction in the overall attack rate by 1.1% and a delay in the epidemic peak by more than 1 week (*162*).

A second group of studies investigated reactive school closures. One detailed study of transmission in a school in Pennsylvania identified no effect of the reactive closure that was implemented when 27% of students already had symptoms (*163*). Two studies conducted in Japan estimated reductions in the epidemic peak and overall attack rate by about 24% and 20% (*164, 165*). A study of reactive school closures in London in 2009 estimated that the closures reduced the reproductive number

from 1.33 (95% CI: 1.11–1.56) to 0.43 (95% CI: 0.35–0.52) (166). A study in the USA suggested that absenteeism could be reduced by about 2–3% after the reopening of school that had been closed due to outbreaks (167), and another study estimated that outbreak duration decreased by 4.98 days for a 2-day closure (168). However, other studies did not show a beneficial effect in reactive school closures in terms of reducing the overall attack rate and influenza duration (169, 170).

A third group of studies investigated the impact of regular school holidays. A study in France estimated that routine school holidays prevented 18% of seasonal influenza cases (18–21% in children) (171). Analysis of data from London from the 2009 pandemic suggested that transmission was substantially lower in the summer holidays of 2009, but resurged after schools reopened (172). An epidemiological analysis in Peru also reported that the number of infected cases declined throughout a school closure period (173). One study in the USA found an unchanged pattern in school-age children, but increasing influenza incidence among adults and children aged under 5 years during planned winter holidays (174). In addition, a cohort study in the USA indicated no difference in post-break absenteeism in schools on holidays compared with schools that remained open at the same time (RR: 1.07, 95% CI: 0.96–1.20) (175). More recently, planned school holidays, including winter or summer holidays with the addition of some public holidays, were estimated to reduce influenza transmission (176-185) in terms of reducing transmission by 10–40% (176, 179-181, 185) and delaying the peak for more than 1 week (183, 184).

> **OVERALL RESULT OF EVIDENCE ON SCHOOL MEASURES AND CLOSURES**
>
> 1. The effect of reactive school closure in reducing influenza transmission varied but was generally limited. Proactive closures and planned school holidays had a moderate impact on transmission.
> 2. Although school closures alone might have an impact, combination with other interventions improved the effectiveness.
> 3. If schools remain open during a pandemic or epidemic, school measures can be considered in order to reduce transmission

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence, and the studies that have been published reported or predicted that school measures and closures have a variable effect on transmission of influenza.

Values and preferences
There was little variability in the importance that populations assign to school closures; for example, in a survey in the USA, 92% of caregivers and 89% of teachers reported that they believed school closures were somewhat effective in reducing influenza cases among school-age children (186). School closures affect families with children.

Balance of benefits and harms

School closures can reduce influenza transmission, but the timing and duration is critical, and mistimed closures could lack impact. On the other hand, closures could have a major impact on the safety, health and nutrition of children in lower income families (*187*); for example, missing work to take care of children can affect income (*125*), and access to free school meals could be an additional concern for low-income families (*188*). School measures would reduce density and contact rates among students, and these interventions may cause mild disruption to schools and communities.

Resource implications

School closure is one of the measures that is found to be potentially not cost-effective (*189*). A review suggested that the cost of proactive closure can be significant, at £0.2 billion – £1.2 billion per week in the United Kingdom of Great Britain and Northern Ireland (which equates to 0.2–1% of the United Kingdom's gross domestic product [GDP]), with similar results found in Australia (*125*). Proactive closure in the USA for 4 weeks could cost US$ 10–47 billion (0.1–0.3% of GDP) (*190*). Another study in the USA also estimated a $21 billion (>3% GDP) loss for an 8-week reactive school closure (*191*). A simulation study predicted that school closures could reduce influenza transmission, but at increased cost to society (*192*). School measures could have some resource implications.

Ethical considerations

School closures raise major ethical issues for families and communities (*125*, *188*). Closures can have a substantial social impact because they may require parents to make other arrangements for care or supervision of their children, which can be particularly challenging for some families, especially if closures are prolonged. Social equity concerns might be exacerbated when closing schools, because children from lower income families may receive subsidized free food at school (*188*). Students' educational advancement could be jeopardized if they miss important exams or class work, and do not have alternative learning strategies (*32*). Moreover, media reporting of school closures may increase pandemic-related fears and concerns among the local community (*32*). Extending the school holidays might increase travel and thus lead to the temporary loss of health care workers from the health care system. Moreover, the availability of parents or caregivers would need to be taken into account when excluding ill children from school; segregation of ill children at school might be an alternative to exclusion in some locations.

Acceptability

Two studies in the USA and Australia suggested that most families (more than 90%) agree to the implementation of school closure as a potential intervention to reduce influenza transmission (*151*, *193*). To accommodate the closure period, the school may be required to extend the school year or offer alternative learning programmes (e.g. online learning), which may require extensive discussions with local authorities, given that extra costs may be incurred in extending the school year. There are also practical difficulties in communicating needs at different levels (national, local, school and individual), particularly in situations where uncertainty and risk assessments may change rapidly (*194*, *195*). Such measures will probably only be acceptable to most stake-holders when the benefits clearly outweigh the negative consequences. According to a review of state government planning documents in the USA, in their published influenza preparedness for schools, 42% of the states mentioned that school measures could promote social distancing (*155*). The acceptability of school measures at a national level is likely to be high.

Feasibility

The feasibility of school closure is questionable. Reactive school closures, rather than proactive school closures, are often implemented for operational reasons (*194*). Proactive school closures have been implemented during seasonal epidemics in some locations (*194*). School closures are most effective if children stay at home rather than engaging in extracurricular activities, although this may be difficult to control (*196, 197*). Most (61%) national pandemic influenza preparedness implementation plans give recommendations about school closures but lack further detail (*65*). There may be considerable variation in social structures and legal frameworks relating to school closures in different Member States (*198, 199*). The guideline development group suggested that a class dismissal intervention could still include a provision for children of low-income families or essential workers to attend school, and this could be a more flexible measure than complete school closure.

> **RECOMMENDATION:**
>
> School measures (e.g. stricter exclusion policies for ill children, increasing desk spacing, reducing mixing between classes, and staggering recesses and lunchbreaks) are conditionally recommended, with gradation of interventions based on severity. Coordinated proactive school closures or class dismissals are suggested during a severe epidemic or pandemic. In such cases, the adverse effects on the community should be fully considered (e.g. family burden and economic considerations), and the timing and duration should be limited to a period that is judged to be optimal.
>
> **Population:** Students and staff in childcare facilities and schools
>
> **When to apply:** Gradation of interventions based on severity; school closure can be considered in severe epidemics and pandemics

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (variable effectiveness)	No RCTs were identified, and the quality of evidence is very low. The effect of school measures and closures in reducing influenza transmission was variable.
Values and preferences	Favourable	There was little variability in the importance that populations assign to school closures.
Balance of benefits and harms	Conditional	The balance between benefits and harms is uncertain for school closures, which may cause the loss of work or salary.
Resource implications	Conditional	School closures were associated with moderate costs but were less cost-effective than stockpiling antiviral drugs or pre-pandemic vaccines.
Ethical considerations	Conditional	School closure has ethical repercussions on families and communities, such as the loss of subsidies for lower income families, and increasing fear and concern in the community (which may be exacerbated by heightened media attention).

FACTORS	ASSESSMENT	RATIONALE
Acceptability	Conditional	Most families would accept the class dismissal decision, but the decision-making authority to close schools in different jurisdictions varies widely. School authorities may fear incurring extra costs by extending the school year. School measures are likely to be highly acceptable at a national level.
Feasibility	Conditional	Because of the uncertainty and variability of influenza transmission, it is difficult to predict whether it will develop into a severe epidemic or pandemic.

Overall strength of recommendation	Conditionally recommended	School measures are likely to be feasible in any epidemic or pandemic. The balance between the advantages and disadvantages of school closures is less certain, but closure may be considered in more severe scenarios.

Knowledge gaps: More research is needed on the best triggers to close and reopen schools, and on the optimal timing and duration of school closures in order to maximize the impact of this disruptive intervention. The difference in compliance between individuals of different social status is still uncertain. There was little research on the impact of school measures on transmission.

RCT: randomized controlled trial.

6.5.   Workplace measures and closures

Summary of evidence

The systematic review identified 12 simulation studies and three epidemiological studies from the systematic review published by Ahmed et al. (200), and four additional studies from the updated search (*117, 137, 201, 202*). Workplace measures included paid-leave policy, telework from home, staggered shifts (e.g. having different activity and meal times, and times of entry and exit from the workplace), reduced contact and weekend extension. The epidemiological and simulation studies included in the review by Ahmed et al. suggested that these measures could reduce the overall number of influenza cases. In addition, the implementation of a workplace measure alone was associated with a median 23% reduction in the cumulative incidence of infections to a reproductive number of 1.9 or less (*200*). Simulation studies also showed a delay and reduction in the peak influenza attack rate; however, the effectiveness was estimated to decline with a higher basic reproductive number or a delay in implementation of the intervention (*200*).

Among the four most recent articles since the review by Ahmed et al., a quasi-cluster RCT in Japan showed that paid sick leave policy in the workplace reduced the overall risk of influenza A (H1N1) by about 20% in one influenza season (*137*). The other two epidemiological studies in the USA illustrated that providing paid sick leave could help to reduce transmission in workplaces resulting in an overall decrease of influenza-related absenteeism (*201*, *202*). Workplace measures combined with other interventions (e.g. school closures, personal protective measures and antiviral drugs) showed greater effectiveness (*117*).

Evidence on the effectiveness of workplace closure is limited; six simulation studies were identified (*114*, *142*, *203-206*). The simulation suggested that large-scale workplace closures could delay the time of peak occurrence for 5–10 days, but such closures were less effective than other interventions (e.g. school closures) (*204*, *205*). Closing all schools and closing 10% of workplaces could only delay the peak time by around 4% (*206*). Some studies predicted that workplace closures combined with school closures would be effective in reducing the spread of influenza by decreasing the overall attack rate by about 15–45% and decreasing the height of the epidemic peak by up to 40% (*114*, *203*, *206*). One simulation study predicted that the single strategy of workplace closure would have little impact; however, the combination of workplace closure, school closure, home isolation and a modest level of antiviral drug coverage would be effective in mitigating the impact of an epidemic (*142*).

OVERALL RESULT OF EVIDENCE ON WORKPLACE MEASURES AND CLOSURES

1. The included studies indicated that workplace measures (e.g. telework from home, staggered shifts, weekend extension and paid-leave policy) could reduce both the overall and the peak number of influenza cases, as well as delaying the occurrence of the peak.
2. The overall effectiveness and feasibility of workplace measures is modest, but combination with other interventions can improve its effectiveness.
3. The strength of evidence on workplace closure is very low because the identified studies are all simulation studies. Large-scale workplace closures could delay the epidemic peak for more than 1 week, and small-scale closures may have a modest impact on attack rate or peak number.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence that workplace measures and closures reduce influenza transmission.

Values and preferences
There was uncertainty and variability in the importance that populations assign to workplace measures to reduce influenza transmission. A study in the Netherlands reported that 30% of respondents believed that staying home from work is an efficacious means of reducing influenza transmission (207); in another study, 93% of New York State residents believed that staying home is effective in preventing influenza transmission (*208*). A study in the USA showed that 28% of

employed respondents reported that they might lose their jobs or businesses as a result of having to stay home from work for 7–10 days in the event of a pandemic influenza outbreak (*127*). This would also cause severe personal economic crises among some members of the public, but less so for those who received pay while they worked remotely (*127*).

Limited studies showed the values and perceptions among the population on the potential consequences of workplace closures. One study mentioned that large-scale workplace closures might raise the public's concern about the potential economic and financial consequences (*209*). Although there is limited evidence, it may be reasonable to expect increased levels of distress among employers and employees in the event of a workplace closure, because of possible operational and financial impacts (*210*).

Balance of benefits and harms
Workplace measures could potentially reduce transmission by about 20–30%, based on the included studies. A review illustrated that telecommuting without pay would be inequitable, and would impact particularly on self-employed people or low-income families, because they have a higher risk of suffering from severe financial problems as a result of workplace measures (*125*). Large-scale workplace closures are likely to have substantial economic consequences. However, if school closures are also implemented, workplace closures may avoid the need for some working parents to make other childcare arrangements.

Resource implications
The guideline development group believed that workplace measures and closures might be an economic burden on the government. Telecommuting was found to be modestly effective in reducing influenza transmission, but also likely to be economically disruptive (*125*). The most costly strategy considered in a simulation study was that of a continuous school closure together with a continuous 50% workplace non-attendance; this scenario has the highest overall cost (US$ 103 million) and the highest cost per prevented case (US$ 9894 per case) (*211*). Workplace closures can also be economically disruptive (*125*), and the cost of full workplace closures for any period of time will have significant economic impact (88).

Ethical considerations
Workplace measures and closures could affect the economy and productivity of a society. A survey in the USA found that self-employed individuals and those unable to work from home might not be able to comply with recommended workplace measures because of job insecurity and financial considerations (*125, 127*). Social equity concerns may be exacerbated by workplace closure due to the lack of income to pay for necessities in lower income families.

Acceptability
Workplace measures may be acceptable if they are well-planned in selected workplaces. Most stakeholders are unlikely to find workplace closures acceptable. The guideline development group encouraged giving isolated and quarantined individuals the opportunity to telework. Employees will accept workplace closures only if there is no anxiety regarding job security and income replacement (*88*). In addition, companies and authorities will not accept this intervention because of high operational costs.

Feasibility
Telework, paid-leave policy and staggered-shift measures are unlikely to be feasible in most circumstances. Workplace closure is also likely to have a number of feasibility issues; for example, many companies provide essential services to the community or facilitate off-site working, and thus cannot be closed. Overall, the guideline development group believed that mandated workplace closure is unlikely to be feasible.

RECOMMENDATION:

Recommendation: Workplace measures (e.g. encouraging teleworking from home, staggering shifts, and loosening policies for sick leave and paid leave) are conditionally recommended, with gradation of interventions based on severity. Extreme measures such as workplace closures can be considered in extraordinarily severe pandemics in order to reduce transmission.

Population: Selected workplaces

When to apply: Gradation of interventions based on severity. Workplace closure should be a last step that is only considered in extraordinarily severe epidemics and pandemics

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very Low (effective)	One quasi-cluster RCT is on workplace measures, and the quality of the rest of the evidence is very low. All identified studies of workplace closure are simulation studies, which provide very low quality of evidence. Workplace measures and closures are effective in reducing influenza transmission in the community.
Values and preferences	Conditional	There is significant uncertainty surrounding people's values and preferences on workplace measures and closures.
Balance of benefits and harms	Conditional	Potentially effective in reducing influenza transmission, but may have economic harms.
Resource implications	Conditional	Workplace measures and closures can be economically disruptive.
Ethical considerations	Conditional	Workplace measures and closures may have adverse impacts on the economy and productivity of a society.
Acceptability	Conditional	Unlikely to be acceptable in all but the most severe pandemics.
Feasibility	Conditional	Many workplaces cannot be closed (e.g. those that provide essential services). Workplace closures may have limited feasibility.

Overall strength of recommendation	Conditionally recommended	The balance between the advantages and disadvantages of implementing workplace measures and closures is uncertain. Some measures may be relatively feasible and may contribute to reduced transmission in the community. Workplace closures may only be warranted as an extreme social distancing measure in an extraordinarily severe pandemic.

Knowledge gaps: As with school closures, more research is needed on the best trigger factors, timing and duration of workplace closures in order to maximize the impact of this highly disruptive intervention. There is a need for a comprehensive review of the ethical issues of workplace measures, as well as a comparison of the benefits and costs of implementing the measures. Other potential workplace measures have not been studied in depth, such as providing segregated working areas for people with mild symptoms. In addition, studies are needed on feasibility and scope of implementation of workplace measures, and the potential impact on families and the public.

RCT: randomized controlled trial.

6.6. Avoiding crowding

Summary of evidence
Three epidemiological journal articles were included in our systematic review (112, 159, 212). One of those studies concerned World Youth Day 2008 pilgrims; it found that sleeping in a small group reduced the transmission of influenza compared with sleeping in one large hall (212). Another two articles were based on the 1918–1919 pandemic; both articles found that timely bans on public gatherings and closure of public places appeared to reduce the excess death rate (Spearman ρ=0.31 and 0.46) (112, 159). However, it is impossible to determine the individual effects of measures to avoid crowding in these studies.

OVERALL RESULT OF EVIDENCE ON AVOIDING CROWDING

1. The effect of measures to avoid crowding alone in reducing transmission is uncertain.

2. Timely and sustained application of measures to avoid crowding may reduce influenza transmission, although the quality of evidence of its effectiveness is very low.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence

There is a very low overall quality of evidence on whether avoiding crowding can reduce transmission of influenza.

Values and preferences

There was uncertainty or variability in the importance that populations assign to avoiding crowding to reduce influenza transmission. A survey in Thailand reported that 54% of respondents believed that avoiding gatherings of five or more people could reduce the spread of diseases during an outbreak (*213*). Surveys in the United Kingdom and the Netherlands also showed a similar result: half of the respondents believed that this intervention would reduce the risk of getting infected with the influenza virus (*87, 207*).

There are differences in perception of expected outcomes from avoiding crowding among different populations. Some participants in a survey in the USA argued that they would approve of avoiding religious activities if it could reduce influenza transmission (*209*); however, other people believed that avoiding gatherings might prevent them from receiving support (e.g. worshipping and praying together) from their religious community during the crisis (*209*).

Balance of benefits and harms

Avoiding crowding, in combination with other social distancing measures, may reduce influenza transmission, but there is no conclusive evidence to determine its effect (*214*). Modification, postponement or cancellation of mass gatherings may have cultural or religious implications, and may incur considerable costs (*88, 209*).

Resource implications

The financial fragility of religious organizations was a concern, and mandatory closure may be seen as a financial hardship for many institutions (*209*). Governments might face legal liabilities for financial losses associated with workplace measures or closures.

Ethical considerations

Avoiding crowding may have cultural or religious implications (*209*). Gatherings are important places to share information during influenza, which can comfort people and reduce fear. The abolition of religious gatherings may violate the devout faith of the participants and make them feel morally guilty. The guideline development group suggested that it would not be possible to cancel some events (e.g. the Hajj).

Acceptability

The acceptability of avoiding crowding among the public may depend on the type and importance of the gathering (*125*). In a survey in Australia in 2007, 94.2% of participants were reported as being willing to avoid public events (*151*), and a polling study in five countries (Argentina, Japan, Mexico, United Kingdom and the USA) in 2010 showed that 11–69% of respondents would like to avoid places where many people gather (e.g. shopping centres or sporting events) during a pandemic (*215*). However, some participants might oppose the mandatory cancellation of religious gatherings during a pandemic (*209*). During a WHO consultation of influenza A(H1N1)pdm09, most reporting countries stated they had not instituted restrictions on mass gatherings, and were taking a wait-and-see approach for any upcoming events in their countries (*216*).

Feasibility

There have been recommendations for the prohibition of mass gatherings but without further details in most (66%) national pandemic influenza preparedness implementation plans (*65*). However, it is still uncertain whether measures to avoid crowding alone would have a large effect.

RECOMMENDATION:

Avoiding crowding during moderate and severe epidemics and pandemics is conditionally recommended, with gradation of strategies linked with severity in order to increase the distance and reduce the density among populations.

Population: People who gather in crowded areas (e.g. large meetings, religious pilgrimages, national events and transportation hub locations).

When to apply: Moderate and severe epidemics and pandemics.

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very Low (unknown)	No RCTs were found and the quality of evidence across all reviewed articles is very low. The effect of measures to avoid crowding alone is unknown.
Values and preferences	Conditional	Some people believe that the outcome of this intervention is conducive to reducing the risk of viral transmission, but others may view it as a barrier to accessing group support and personal freedom.
Balance of benefits and harms	Conditional	The effect of measures to avoid crowding alone is uncertain, and this intervention may have cultural or religious implications.
Resource implications	Conditional	There might be cost considerations among organizers, attendees and employees.
Ethical considerations	Conditional	There may be cultural or religious issues.
Acceptability	Conditional	Likely to be acceptable in severe pandemics.
Feasibility	Conditional	The programmatic considerations and existing infrastructure may hinder the implementation of avoiding crowding.
Overall strength of recommendation	**Conditionally recommended**	**The balance between the advantages and disadvantages of avoiding crowding is less certain, but may be justifiable in severe pandemics.**

Knowledge gaps: There are still major gaps in our understanding of person-to-person transmission dynamics. The reduction of mass gatherings is likely to reduce transmission in the community, but its potential effects are difficult to predict with accuracy. Large-scale RCTs are unlikely to be feasible.

RCT: randomized controlled trial.

7. TRAVEL-RELATED MEASURES

7.1.   Travel advice

Summary of evidence
There is no evidence measuring the effect of travel advice on influenza transmission.

Summary of considerations of members of the guideline development group
for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
The quality of evidence cannot be judged because no study was identified.

Values and preferences
Travel advice helps the public make informed decisions when travelling, and offers them an objective assessment of the risks involved in travelling during an epidemic or pandemic (*217*). Travel advice increases travellers' awareness of travel risk in affected regions. No literature on the values and preferences of travel advice was identified in the systematic review.

Balance of benefits and harms
Travel advice can potentially reduce travellers' exposure to influenza viruses and limit the spread by deterring travel to regions affected by epidemics or pandemics (*218*). However, travel advice that recommends public avoidance of travel or trade may have financial consequences to the local and global economy (*219*). The systematic review did not identify any literature that demonstrated benefits and harms related to travel advice.

Resource implications
The resource implications of providing information to individuals depend on the approach used to disseminate travel advice. However, the overall resource implications of providing travel advice are uncertain.

Ethical considerations
Strategies to maintain public trust and increase compliance with the travel advice should be carefully considered (*219*).

Acceptability
Public health authorities have generally included public awareness campaigns as part of their ongoing strategy to increase travellers' awareness of infectious disease risks, including influenza, during travel. Issues with acceptability of travel advice are unlikely, but cultural issues and potential economic consequences should be considered.

Feasibility
Member States routinely provide travel advice for infectious diseases (e.g. dengue, malaria and Middle East respiratory syndrome), and they did provide advice in the early stages of the 2009 H1N1 pandemic.

RECOMMENDATION:

Travel advice is recommended for citizens before their travel as a public health intervention in order to avoid potential exposure to influenza and to reduce the spread of influenza.

Population: Citizens before travelling

When to apply: Early phase of pandemics

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	None	No scientific evidence identified in the systematic review.
Values and preferences	Favourable	Travel advice can increase travellers' awareness of travel risk in areas where they may be exposed to circulating influenza viruses.
Balance of benefits and harms	Favourable	Although travel advice may contribute to the reduction of potential exposure and onward transmission of infections, there may be economic consequences of reduced travel.
Resource implications	Favourable	Uncertain. May have consequences for countries affected early if travel advisories are issued against those countries.
Ethical considerations	Favourable	No major ethical issues.
Acceptability	Favourable	Travel advice is likely to be acceptable in most settings.
Feasibility	Favourable	Travel advice is already used for other infections and in previous pandemics; there are no anticipated feasibility issues.
Overall strength of recommendation	**Recommended**	**No scientific evidence was identified for the effectiveness of travel advice against pandemic influenza; however, providing information to travellers is simple, feasible and acceptable.**

Knowledge gaps: Studies measuring the effect of travel advice on influenza transmission would be welcome.

7.2. Entry and exit screening

Summary of evidence
Ten articles related to entry and exit screening were included in this review (*185, 220-228*). Observational studies conducted at airports estimated that the sensitivity of entry screening was low (*226-228*). Among arriving international travellers, half of the influenza cases were identified more than a day after arrival (through passive case finding and contact tracing in the community), although 37% of the influenza cases were screened while passing through the border entry site (*185*). Simulation studies estimated that screening international travellers may help to delay the epidemic by less than 2 weeks (0–12 days) (*220-222*).

OVERALL RESULT OF EVIDENCE ON ENTRY AND EXIT SCREENING

1. Ten studies were included in this review.
2. Considering the asymptomatic period of infected patients and the sensitivity of screening devices, the effectiveness of screening travellers is likely to be very limited.

Summary of considerations of members of the guideline development group for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence that entry and exit screening can delay the introduction of infection to a country and local transmission.

Values and preferences
The sensitivity of screening can have an impact on the effectiveness of traveller screening at entry and exit points. Screening measures included health declarations, visual inspections and thermography to detect disease symptoms (*229*). One of the major criteria for screening travellers for influenza infections is fever, and screening sensitivity is largely reliant on detecting fever by available instruments. Infrared thermometers are used at some borders due to the instantaneous and non-invasive nature of their use. A study conducted in Japan during the influenza pandemic A(H1N1)pdm09 in 2009 reported that the sensitivity of infrared thermometers was 50.8–70.4% and the specificity 63.6–81.7% (*224*). A study conducted in New Zealand reported that the sensitivity of infrared thermal image scanners was 84–86% and the specificity 31–71% (*225*). It is possible that some travellers with fever might opt to take antipyretics to reduce their symptoms before travel, to avoid detection of their fever by thermal scanners or thermometers.

Molecular diagnostics such as polymerase chain reaction (PCR) can be used at ports of entry, but these are generally more cost and resource intensive, and are unlikely to be applied to a large number of travellers (*223*). Point-of-care antigen detection tests might be more feasible but would also be costly (*223*).

Balance of benefits and harms
The systematic review identified no literature on the harm of screening travellers. Influenza cases may remain asymptomatic for a few days (up to 2 days for seasonal influenza) (*185*), symptom presentation varies and screening methods are imperfect (*230*); therefore, traveller screening for symptoms of influenza virus infection has major limitations in preventing the introduction of influenza into a location, and reducing the overall attack rate and duration of an epidemic (*228*).

Resource implications

Substantial public health resources would be required, including adequate numbers of trained staff, screening devices and laboratory resources, and adequate infrastructure to conduct effective screening of travellers *(228)*.

Ethical considerations

Involuntary screening needs to be considered and implemented with care to respect the privacy of travellers *(219)*.

Acceptability

Screening travellers using infrared thermometers continues to be used in some ports of entry and is generally accepted by policy-makers as a "visible" public health measure. Exit screening was not implemented in the 2009 influenza pandemic, and its acceptability for preventing or delaying the introduction of influenza infections to a location is uncertain.

Feasibility

Entry screening is used in some ports of entry and has been shown to be feasible.

RECOMMENDATION:

Entry and exit screening for infection in travellers is not recommended, because of the lack of sensitivity of these measures in identifying infected but asymptomatic (i.e. pre-symptomatic) travellers.[a]

Population: N/A

When to apply: N/A

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (lack of effectiveness in reducing influenza transmission)	The overall quality of available evidence was very low, and the overall effectiveness of entry and exit screening on influenza pandemics is ineffective due to the sensitivity of screening measures and asymptomatic period of infected patients.
Values and preferences	Conditional	One of the major criteria used in the screening of travellers for influenza infections is fever. Thus, screening sensitivity is largely reliant on the detection of fever.
Balance of benefits and harms	Conditional	There was no literature on the benefits and harms of traveller screening.
Resource implications	Conditional	Substantial public health resources are required, which may be better used elsewhere.

[a] Some locations routinely monitor the temperature of incoming travellers; for example, in an effort to identify incoming travellers with symptoms of Ebola virus disease, avian influenza, Middle East respiratory syndrome or some other emerging infectious disease. The recommendation here to not implement entry or exit screening is specific to seasonal and pandemic influenza.

FACTORS	ASSESSMENT	RATIONALE
Ethical considerations	Conditional	Involuntary screening may have ethical or legal implications.
Acceptability	Favourable	Screening is likely to be acceptable in general.
Feasibility	Favourable	Feasibility has been demonstrated for several infectious diseases.

Overall strength of recommendation	Not Recommended	**Not recommended due to the overall ineffectiveness in reducing the introduction of infection and delaying local transmission.**

Knowledge gaps: There were no high-quality studies on the effectiveness of entry and exit screening. Studies on the best approaches to screening travellers at different times, with different measures and for different pathogens are required to understand the potential advantages of screening travellers (*230*).

N/A: not applicable.

7.3. Internal travel restrictions

This section covers internal travel restrictions only – international travel restrictions are not covered in this document[1].

Summary of evidence

One epidemiological study (*231*) and four simulation studies (*114, 162, 232, 233*) related to internal travel restrictions were included in this review. A time-series analysis study conducted in the USA showed that frequency of domestic airline travel is temporally associated with the rate of influenza spread, and following the September 11 attacks in 2001, a reduction in such travel delayed the epidemic peak by 13 days compared with the average for other years (*231*). A simulation study predicted that implementation of a strict travel restriction (95% travel restriction, enforced for 4 weeks) could reduce the epidemic peak by 12%, and a moderate restriction (50% travel restriction, enforced for 2–4 weeks) could delay the pandemic peak by 1–1.5 weeks (162). Another simulation study predicted that an internal travel restriction of more than 80% could be beneficial (*232*). A strict internal travel restriction (90%) was also consistently found to delay the epidemic peak by 2 weeks in the United Kingdom, and by less than 1 week in the USA (114). However, a 75% restriction had almost no effect (*114*).

OVERALL RESULT OF EVIDENCE ON INTERNAL TRAVEL RESTRICTIONS

1. Five studies were included, four of which were simulation studies.
2. The effectiveness of internal travel restrictions depends on the level of restriction – only very strict restrictions would be expected to have an impact on influenza transmission.

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[1] The WHO IHR secretariat is in the process of developing a guidance on the effectiveness of travel and trade restrictions to prevent, delay or control international spread of diseases, including pandemic influenza.

Summary of considerations of members of the guideline development group
for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence that internal travel restrictions can reduce influenza transmission.

Values and preferences
Values and preferences related to internal travel restrictions are uncertain.

Balance of benefits and harms
Legal and ethical issues surrounding restrictions on freedom of movement of persons (*219*) and economic consequences are potential harms that may result from internal travel restrictions (*234*).

Resource implications
Restricting internal travel would require a large amount of public resources, including the provision of public advice and a large number of staff. Furthermore, there would be consequences for the supply chains of food and essential medicines due to the disruption of movement.

Ethical considerations
The human right to freedom of movement should be considered (*219*), as should potential adverse economic impacts, particularly in vulnerable populations such as migrant workers and individuals who need to travel to seek medical attention (*219).*

Acceptability
There is limited evidence for the effectiveness of internal travel restrictions, and it has legal, ethical and economic implications. Although 37% of national pandemic preparedness plans of Member States have travel restriction plans as a component of NPIs (*65*), the acceptability is still undetermined.

Feasibility
Some countries have already included travel restriction plans in their national pandemic preparedness plans. However, some countries cannot implement those plans because of their own laws. Therefore, travel restriction plans may be challenging to implement because of legal, ethical, economic and resource implications.

RECOMMENDATION:

Internal travel restrictions are conditionally recommended during an early stage of a localized and extraordinarily severe pandemic for a limited period of time. Before implementation, it is important to consider cost–effectiveness, acceptability and feasibility, as well as ethical and legal considerations in relation to this measure.

Population: General public

When to apply: Early phase of extraordinarily severe pandemics

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FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (effective)	The overall quality of the evidence was very low for the effectiveness of internal travel restrictions in an influenza epidemic or pandemic. Very strict internal travel restrictions are effective in reducing influenza transmission in the community.
Values and preferences	Conditional	Uncertain.
Balance of benefits and harms	Conditional	Internal travel restrictions can have important economic consequences. There is no published evidence of potential benefits, but theoretically transmission would be reduced.
Resource implications	Conditional	Substantial implementation cost may be incurred.
Ethical considerations	Conditional	The human rights of free movement should be considered, as should the adverse economic effects, particularly in vulnerable populations such as migrant workers and individuals who need to travel to access medical care.
Acceptability	Conditional	Uncertain.
Feasibility	Conditional	Some countries already have travel restriction plans in place in the event of an epidemic or pandemic; however, some countries cannot implement these because of their own laws.

Overall strength of recommendation	Conditionally recommended	This measure can be conditionally recommended during the early stage of a localized extraordinarily severe pandemic for a limited period of time.

Knowledge gaps: No high-quality studies for the effectiveness of internal travel restrictions were identified. Studies to assess the effectiveness of internal travel restrictions and the cost–effectiveness of this measure would be valuable to inform decisions on its use and to identify potential barriers to its implementation.

7.4. Border closure

Summary of evidence
Eleven articles related to border closure were included in the systematic review (*114, 135, 204, 231, 235-239*). Two were epidemiological studies (*135, 231*) and nine were simulation studies (*114, 204, 234-240*). An epidemiological study suggested an important influence of international air travel on the timing of influenza introduction (*231*). Another historical analysis of the 1918–1919 pandemic suggested that strict border control was a successful method for delaying and preventing influenza from arriving in South Pacific islands (*135*).

A simulation study predicted that 99% restriction of cross-border travel between Hong Kong SAR and mainland China may delay the epidemic peak by about 3.5 weeks compared with non-travel restriction (*235*). Another simulation study conducted in Italy predicted that international air travel restriction would delay the peak of epidemic by about 1–3 weeks, depending on the transmission rate and the level of restriction (*204*). However, the attack rate was not significantly affected (*204*). Furthermore, simulation studies based on a global scale model also predicted that international travel restriction would delay epidemics by about 2–3 weeks (*236*) and significantly delay its global spread (5–133 days) (*237*). Strict border control of 99.9% may be effective in delaying the epidemic peak by 6 weeks, while 90% and 99% border control would delay the epidemic peak by 1.5 and 3 weeks, respectively (*114*). International travel restriction is estimated to slow the importation of infections (*234, 238*), but would not reduce the epidemic duration (*238*). Because the supply of essential items to a population, such as food and medical supplies, often relies on importation, strict border closures need to be carefully considered before implementation in island countries and territories (*239*).

> **OVERALL RESULT OF EVIDENCE ON BORDER CLOSURE**
>
> 1. Eleven studies were included in this review.
> 2. Generally, only strict border closures are expected to be effective within small island nations.
> 3. For island nations, border closure should be carefully considered because it may affect the supply of essential items to the population.

Summary of considerations of members of the guideline development group
for determining the direction and strength of the recommendations
The guideline development group, with the support of the steering group, formulated recommendations that were informed by the evidence presented and took into account quality of evidence, values and preferences, balance of benefits and harms, resource implications, ethical considerations, acceptability and feasibility, as outlined below.

Quality of evidence
There is a very low overall quality of evidence that border closure has an effect on transmission of influenza, and studies in the literature reported or predicted variable effectiveness.

Values and preferences
Values and preferences related to border closure are uncertain.

Balance of benefits and harms
No scientific evidence of the harm of border closure for individuals was identified. However, it is reasonable to expect that strict border control could affect daily life and have serious economic consequences.

Resource implications

No costing studies on border closure were identified; however, the cost will be prohibitive in most countries because of the closure of borders (air, land and sea). Substantial public resources would be needed, including the provision of public advice and large numbers of staff to restrict cross-border travel. Furthermore, there would be consequences for the supply chain for food and essential medicines, as well as broader economic consequences.

Ethical considerations

The right to free movement of persons should be considered (*219*). As with internal travel restrictions, border closure applied by nations should be done voluntarily as much as possible, and compulsory intervention should be involved as a last resort (219). Furthermore, the stigmatization and discrimination of individuals from affected areas and economic impacts of border closures should also be carefully considered (*219, 241*).

Acceptability

There is limited evidence for the effectiveness of border closures, and it has legal, ethical and economic implications.

Feasibility

Border closure in severe pandemics is technically feasible, and it may be most effective if implemented in the very early phase of a pandemic. However, the above-mentioned ethical, economic and resource implications affect its feasibility.

RECOMMENDATION:

Border closure is generally not recommended unless required by national law in extraordinary circumstances during a severe pandemic, and countries implementing this measure should notify WHO as required by the IHR (2005).

Population: General Public

When to apply: N/A

FACTORS	ASSESSMENT	RATIONALE
Quality of evidence	Very low (variable effectiveness)	The overall quality of evidence for the effectiveness of border closure was very low. The effect of border closure in reducing influenza transmission is varied.
Values and preferences	Conditional	Uncertain.
Balance of benefits and harms	Conditional	May be effective in delaying importation of new cases but at major economic cost.
Resource implications	Conditional	A large amount of public resources would be needed and there would be considerable economic consequences.
Ethical considerations	Conditional	Ethical issues relating to restrictions of free movement should be carefully considered.

FACTORS	ASSESSMENT	RATIONALE
Acceptability	Conditional	There is limited evidence for the effectiveness of border closure, and it has legal, ethical and economic consequences. However, the acceptability is still unclear.
Feasibility	Conditional	Likely not to be feasible in most locations.

Overall strength of recommendation	**Not Recommended**	**Overall, border closure is not recommended unless required by national law or in extraordinary circumstances during a severe pandemic, and countries should notify WHO as required by IHR. This is due to the very low quality of evidence, economic consequences, resource implications and ethical implications.**

Knowledge gaps: Due to the lack of high-quality evidence, the benefit of border closure is still uncertain (*231*). Cost–benefit studies to assess the advantages and disadvantages of border closure are needed.

IHR: International Health Regulations; N/A: not applicable; WHO: World Health Organization.

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