ECDC Advisory Forum

Fifty-eighth Meeting

Stockholm, 24-25 September 2019

Expert opinion on non-pharmaceutical countermeasures against pandemic influenza

Document number: AF58/05	Date: 3 September 2019
Summary:	In an effort to support national and regional pandemic preparedness activities, ECDC has reviewed the evidence base for non-pharmaceutical countermeasures (NPC) against pandemic influenza, thus updating the available documentation from 2009. A literature review was procured in 2018 and the draft document reviewed with an international panel of experts in May 2018. This expert opinion will be opened for a public consultation immediately after the AF opinion.
Action:	The Advisory Forum is requested to provide views on: 1) Are the NPCs selected for this Expert Opinion comprehensive and relevant? 2) Are the conclusions for each measure balanced and appropriate in light of the limitations of the evidence base? 3) How can ECDC and the public health institutes promote further research into the knowledge gaps in an effective way?
Background:	The purpose of this expert opinion is to summarise to public health decision makers in the EU/EEA Member States, EU institutions and other interested parties, the evidence base on the effectiveness of NPCs and provide an expert opinion on the use of the NPCs that have been proposed for reducing the risk and transmission of human pandemic influenza to date.

Contents

Summary

1. The purpose of this expert opinion is to summarise to public health decision makers in the EU/EEA Member States, EU institutions and other interested parties, the evidence base on the effectiveness of NPCs and provide an expert opinion on the use of the NPCs that have been proposed for reducing the risk and transmission of human pandemic influenza to date.
2. In this document, these measures are categorised into personal protective, environmental, social distancing and travel-related measures. The document also aims to identify gaps in research and inform the planning and design of scientific studies, and of in-depth systematic reviews for specific types of interventions.
3. This Expert Opinion is based upon a review of literature reviews since the 2009 pandemic on the effectiveness of the various NPCs. The document builds on the previous ECDC technical document 'Guide to public health measures to reduce the impact of influenza pandemics in Europe: "The ECDC Menu"', published in 2009, with updated information and lessons learned from the 2009 influenza pandemic.
4. An international panel of experts reviewed the draft document in May 2018 and it will be open for public consultation, immediately after the AF opinion.
5. The NPCs ranged from personal protective actions taken by individuals (personal protective, environmental measures) to actions that require extensive preparation by communities, authorities or states (social distancing and travel-related measures). Their use varied in the different countries and settings during the previous pandemics.
6. Overall, there is a limited and sometimes contradictory evidence base on the effectiveness of NPCs against influenza infection especially in community settings. A lot of evidence is indirect, i.e. it comes from studies not directly applicable to pandemic influenza, but on other infectious diseases or respiratory viruses or seasonal influenza. Studies focused on laboratory confirmed influenza are rare. After December 2018, new studies have been published on the effectiveness of the different NPCs. For example, two recent studies (Ali et al., 2018 and Litvinova M et al., 2019) have recently shown that reactive school closures before or around the peak of an epidemic may reduce influenza virus transmission; these are out of scope of this expert opinion but are examples that show that the evidence is evolving.

Background

7. Influenza is a viral respiratory infection spreading efficiently from person to person by direct and indirect contact. Influenza pandemics account for millions of cases of illness, hospitalization and death and a significant global societal and economic burden. Production and distribution of vaccines and antiviral drugs, complemented with enhanced surveillance, case reporting, early rapid viral diagnosis, and administrative controls, including risk communication, education, training and health care (HC) administration will form the essential response to a pandemic.
8. A reduction in the impact or severity of the pandemic could also be attempted by a variety of non-pharmaceutical countermeasures (NPCs). Several NPCs have been proposed and used as public health responses. The main objective of the use of NPCs is to reduce the impact of the pandemic by reducing viral transmission. The reduction in transmission may delay the epidemic peak, reduce the overall number and peak number of cases, including severe and fatal cases, complementing pharmaceutical countermeasures during a pandemic.

Objectives

9. The purpose of this expert opinion is to summarise to public health decision makers in the EU/EEA Member States, EU institutions and other interested parties, the evidence base on the effectiveness of NPCs and provide an expert opinion on the use of the NPCs that have been proposed for reducing the risk and transmission of human pandemic influenza to date. In this document, these measures are categorised into personal protective, environmental, social distancing and travel-related measures. The document also aims to identify gaps in research and inform the planning and design of scientific studies, and of in-depth systematic reviews for specific types of interventions.

Methods in short

10. This document is a review of literature reviews since the 2009 pandemic on the effectiveness of the various NPCs. The document builds on the previous ECDC technical document 'Guide to public health measures to reduce the impact of influenza pandemics in Europe: "The ECDC Menu"', published in 2009, with updated information and lessons learned from the 2009 influenza pandemic.
11. A literature search was restricted to PubMed based on titles and abstracts to retrieve review articles on NPCs related to effectiveness against pandemic influenza and/or other respiratory infections that were published between January 2009 and December 2018. The reference lists of all articles were checked for additional relevant literature, including national and international guidance documents. The search terms that were used to identify review articles can be found in the Annex. Articles were selected based on the following inclusion criteria: 1) English language; 2) Reviews; 3) Publication date; 4) Included evidence on effectiveness against pandemic influenza and/or other respiratory infections. Articles were selected based on their title, abstract and text, in this order. During this process, articles that did not fit the criteria were eliminated. The information was sorted by intervention type and separated into the relevant chapters.
12. An expert meeting took place in May 2018. The discussion panel consisted of scientific content and policy experts from Germany, the Netherlands, Norway, Hong Kong, Poland, Spain, Sweden, the United Kingdom, European Commission DG SANTE.C3, the United States, WHO HQ and ECDC with a scope to discuss the evidence base for effectiveness of NPCs and to revise the draft document accordingly.

Results in short

13. The NPCs ranged from personal protective actions taken by individuals (personal protective, environmental measures) to actions that require extensive preparation by communities, authorities or states (social distancing and travel-related measures). Their use varied in the different countries and settings during the previous pandemics.

14. Overall, there is a limited and sometimes contradictory evidence base on the effectiveness of NPCs against influenza infection especially in community settings. A lot of evidence is indirect, i.e. it comes from studies not directly applicable to pandemic influenza, but on other infectious diseases or respiratory viruses or seasonal influenza. Studies focused on laboratory confirmed influenza are rare. Effectiveness of the measures will depend on additional factors, for example proper use, frequency of use, combination of measures, duration of and adherence to the measures. Although compliance and adherence to NPCs is and is expected to be variable, public anxiety may increase rates of adherence to NPCs during a pandemic, increasing the effectiveness of the measures. Many reviews have studied the layered approach, using a combination of measures to increase effectiveness; for this reason, it is difficult to disentangle the effects of specific interventions. In this situation (limited and often conflicting evidence), expert panel suggestions are based on expert judgements, taking into account theoretical consideration, common practice and current guidelines and recommendations of public health organisations.
15. Personal protective measures (PPMs) (hand hygiene, respiratory etiquette and other measures) and environmental measures are commonly recommended and undertaken during seasonal influenza epidemics and pandemics. The evidence of PPM effectiveness to mitigate the pandemic is variable and sometimes conflicting, but they are generally inexpensive, easy to implement and with limited associated risks. Personal protective equipment (i.e. gloves, gowns, eye protection) is mainly used in health care settings (HCSs) and high-risk situations and most evidence of effectiveness originates from such studies. Other NPCs for use during pandemics include voluntary quarantine of exposed household members, school closures and other social distancing and travel-related measures. Proactive school closures may reduce influenza transmission but the timing and duration will determine whether they achieve the mitigation objectives. Travel-related measures, such as travel restrictions and border closures may have some effect in delaying the viral spread but only if they achieve almost complete isolation of the country and at very early pandemic phases, which can be done in specific contexts, such as on small island nations. They are generally impracticable due to major societal and economic costs. Border screening is unlikely to be effective because current screening methods (e.g. thermal scanners) have low sensitivity and cannot identify asymptomatic or pre-symptomatic infections. The ECDC expert opinion on options for action based on the evidence of effectiveness for each measure are summarised in Table 1.
16. For each measure, the review considers, where applicable, the following aspects: objectives, rationale, evidence base of effectiveness and benefits, operational considerations (direct and indirect costs, risks, and potential adverse effects), likely acceptability in Europe, and on the basis of these considerations provides an expert opinion on options for action.

Personal Protective Measures	Summary of evidence of effectiveness
Hand hygiene	Evidence supports the use of this measure during epidemics and pandemics as it reduces the risk of infectious diseases in general, although evidence on effectiveness of this measure against laboratory-confirmed and pandemic influenza is variable and sometimes contradicting. Effectiveness is dependent on frequency of hand washing. Effectiveness will increase when used in combinatior with other measures (e.g. facemasks). Compliance may increase during a pandemic, increasing effectiveness.
Respiratory etiquette	There are theoretical considerations for promoting this measure, and it is recommended in major guidelines, however, evidence for its real-world effectiveness is lacking. Appropriate disposal of tissues and combination with hand hygiene play an important role.

Use of surgical facemasks	There is lack of evidence for the use of surgical facemasks in the community and against laboratory-confirmed influenza. The majority of evidence originates from studies in health care settings. It has been shown to be beneficial when used by infected people, or people in close contact with patients or at high-risk situations (e.g. in health care settings). There is evidence that effectiveness will increase when used in combination with other measures (e.g. hand hygiene). Compliance may increase during a pandemic, increasing effectiveness.
Use of respirators	Current evidence does not support the wide use of respirators instead of surgical masks, although respirators are considered beneficial in health care settings for aerosol generating procedures.
Other personal protective equipment	Evidence supports the use of gowns, gloves and eye protection in health care settings depending on the situation, the performed procedure and the risk assessment in epidemic or pandemics.
Environmental Measures	
Surface and object cleaning	Evidence indirectly supports the use of environmental measures during epidemics and pandemics due to the transmission modes of influenza viruses and the potential of these measures to reduce transmission. There is lack of direct evidence on effectiveness against laboratory-confirmed and effectiveness on mitigating the pandemic.
Room air ventilation	Evidence indirectly supports use of fresh air natural ventilation in various settings and appropriate ventilation in HC facilities due to the potential to reduce transmission.
Social distancing measures	
Voluntary isolation of ill persons	Evidence supports voluntary home isolation of ill persons with uncomplicated illness, during epidemics and pandemics.
Voluntary quarantine of exposed persons	Evidence supports use of this measure in pandemics, especially of higher severity. Societal and economic costs and consequences will be substantial if this measure is widely used and enforced.
Interventions in educational and child care settings	Evidence supports proactive school closures in moderate to high impact situations, although they can be associated with significant societal and economic costs. Depending on the severity level of the pandemic, reactive school closures might be necessary, for operational reasons. Decision on optimal timing and duration of school closures is crucial in order to limit the pandemic impact. Planning to mitigate transmission in schools, while schools are open, is always supported during epidemics and pandemics.

Measures in the workplace and other public places	Evidence supports the use of teleworking and inter-personal distancing measures within workplaces and other public places during pandemics, in combination with personal protective and environmental measures. Workplace closures might be necessary and considered in exceptional cases, although limited data exist on their effectiveness to mitigate a pandemic. Societal and economic costs of broad workplace closures are likely to be prohibitively high.
Measures at mass gatherings	Evidence shows that mass gatherings are associated with increased respiratory virus transmission, and therefore mitigation measures are likely to have some effect in reducing influenza transmission. The decision of event planners to cancel, re-arrange or postpone the mass gathering should be based on a risk assessment in coordination with public health authorities.
Travel-related measures	
International and domestic travel advice	No evidence to quantify the effectiveness of travel advice to mitigate a pandemic, however this measure has been widely implemented during past severe epidemics and pandemics and is supported by the reviews. Travel recommendations may also be given on the use of preventative measures during traveling to minimise the risk of developing influenza and complications.
Entry and exit screening at national borders	Evidence does not support use of this measure, because of low sensitivity to identify influenza infections.
Domestic travel restrictions	Evidence supports travel restrictions in early phases of moderate to high impact pandemic situations based on the risk assessment of the situation. They may slightly delay introduction of infections and can be associated with significant societal and economic costs.
Border closures	Evidence shows that they may delay the viral spread, only if they are almost complete and rapidly implemented in the early pandemic phases, which can be done in specific contexts, such as on small island nations. They are generally considered to be undesirable, as there will be large secondary effects.

Conclusions

17. In the case of an influenza pandemic, NPCs aim to reduce transmission, delay the peak and relieve the peak burden to the HC system. Several NPCs may be used and have been used in the past influenza pandemics, at least since 1918. A layered approach of using a combination of measures simultaneously has been suggested to be the most effective and should be considered in preparedness plans. In the early pandemic phase, such an approach may delay viral transmission and spread, giving unaffected areas more time to prepare. As the pandemic progresses, a synergistic effect may increase effectiveness of individual measures. Overall, measures that are implemented early in the pandemic phases and for longer periods have been shown to have a higher impact. Although personal protective and environmental measures are minimally disruptive to everyday activity, and so are likely to be highly acceptable, and can also be undertaken during seasonal epidemics, social distancing and travel-related measures may be less acceptable and/or have higher societal, legal, ethical and economic consequences. Risk communication and appropriate training are essential for a successful response. Actions will need to be tailored to the pandemic severity, the local situation and to the different population groups and community settings.

18. This document collates the recent scientific evidence in order to assist European Union (EU) and European Economic Area (EEA) Member States to update their pandemic preparedness plans and national recommendations, decide on which measures they may plan to apply and in which circumstances, in the case of an influenza pandemic. Many of the same considerations may also apply to seasonal influenza epidemics. Overall, the evidence base for NPCs is limited and further research is needed to support pandemic preparedness activities.

Annex I: Expert opinion on non-pharmaceutical countermeasures against pandemic influenza

Draft for public consultation 27 August 2019

ECDC SCIENTIFIC ADVICE

Expert opinion on non-pharmaceutical countermeasures against pandemic influenza

Acknowledgements

This report was drafted by 5.1.2e and 5.1.2e (ECDC) based on the ECDC technical document 'Guide to public health measures to reduce the impact of influenza pandemics in Europe: 'The ECDC Menu', published in 2009. Chloe Sellwood contributed with drafting the 'Administrative controls to health care' chapter. The scientific expert panel that participated to the Expert Meeting in May 2018, Stockholm, Sweden and contributed to the report consisted of the following experts: 5.1.2e (NL), 5.1.2e (DE), 5.1.2e 5.1.2e (SE), 5.1.2e (HK), 5.1.2e (PL), 5.1.2e (UK), 5.1.2e (SE), 5.1.2e (NO), 5.1.2e (UK), 5.1.2e (UK), 5.1.2e (ES), 5.1.2e 5.1.2e (UK), 5.1.2e (NL) and 5.1.2e (US CDC), 5.1.2e (WHO HQ), 5.1.2e 5.1.2e (European Commission DG SANTE.C3). ECDC experts that participated to the meeting were: 5.1.2e 5.1.2e, 5.1.2e, 5.1.2e, 5.1.2e and 5.1.2e. The report has been reviewed by 5.1.2e (ECDC).

Contents

Abbreviations

AR Attack Rate

ARI Acute Respiratory Infections

CDC U.S. Centers for Disease Control and Prevention

CI Confidence Interval

ECDC European Centre for Disease Prevention and Control

ERLI-net European Reference Laboratory network for Influenza

GISRS Global Influenza Surveillance and Response System

HC Health Care

HCAI Health Care Associated Infections

HCS Health Care Setting

HCW Health Care Workers

ICU Intensive Care Units

IHR International Health Regulations

ILI Influenza-Like-Illness

LCI Laboratory Confirmed Influenza

LTCF Long Term Care Facilities

MERS-CoV Middle East Respiratory Syndrome Corona Virus

NIC National Influenza Centre

1 NHS National Health Service

2 NPC Non-pharmaceutical countermeasure

3 OD Odds Ratio

4 PHE Public Health England

5 PPE Personal Protective Equipment

6 PPM Personal Protective Measure

7 RCT Randomised Controlled Trial

8 RR Risk Ratio

9 SARI Sever Acute Respiratory Infections

10 SARS-CoV Severe Acute Respiratory Syndrome Corona Virus

11 WHO World Health Organization

12

13

Executive summary

Background

Influenza is a viral respiratory infection spreading efficiently from person to person by direct and indirect contact. Influenza pandemics account for millions of cases of illness, hospitalization and death and a significant global societal and economic burden. Production and distribution of vaccines and antiviral drugs, complemented with enhanced surveillance, case reporting, early rapid viral diagnosis, and administrative controls, including risk communication, education, training and health care (HC) administration will form the essential response to a pandemic.

A reduction in the impact or severity of the pandemic could also be attempted by a variety of non-pharmaceutical countermeasures (NPCs). Several NPCs have been proposed and used as public health responses. The main objective of the use of NPCs is to reduce the impact of the pandemic by reducing viral transmission. The reduction in transmission may delay the epidemic peak, reduce the overall number and peak number of cases, including severe and fatal cases, complementing pharmaceutical countermeasures during a pandemic.

Objectives

The purpose of this expert opinion is to summarise to public health decision makers in the EU/EEA Member States, EU institutions and other interested parties, the evidence base on the effectiveness of NPCs that have been proposed for reducing the risk and transmission of human pandemic influenza to date and to review these measures in light of operational feasibility and acceptability. In this document, these measures are categorised into personal protective, environmental, social distancing and travel-related measures. The document also aims to identify gaps in research and inform the planning and design of scientific studies, and of in-depth systematic reviews for specific types of interventions.

Methods in short

This document is a review of literature reviews since the 2009 pandemic on the effectiveness of the various NPCs. The document builds on the previous ECDC technical document 'Guide to public health measures to reduce the impact of influenza pandemics in Europe: 'The ECDC Menu', published in 2009, with updated information and lessons learned from the 2009 influenza pandemic.

A literature search was restricted to PubMed based on titles and abstracts to retrieve review articles on NPCs related to effectiveness that were published between January 2009 and December 2018. The reference lists of all articles were checked for additional relevant literature, including national and international guidance documents. The search terms that were used to identify review articles can be found in the Annex. Articles were selected based on the following inclusion criteria: 1) English language; 2) Reviews; 3) Publication date; 4) Included evidence on effectiveness. Articles were selected based on their title, abstract and text, in this order. During this process, articles that did not fit the criteria were eliminated. The information was sorted by intervention type and separated into the relevant chapters.

An expert meeting took place in May 2018. The discussion panel consisted of scientific content and policy experts

from Germany, the Netherlands, Norway, Hong Kong, Poland, Spain, Sweden, the United Kingdom, United States, European Commission DG SANTE.C3, the U.S. CDC, WHO HQ and ECDC with a scope to discuss the evidence base for effectiveness of NPCs and to revise the draft document accordingly.

Results in short

The NPCs ranged from personal protective actions taken by individuals (personal protective, environmental measures) to actions that require extensive preparation by communities, authorities or states (social distancing and travel-related measures). Their use varied in the different countries and settings during the previous pandemics.

Overall, there is a limited and sometimes contradictory evidence base on the effectiveness of NPCs against influenza infection especially in community settings. A lot of evidence is indirect, i.e. it comes from studies not directly applicable to pandemic influenza, but on other infectious diseases or respiratory viruses or seasonal influenza. Studies focused on laboratory confirmed influenza are rare. Effectiveness of the measures will depend on additional factors, for example proper use, frequency of use, combination of measures, duration and adherence to the measures. Although compliance and adherence to NPCs is and is expected to be variable, public anxiety may increase rates of adherence to NPCs during a pandemic, increasing the effectiveness of the measures. Many reviews have studied the layered approach, using a combination of measures to increase effectiveness; for this reason, it is difficult to disentangle the effects of specific interventions. In this situation (limited and often conflicting evidence), expert panel suggestions are based on expert judgements, taking into account theoretical considerations, common practice and current guidelines and recommendations of public health organisations.

Personal protective measures (PPMs) (hand hygiene, respiratory etiquette, facemasks and respirators, and other measures) and environmental measures are commonly recommended and undertaken during seasonal influenza epidemics and pandemics. The evidence of PPM effectiveness to mitigate the pandemic is variable and sometimes conflicting, but they are generally inexpensive, easy to implement and with limited associated risks. Personal protective equipment (i.e. gloves, gowns, eye protection) is mainly used in health care settings (HCSs) and high-risk situations and most evidence of effectiveness originates from such studies. NPCs for the use during pandemics include voluntary quarantine of exposed household members, wider use of facemasks, school closures and other social distancing and travel-related measures. Proactive school closures may reduce influenza transmission but the timing and duration will determine whether they achieve the mitigation objectives. Travel-related measures, like travel restrictions and border closures may be somewhat effective in delaying the viral spread but only if they achieve almost complete isolation of the country and at very early pandemic phases, which can be done in specific contexts, such as on small island nations. They are generally undesirable due to major societal and economic costs. Border screening will unlikely be successful because current screening methods (e.g. thermal scanners) have low sensitivity and cannot identify asymptomatic or pre-symptomatic infections. The ECDC expert opinion on options for action based on the evidence of effectiveness for each measure are summarised in Table 1.

1 **Table 1. Summary of non-pharmaceutical countermeasures and evidence of effectiveness**

Personal Protective Measures	Summary of evidence of effectiveness
Hand hygiene	Evidence supports the use of this measure during epidemics and pandemics as it reduces the risk of infectious diseases in general, although evidence on effectiveness of this measure against LCI and pandemic influenza is variable and sometimes contradicting. Effectiveness is dependent on frequency of hand washing. Effectiveness will increase when used in combination with other measures (e.g. facemasks). Compliance may increase during a pandemic, increasing effectiveness.
Respiratory etiquette	There are theoretical considerations for promoting this measure, and it is recommended in major guidelines, however, evidence for its real-world effectiveness is lacking. Appropriate disposal of tissues and combination with hand hygiene play an important role.
Use of surgical facemasks	There is lack of evidence for the use of surgical facemasks in the community and against LCI. The majority of evidence originates from studies in HCSs. It has been shown to be beneficial when used by infected people, or people in close contact with patients or at high-risk situations (e.g. in HCSs). There is evidence that effectiveness will increase when used in combination with other measures (e.g. hand hygiene). Compliance may increase during a pandemic, increasing effectiveness.
Use of respirators	Current evidence does not support the wide use of respirators instead of surgical masks, although respirators are considered beneficial in HCSs for aerosol generating procedures.
Other personal protective equipment	Evidence supports the use of gowns, gloves and eye protection in HCSs depending on the situation, the performed procedure and the risk assessment in epidemic or pandemics.
Environmental Measures	
Surface and object cleaning	Evidence indirectly supports the use of environmental measures during epidemics and pandemics due to the transmission modes of influenza viruses and the potential of these measures to reduce transmission. There is lack of direct evidence on effectiveness against LCI and effectiveness on mitigating the pandemic.
Room air ventilation	Evidence indirectly supports use of fresh air natural ventilation in various settings and appropriate ventilation in HC facilities due to the potential to reduce transmission.
Social distancing measures	

Voluntary isolation of ill persons	Evidence supports voluntary home isolation of ill persons with uncomplicated illness, during epidemics and pandemics.
Voluntary quarantine of exposed persons	Evidence supports use of this measure in pandemics, especially of higher severity. Societal and economic costs and consequences will be substantial if this measure is widely used and enforced.
Interventions in educational and child care settings	Evidence supports proactive school closures in moderate to high impact situations, although they can be associated with significant societal and economic costs. Depending on the severity level of the pandemic, reactive school closures might be necessary, for operational reasons. Decision on optimal timing and duration of school closures is crucial in order to limit the pandemic impact. Planning to mitigate transmission in schools, while schools are open, is always supported during epidemics and pandemics.
Measures in the workplace and other public places	Evidence supports the use of teleworking and inter-personal distancing measures within workplaces and other public places during pandemics, in combination with personal protective and environmental measures. Workplace closures might be necessary and considered in exceptional cases, although limited data exist on their effectiveness to mitigate a pandemic. Societal and economic costs of broad workplace closures are likely to be prohibitively high.
Measures at mass gatherings	Evidence shows that mass gatherings are associated with increased respiratory virus transmission, and therefore mitigation measures are likely to have some effect in reducing influenza transmission. The decision of event planners to cancel, re-arrange or postpone the mass gathering should be based on a risk assessment in coordination with public health authorities.
Travel-related measures	
International and domestic travel advice	No evidence to quantify the effectiveness of travel advice to mitigate a pandemic, however this measure has been widely implemented during past severe epidemics and pandemics and is supported by the reviews. Travel recommendations may also be given on the use of preventative measures during traveling to minimise the risk of developing influenza and complications.
Entry and exit screening at national borders	Evidence does not support use of this measure, because of low sensitivity to identify influenza infections.
Domestic travel restrictions	Evidence supports travel restrictions in early phases of moderate to high impact pandemic situations based on the risk assessment of the situation. They may slightly delay introduction of infections and can be associated with significant societal and economic costs.
Border closures	Evidence shows that they may delay the viral spread, only if they are

	almost complete and rapidly implemented in the early pandemic phases, which can be done in specific contexts, such as on small island nations. They are generally considered to be undesirable, as there will be large secondary effects.

For each measure, the review considers where applicable: objectives, rationale, evidence base of effectiveness and benefits, operational considerations (direct and indirect costs, risks, and potential adverse effects), likely acceptability in Europe and provides an expert opinion on options for action.

Conclusions

In the case of an influenza pandemic, NPCs aim to reduce transmission, delay the peak and relieve the peak burden to the HC system. Several NPCs may be used and have been used in the past influenza pandemics, at least since 1918. A layered approach of using a combination of measures simultaneously has been suggested to be the most effective and should be considered in preparedness plans. In the early pandemic phase, such an approach may delay viral transmission and spread more efficiently, giving unaffected areas more time to prepare. As the pandemic progresses, a synergistic effect may increase effectiveness of individual measures. Overall, measures that are implemented early in the pandemic phases and for longer periods have been shown to have a higher impact. Although personal protective and environmental measures are everyday actions that will be highly acceptable and undertaken also during seasonal epidemics, social distancing and travel-related measures may be less acceptable and/or have higher societal, legal, ethical and economic consequences. Risk communication and appropriate training are essential for a successful response. Actions will need to be tailored to the pandemic severity, the local situation and to the different population groups and community settings.

This document collates the recent scientific evidence in order to assist European Union (EU) and European Economic Area (EEA) Member States to update their pandemic preparedness plans and national recommendations, decide on which measures they may plan to apply and in which circumstances, in the case of an influenza pandemic. Many of the same considerations may also apply to seasonal influenza epidemics. Overall, the evidence base for NPCs is limited and further research is needed to support pandemic preparedness activities.

1. Background

Influenza virus infections and seasonal epidemics are responsible for hundreds of thousands of hospitalizations, tens of thousands of deaths and considerable economic burden in Europe [1]. On the other hand, there is a continuous threat of a new emergent influenza virus strain to which humans possess little or no immunity resulting in an influenza pandemic with unpredictable consequences. Such pandemics with varying degrees of severity and impact have occurred repeatedly at unforeseeable intervals: the 1918 "Spanish flu", the 1957 "Asian flu", the 1968 "Hong Kong flu" and the 2009 pandemic being the most recent examples. These pandemics accounted for millions of cases of illness, hospitalization and death and a significant global societal and economic burden [2-4].

Rationale

Influenza is a viral respiratory infection spreading efficiently from person to person by direct and indirect contact. Direct spread occurs primarily through person-to-person contact and through aerosols, respiratory droplets produced when infected people cough and sneeze. Indirect spread occurs when respiratory secretions settle on surfaces and objects that are touched by uninfected people, who then infect themselves. A reduction in the impact or severity of influenza pandemics and epidemics (mitigation or damage limitation) may therefore be accomplished by using a variety of non-pharmaceutical countermeasures (NPCs) that interrupt or decrease transmission, in addition to pharmaceutical measures (vaccine and antiviral drug use, if and when they become available).

Objectives of non-pharmaceutical measure use

The primary objective of the NPCs is to reduce the impact of the pandemic by reducing viral transmission. The epidemic peak may be delayed, and the overall number of cases, peak number of cases, and total number of severe illness cases and deaths may be reduced, complementing pharmaceutical countermeasures.

Secondary objectives are to:

- Gain time for the development, production and distribution of pandemic vaccines and procurement, stockpiling and distribution of antiviral drugs;
- Reduce the peak burden on HC and other key systems by decreasing the number of cases during the epidemic peak and spreading cases over a longer period.

Pharmaceutical measures

Pharmaceutical countermeasures, most importantly vaccination and antiviral drugs use are generally effective against influenza viruses [5-10]. ECDC manages a program monitoring influenza vaccine effectiveness on a seasonal basis, and is able to activate it also for pandemic vaccine purposes [11]. ECDC is also supporting the European Commission with technical advice on a joint procurement programme for several EU Member States. The most important measure against a pandemic virus, as is for seasonal influenza viruses, will be a specific pandemic vaccine timely available for the whole population. However, vaccines that match the pandemic strain of influenza virus cannot be developed, produced and be available in sufficient quantities until some months after the pandemic starts. In 2009, the first pandemic vaccines were available around six months after the declaration

of the pandemic, while the bulk of the production could only be delivered in subsequent months. Demand for vaccines will exceed global supply in the early phases of the pandemic. It will also require about two weeks following the vaccination until sufficient protective antibodies are produced in the vaccinated individual. Candidate vaccine viruses with pandemic potential are proposed during each WHO Vaccine Composition Meeting in February for the northern hemisphere and September for the southern hemisphere [12], however specific vaccines are at present unlikely to be available for the first wave of a pandemic strain. If the pandemic vaccine is produced and distributed in a timely manner, this should mitigate the impact of the second and subsequent waves. Preparations for vaccine acquisition, prioritisation and deployment are essential steps in national pandemic preparedness planning.

Antiviral medicines, specifically neuraminidase inhibitors, and potentially protease inhibitors, may play a crucial role in reducing the impact of the pandemic and its clinical implications. They can both protect and treat the individual and reduce virus transmission to others. However, they are mostly effective when administered within 24 to 48 hours after the onset of illness for treatment of patients, or as post-exposure prophylaxis of exposed persons [13,14]. Prophylaxis would be beneficial in public health terms, though in many countries antivirals may be in too limited supply for such use. The effectiveness of the available antiviral drugs against the pandemic virus needs to be ascertained and monitored for every novel virus, since the virus could be inherently resistant to the available drugs, or acquire resistance as a consequence of antiviral drug administration [13,15]. Acquisition of sufficient stockpiles of antibiotics will also be essential for the treatment of increased number of bacterial pneumonia cases that are common after influenza infections and may increase morbidity and mortality during a pandemic.

Influenza virus transmission

The characteristics of influenza virus transmission drive the effectiveness of the various NPCs. The influenza virus may be transmitted among humans via direct contact with infected individuals, via contact with contaminated objects and surfaces or via inhalation of virus-containing aerosols [16,17]. The median basic reproductive number (R_0) is estimated to be 1.28 for seasonal influenza and between 1.46 and 1.80 during the past pandemics [18].

Respiratory transmission depends upon the production of aerosols that contain virus particles. Activities such as breathing and speaking produce aerosols, while coughing and sneezing cause forceful expulsion of viral particles [19,20]. Recommendations to control influenza virus transmission in various community settings include measures that reduce transmission and spread by aerosol and fomite mechanisms. Aerosolized particles are particles of different sizes; the largest droplets will transmit an infection only to those in the immediate vicinity, while smaller droplets travel a distance determined by their size. Those 'droplet nuclei' are 1-4 microns in diameter and may remain suspended in the air for longer periods, travel longer distances, and reach the lower respiratory tract. Inhalation of droplets and droplet nuclei places virus particles in the upper respiratory tract, where they may initiate infection [19,21,22].

Nasal secretions also contain virus particles. They are responsible for transmission by direct contact or by contaminated objects [16]. Infected persons will frequently touch their nose or conjunctiva, placing virus on their hands. Contact will transfer the virus from one person to another, who will then self-infect by touching their nose or eyes. Studies have shown that the influenza virus remains viable on the hands for 3-5 minutes and may remain on the fingers for at least 30 minutes after contamination [23-25]. When contaminated hands touch other objects, the virus is transferred to them and remain up to 48 hours after attachment to a surface [23,24,26,27].

It is unclear how much transmission of influenza takes place through indirect transmission by hands [28]; most studies on inter-human transmission routes are inconclusive, and the relative importance of respiratory virus transmission routes is not known [16,17]. In human infections, maximum levels of virus shedding may occur about a day before the peak of symptoms. Asymptomatic infections also occur and spread of the virus is feasible even through asymptomatic hosts [21].

Though there are several research studies on this area, there is uncertainty regarding the relative importance of droplet, contact or airborne routes of transmission in influenza infection [17,29,30]. This is important as it would influence the effectiveness of NPCs, depending on the route that they are targeting (e.g. hand hygiene for contact transmission, respiratory etiquette and facemask use for airborne and droplet transmission). Studies on animal models have shown that temperatures over 30°C have no effect on contact transmission, but prevent aerosol transmission of influenza [31]. Differences in absolute humidity provide an explanation for the observed variability of influenza virus survival, transmission and seasonality in temperate regions [32]. Low relative humidity (20–30%) has been shown to prolong influenza virus survival in the air, increasing aerosol and droplet transmission that are inhibited at high relative humidity (≥80%) [17,31]. Colder temperatures (≤4 °C) tend to prolong the environmental persistence of influenza A, which could potentially increase the relative burden of contact and aerosol transmission [30]. The role of different routes of transmission may shift during influenza pandemics, given their unpredictable seasonality compared to the northern hemisphere influenza season, which tends to start in October and end in March with a peak between December and February [33].

The different transmission patterns of the pandemic strain may also alter the effectiveness of PPMs during an influenza pandemic compared to a seasonal epidemic. These uncertainties pose challenges to the public health policy makers and highlight the need to report and review previous experiences and lessons learnt [17].

Surveillance: case reporting, contact tracing and early rapid viral diagnosis

Successful containment or control of pandemic influenza will rely on early recognition of sustained human-to-human transmission, which requires a system for outbreak detection, data collection, timely reporting, data analysis and assessment [34,35]. Early detection at the start of a pandemic is crucial to rapidly implement measures to limit the spread of the pandemic at its source. Some situations may warrant case and contact tracing and management by public health authorities in the early stages of the pandemic [36]. The extent of the investigation and recommended measures should be feasible and relevant to the situation [37-39].

As part of national pandemic preparedness planning, each country should prepare for enhanced surveillance to detect the emergence of the new disease, characterize the disease (epidemiology, clinical manifestations, severity) and monitor its progress [40]. A surveillance system for monitoring the compliance and effectiveness of public health interventions will need to be implemented. In the case of a novel virus, case reporting and early rapid viral diagnosis will support a range of necessary preparedness activities, including: a) providing information regarding the presence and epidemiology of the virus in the community, b) determining and implementing appropriate interventions, including timely targeted implementation of NPCs and c) generating current accurate information for policy makers, public health officials, providers and the public [41].

In the light of the most recent experience with SARS and the 2009 pandemic, enhanced level of national and international surveillance has been proven crucial in order to contain the spread of a pandemic. Influenza surveillance at a global level is achieved through an experienced network of laboratories, the Global Influenza

Surveillance and Response System (GISRS) and at a European level through the European Reference Laboratory of Influenza network (ERLI-net) supported by WHO and ECDC.

Contact tracing on board aircraft

In order to assist national public health authorities in the European Union to assess the risks associated with the transmission of infectious agents on board aircrafts, ECDC initiated in 2007 the RAGIDA project (Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft). RAGIDA consisted of two parts: the production of systematic literature reviews and disease-specific guidance documents [42,43].

Considering the lack of published data available on evaluating the risk of transmission of most infectious agents on board aircrafts, and taking into account the key factors that influence the decision making, the RAGIDA guidance provides a viable evidence based tool for public health authorities determining triggers and making decisions on whether to undertake contact tracing in air travellers or crew, in the early stages of a pandemic. These guidance documents may be adapted to the local situation, national and international regulations or preparedness plans [43,44].

Overall, for influenza virus, the evidence in the published literature was not adequate to assess the risk for transmission on-board aircraft and the effectiveness of contact tracing measures remains unclear; it has been suggested that air transportation appears important in accelerating and amplifying influenza propagation [45]. Transmission occurs aboard aeroplanes, at the destination and possibly at airports [45]. Control measures to prevent influenza transmission on cruise ships are needed to reduce morbidity and mortality [45]. The feasibility and cost benefit of contact tracing needs to be carefully assessed. Please refer to the relevant document for more information [43].

Contact tracing should not be undertaken by default, but rather in exceptional situations, if indicated by the outcome of the situational risk assessment. In order to reduce transmission, contact tracing should be performed at early pandemic stages. This situational risk assessment should take into account how the index case was classified (probable or confirmed), the time of travel in relation to onset of symptoms, the epidemiological situation in the country of destination and in the country of departure, and the purpose of the contact tracing. Please refer to the options for action in the relevant document [43].

Administrative controls in healthcare

Administrative controls are measures taken to ensure that the entire HC system is working effectively. The HC facility management team needs to ensure that resources are available for implementation of necessary measures. These resources include the establishment of sustainable infrastructures and activities, clear policies and guidelines on early recognition of infections, access to rapid laboratory testing, appropriate hospital triage and placement of patients and organisation of services [46]. They include risk communication policies, designation of responsibilities, education of employees about the hazards to which they are exposed and training on the proper use and disposal of Personal Protective Equipment (PPE) as well as provision of means by which to avoid infection, while establishing appropriate programmes for staff vaccination and antiviral drug prophylaxis [47].

Specimen/patient transport

All human specimens of respiratory secretions and excretions should be considered as potentially infectious [48]. Precautions should be taken during patient transport within healthcare facilities, as respiratory secretions from

influenza-infected patients are the main source of infectious material in HCSs [49]. The movement and transport of patients to and from the isolation areas should be limited and if possible through dedicated corridors and elevators. The receiving facility should be informed prior to the patient's arrival of the patient diagnosis and of the precautions that are indicated. The use of mobile diagnostic devices should be encouraged when available. In case transport outside the isolation room is required, the patient should wear appropriate PPE and perform hand hygiene after contact with respiratory secretions.

Hospital triage and cohorting

Hospital triage and cohorting of patients has the objective of isolating potentially infectious patients and using appropriate protective measures and treatment rapidly thereby mitigating the impact of the pandemic on the rest of the HC services [47]. Hospital triage procedures are the process of prioritising patients on first contact based on their need for immediate medical care and treatment as compared to the chance of benefiting from such care. These procedures may allow triage of potentially infectious patients before the entry into the facilities (for example use of a flu Emergency Department (ED) and a non-flu ED where space allows), and appropriate protective measures and treatment to be applied rapidly, reducing the impact of the infection on the rest of the HC services. It is used in emergency rooms, disasters, and wars, when limited medical resources are allocated to maximize the number of survivors. Cohorting patients into wards or areas in the facility with clear designation of 'flu dirty' and 'flu clean' areas also offers the potential to reduce nosocomial spread if applied successfully.

No empirical studies have quantified the effectiveness of hospital triage protocols for containing pandemic influenza. Hospitals may use available guidelines for HCSs to be able to categorise patients in case of a pandemic. Early recognition of patients with suspected influenza will allow for appropriate patient management and reduced risk of transmission within the HC facilities. All staff will need to be able to recognise the symptoms and signs of the disease that fit with the current 'case definition' of the pandemic in patients and respond appropriately [60]. Guidelines must be developed with public health, scientists, and legislative authorities to help clinicians define, adopt, and communicate to the public those practice standards that will be followed in case of a pandemic [61].

Triaging procedures may require changes to emergency room facilities, additional temporary facilities and protective measures for first-line responders and might require reallocation of staff. During a pandemic, health authorities will provide a more specific case definition or testing algorithm to detect cases. Definitions used by health authorities to identify cases of pandemic influenza may change at different phases of a pandemic, as knowledge of the disease increases. General practices need to maintain good communication pathways with state and territory health authorities to ensure timely notification of any changes to case definitions or clinical management [50].

Non-pharmaceutical countermeasures to reduce transmission

Several NPCs have been proposed and used as public health responses during the past pandemics. In this document, these measures are categorised in:

- Personal protective measures;
- Environmental measures;

- Social distancing measures;
- Travel-related measures.

A range of measures have been previously recommended by WHO and a guide specific for the prevention and control of influenza in long-term care facilities [51-57]. ECDC in 2009 published a technical report that is a guide to public health measures to reduce the impact of influenza pandemics in Europe [42,58,59]. The U.S. CDC has recently updated the 2007 guide Community Mitigation Guidelines to Prevent Pandemic Influenza [58]. Several other guidance documents that include NPC use are available from national public health institutes and agencies, such as the Public Health England (PHE) [60-62], Public Health Canada (PHAC) [37], Robert Koch Institute [63], Ministry of Health Singapore [64], New Zealand [65], Australia[66], as well as professional organisations, such as The Royal Australian College of General Practitioners (RACGP) [67] and other government-funded bodies, such as the UK National Health Service (NHS) [61].

All of the reviewed guidelines agree that NPC implementation is crucial at all phases prior, during and after the pandemic. There are important issues to consider when planning and implementing such public health measures. One of the key issues is to identify and define the triggers that will be used for the implementation of NPCs at each pandemic stage. The measures should ideally be used in combination, in a layered approach, as the effectiveness of each individual measure may be limited when implemented on its own [9,68]. In the early pandemic phases, combination approaches may contain the virus or delay its spread, allowing unaffected areas to activate preventive measures. During a pandemic, a synergistic effect may increase effectiveness of individual measures, whilst reducing the societal and economic impact of individual measures [68]. Despite the anticipated effectiveness of each measure, NPCs are often evaluated in terms of their perceived necessity, efficacy, acceptability, and feasibility. To enhance uptake, it will be necessary to address key barriers, such as beliefs about transmission of the virus, rejection of personal risk of infection and concern about the potential costs and stigma associated with some interventions [69-72]. Intercountry variability and differences between populations within a single country suggest that one-size-fits-all plans may be less effective [71]. Planned public health actions should therefore be tailored to the pandemic impact, severity and local situation.

2. Methods

The purpose of this document is to summarise to public health decision makers in European Member States, EU institutions and other interested parties, the evidence base on the effectiveness of NPCs for reducing the risk and transmission of human pandemic influenza, to aid the connection between science and policy. It is a comprehensive review of literature reviews since the 2009 pandemic on the NPC effectiveness. Risks and secondary consequences associated with their use, their likely acceptability, the probable public health expectations and the knowledge gaps are also discussed.

We searched PubMed for reviews on the effectiveness of NPCs from January 2009 until December 2018 (last search on 18 December 2018), using the combination of search terms that are listed in the Annex. The following search terms were used to identify review articles: 'influenza', 'pandemic', 'respiratory infection', 'respiratory tract infection', 'respiratory virus', 'non-pharmaceutical measures', 'public health measures', 'non-pharmaceutical interventions', 'personal protective measures', 'personal protective equipment', 'environmental', 'cleaning', 'surface', 'humidification', 'ventilation', 'disinfectants', 'disinfection', 'copper', 'alloy', 'sunlight', 'hand hygiene', 'mask', 'respirator', 'hand disinfection', 'social distancing', 'voluntary isolation', 'workplace', 'quarantine', 'mass gatherings', 'Hajj', 'school closure', 'entry screening', 'exit screening', 'border closure', 'travel advice', 'travel measures'. Duplicate search results were removed. Following the initial search results, the titles and abstracts (in this order) were reviewed to exclude those outside the scope. If the paper described the NPC and its effectiveness against influenza transmission, the full-length text was read and relevant data were extracted. Articles were selected based on the following inclusion criteria: 1) English language; 2) Reviews; 3) Publication date; 4) Included evidence on effectiveness. During this process, articles that did not fit the criteria were eliminated. The final list of papers was reviewed. The information was sorted by intervention type and separated into the relevant chapters.

The document is building on the ECDC technical document 'Guide to public health measures to reduce the impact of influenza pandemics in Europe: 'The ECDC Menu', published in 2009, with updated information including the most recent data, guidance documents and lesson's learned from the 2009 influenza pandemic [58]. Between 2009 and 2018, a substantial amount of studies, reviews and guidelines have been published [9,62,65,69,73-87].

We examined infection control policies and guidelines from WHO, US Centers for Disease Control and Prevention (CDC) and other aforementioned health organisations for recommendations on the use of NPCs. We also included previous ECDC guidelines. Such guidance documents, e.g. the WHO's 2005 Pandemic Plan [51] as well as more recent WHO documents [56,57,88,89] and WHO's 2009 guidance on NPCs [90], the CDC Interim Pre-pandemic planning guidance 2007 [91] and the Community Mitigation guidelines to prevent pandemic influenza, United States, 2017 [24,74] provide clear recommendations for national and subnational authorities. In this review, and it's previous version [58], no explicit recommendations are formulated, although an expert opinion for options for action based on the evidence is provided. The content is intended to collate the available scientific evidence in order to assist European Member States to update their pandemic preparedness plans, decide on which measures they may plan to apply and in which circumstances, in the case of an influenza pandemic. Many of the same considerations may apply to seasonal influenza epidemics and especially to more severe epidemics.

ECDC convened a group of experts in 16-17 May 2018 in Solna, Sweden with the participating panel consisting of public health policy and scientific experts from Germany, the Netherlands, Norway, Hong Kong, Poland, Spain, Sweden, the United Kingdom, United States, European Commission DG SANTE.C3, U.S. CDC, WHO HQ and ECDC. The main objectives of this meeting were to present and discuss the evidence base for the following subjects and review the related draft guidance: PPMs in HC and long-term facilities, PPMs in community and workplaces, environmental measures, social distancing measures, travel measures and restrictions on international travel. Moreover, the following topics were discussed: pandemic preparedness, non-pharmaceutical approaches in non-EU Countries, WHO related guidelines. The opinions of the experts were noted and taken into account in producing the final ECDC expert opinion. The experts also suggested the inclusion of a number of relevant studies which were not captured in the initial literature review, such as epidemiological modelling studies and health economic analysis.

The NPCs range from personal protective actions taken by individuals (personal protective, environmental measures) to actions that require extensive preparation by communities, authorities or states (social distancing and travel-related measures). Their use has varied for each measure and from one country to another during the previous pandemics [41,92-95]. Evidence for effectiveness was stronger for some of the measures (e.g. school closures) and weak (e.g. entry/exit screening at national borders) or limited for others (e.g. respiratory etiquette). PPMs (hand hygiene, respiratory etiquette), few social distancing measures (voluntary home isolation) and environmental measures are commonly recommended and undertaken during influenza epidemics. They are generally inexpensive and easy to implement, though their effectiveness during seasonal influenza epidemics may differ from an influenza pandemic, due to the uncertain characteristics of the pandemic and the pandemic strain. Facemasks and other PPMs (gloves, gowns, eye protection) are mainly used in HCSs and most evidence of effectiveness originates from such studies. Although compliance and adherence to the measures is variable, public anxiety may actually increase rates of adherence to the public health interventions. NPCs for the use during pandemics include voluntary quarantine of exposed household members, wider use of facemasks, other social distancing and travel-related measures. The summary of the evidence and expert opinion for each measure is in Table 1.

The PubMed search for literature reviews on the NPCs after 2009, using the search terms that are listed in the Annex generated 2 253 results. The following study designs were included in the considered reviews and are specified in the respective table for each measure were applicable (See Tables 2-10): randomised controlled trials (RCTs) and observational studies, including cohort, case-control, cross-over, before-after, time series and other modelling studies. Following duplicate paper removal and review of the titles, abstracts and full texts (in this order) of the initial search results to exclude those outside the scope, the final number of review papers included in this review was 21 for hand hygiene, 3 for respiratory etiquette use, 25 for facemask use, 9 other personal protective equipment, 17 for environmental measures, 5 for voluntary isolation/voluntary quarantine, 6 for school closures, 6 for workplace measures, 6 for mass gatherings and 10 for travel-related measures (excluding contact tracing on board aircrafts, for which only the ECDC risk assessment guidelines (RAGIDA) have been referred). Some reviews referred to more than one NPC. A summary of included reviews per measure is provided in the tables following the respective measure chapters in 'Discussion and conclusions'.

The following NPCs have been included, categorised as follows:

Personal protective measures

- Hand hygiene;

- Respiratory hygiene;
  - Respiratory etiquette;
    - Use of facemasks and respirators outside home;
    - in healthcare settings;
    - situations with high exposure risk;
    - by people and patients with respiratory symptoms.
- Other personal protective equipment.

Environmental measures

- Surface and object cleaning;
- Room air ventilation.

Social (inter-personal) distancing measures

- Voluntary isolation of ill persons;
- Voluntary quarantine of exposed persons;
- Interventions in educational and child care settings;
  - Reactive school closures;
  - Proactive school closures;
- Measures in the workplace and other public places;
- Measures at mass gatherings.

Travel-related measures

- International and domestic travel advice;
- Entry and exit screening at national borders;
- Domestic travel restrictions;
- Border closures;

For each measure, the review considers where applicable: the objective, rationale, evidence base of effectiveness and benefits, operational considerations (direct and indirect costs, risks, and potential adverse effects), acceptability in Europe and provides the ECDC expert opinion for options for action.

Limitations

Evidence of effectiveness is lacking or is limited for some of the measures and literature reviews are lacking for some of the measures; for those measures, options for action are provided based on the experts' opinion, existing evidence and WHO and other international guidelines. The expert opinion includes only PubMed papers and only in the English language. The potential impact of each measure was not quantified or compared to the other measures. The methodological quality of included reviews and studies has not been assessed; some of the reviews have identified and/or included poor quality studies. This review has taken into account all of the reviews that have assessed effectiveness of NPCs against LCI and/or ARI and/or ILI and/or respiratory infections irrespective of which one; the focus of each included review has been described in the summary table at the respective chapter. Cost-effectiveness studies have not been included in this review.

3. Results

Personal protective measures

PPMs refer to, hand and respiratory hygiene, respiratory etiquette, and respirator or facemask use; these are commonly recommended and undertaken during influenza outbreaks and they are generally inexpensive and easy to implement [41,96-98]. Their effectiveness during seasonal influenza epidemics may differ from an influenza pandemic, due to the uncertain characteristics of the pandemic strain, while public anxiety may actually increase rates of adherence [99-103]. Despite persisting knowledge gaps in relative effectiveness between the different PPMs and across population groups, results suggest that campaigns to increase the frequency of PPMs use in situations with a high risk of exposure are likely to contribute to preventing pandemic influenza infection [71,73].

Hand hygiene

Hand hygiene refers to hand washing with soap and water or cleaning with alcoholic solutions, gels or tissues.

Objective: Proper hand hygiene aims to reduce transmission from person to person by direct or indirect contact in any community setting. Proper hand hygiene will prevent other communicable diseases that may add burden during a pandemic if they occur simultaneously.

Rationale: Influenza transmission can be direct or indirect through hand-mediated transfer and could be reduced by washing hands often with soap and water or alcohol-based hand cleansers.

Evidence of effectiveness: Ignaz Semmelweiss documented the dramatic effectiveness of handwashing and disinfection in decreasing mortality from puerperal fever in 1847, before the germ theory had emerged. More recent studies have shown that the influenza virus remains viable on the hands for 3-5 minutes and may remain on the fingers for at least 30 minutes after contamination [23,25]. Several studies and reviews have evaluated hand washing effectiveness against respiratory infections both before [41,99,100,104-109] and after the 2009 pandemic [9,73,79,84-86,98,110-126]. Overall, the evidence supports the use of this common measure to reduce the risk of infectious diseases in various settings: HCSs, households, educational settings, workplaces. In meta-analyses, the highest quality cluster-randomised control trials (RCTs) suggested respiratory virus spread can be reduced by hygienic measures, such as handwashing [127-129] and this is especially evident around younger children that are less capable of hygienic behaviour themselves and have longer-lived infections and increased social contact, acting as portals of infection into the household [127,128,130]. Some studies suggest that use of an alcohol-based hand sanitizer is more effective in preventing direct spread of most infections compared to antimicrobial soap or no hand washing, but antimicrobial hand washing products have not been shown to offer an advantage over soap and water [41,131,132].

In an attempt to quantify the effectiveness of PPMs specifically in preventing influenza transmission, several systematic reviews and meta-analyses were conducted, some of which concluded that regular hand hygiene provided a significant protective effect specifically against influenza infection [73,86,127,128], however many studies on the effectiveness of this measure were not focused on LCI. Studies in schools reported that the incidence and proportion of school absenteeism decreases where hand hygiene measures are implemented at

school settings [84,110,130]. Another study showed that hand hygiene in combination with facemask use reduced the risk of secondary influenza infection [83,85], while a single cohort study reported that an increase in HCW adherence to hand hygiene recommendations resulted to a reduction of the risk of influenza infection [113]. There was contradicting evidence from RCTs and most showed limited effectiveness against LCI. A systematic review of RCTs from seasonal influenza epidemics, which evaluated hand hygiene effectiveness, found a significant protective effect associated with a combination of hand hygiene and facemask use, but no significance in hand washing alone in preventing seasonal influenza infections [83]. Statistically non-significant risk reductions associated with hand hygiene and facemask use for LCI and ILI were also found in other studies as well [9,84,133].

The frequency of hand washing is an important factor that may influence the effectiveness of the intervention. Studies from the 2009 influenza pandemic showed that the increased frequency of hand washing had a significant protective effect to reduce the risk of influenza infection [79,111,115]. Hand hygiene that was motivated by influenza exposure, was found to be significantly protective in two studies. Occasional hand hygiene both following contact with an index case [112,114,115] and following contact with contaminated surfaces [79,111] was found to have a protective effect against a laboratory-confirmed pandemic influenza infection [73]. It is unclear what constitutes an appropriate "threshold" for adequate, protective hand hygiene; it is likely that this may vary depending on individual factors such as exposure, susceptibility and risk of severe outcomes [73]. The significant protective effect of hand hygiene following contact with infected individuals, supports the notion that protective measures both during and immediately following viral exposure will increase intervention effectiveness [134]. The frequency of performing hand washing may need to increase in pandemic situations, when attack rates and viral loads are likely to be higher than during seasonal epidemics, increasing the frequency of exposure events [128]. Hand washing may also infer indirect protection, through minimising the influenza virus surface contamination in households [86,116]. One study has shown that increased frequency of hand washing reduced surface contamination with influenza virus, which in turn reduced the risk of infection via fomites [24,131].

Operational considerations: There will be moderate direct costs. The major limiting factor would be the availability of facilities for hand washing and of hand sanitisers (tissues, gels, solutions). In many settings, it will be difficult to increase the amount of resources to build special facilities for hand washing only for a pandemic response. Such facilities and practices would be advisable for other hygienic reasons, without considering the pandemic, in many communal settings, such as schools, day-care centres, restaurants, cafeterias and churches or religious institutions. Some irritation from alcohol-based solutions or very frequent hand washing has been reported. There is no consensus on the duration, frequency or type of hand washing (soap and water versus alcohol solutions) and an evidence based review concluded both were effective [117]. Regarding hand washing techniques, there is evidence that the WHO-recommended technique reduced microbial load on HCWs hands, although the most effective hand hygiene technique was not identified [135].

Likely acceptability: Hand hygiene is broadly acceptable and easy to implement, while giving people a practical way to enact it [71]. Based on a systematic review of public perceptions of NPCs for reducing transmission of respiratory infections, hand hygiene was viewed as a familiar and socially responsible action to take [69]. Multimodal strategies to enhance hand hygiene compliance was shown to achieve slight to moderate improvements [136]. Compliance with good hand hygiene practices may be higher than that for facemasks, which have been less acceptable in the past [71,102]. The international experience shows that the level of hand washing can be increased, if the easiness of hand washing is increased. Addressing determinants such as

knowledge, awareness, action control, social influence, attitude, self-efficacy and intention will enhance effectiveness of hand hygiene improvement activities [137].

Expert opinion: Although the evidence on effectiveness of hand hygiene in reducing LCI is limited, the use of hand hygiene is supported in all community settings (home, schools, workplaces etc.) at all times as frequently as possible, especially following possible exposure to infectious agents [47,138]. Effectiveness will increase when used in combination with other measures (e.g. facemasks). Compliance may increase during a pandemic, increasing effectiveness. It is essential in HC and long-term care settings, which manage vulnerable individuals. It is considered a rational precaution, with limited costs and no associated risks [139]. Educational programmes for proper and frequent hand washing will be needed, but these can be implemented during ordinary seasonal influenza seasons and during pandemics [140]. Sanitising gels should not replace hand washing and if sanitising gels are used, then solutions based on >70% alcohol content should be preferred [24].

Table 2. Summary of reviews and meta-analyses on hand hygiene effectiveness

Hand hygiene - Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Hansen et al., 2018	Workplace settings	Infectious diseases	Moderate evidence to support hand hygiene programs.
McGuinness et al., 2018	Childcare, school, domestic settings	ARI	Evidence suggests that hand-hygiene interventions can reduce ARI morbidity, but effectiveness varies according to setting, intervention target and compliance.
Zivich et al., 2018	Workplace settings (11 studies)	Infectious diseases	Minimal hand-hygiene interventions effective at reducing the incidence of employee illness.
Kumar et al., 2017	Various settings-Children	Influenza	Cough etiquette, use of facemasks and hand hygiene are the most important measures to reduce the risk of infection transmission from person to person.
Mbakaya et al., 2017	Various settings-children (8 studies)	Respiratory and other infections	Multi-level hand-washing interventions can reduce the incidence of diarrhoea, respiratory infections, and school absenteeism.
Saunders-Hasting et al., 2017	Community (2 RCTs, 8 case-control studies, 4 cohort studies, 2 cross-sectional surveys)	Pandemic influenza 2009 infections	Hand hygiene provided a significant protective effect.
Kingston et al., 2016	HCSs (16 clinical trials)	HC associated infections	Adopting a multimodal approach to hand hygiene achieved slight to moderate improvements in hand hygiene compliance.
Willmott et al., 2016	Educational settings (18 RCTs)	Respiratory and gastrointestinal pathogens	Evidence of the effect of hand hygiene interventions on infection incidence in educational settings is mostly equivocal but they may decrease respiratory infection among children.
Hocine et al., 2015	Nursing homes (56 studies)	Various infections	Infection control strategies were more effective when a hand hygiene measure was implemented (70% vs 30% with no

			implementation). 25% of randomised trials concluded that hand hygiene-related interventions led to a reduction of infectious risk.
Lidal et al., 2015	Day-care centres	Respiratory and other infections	Attention to hand hygiene reduces respiratory infections by 17-43%, absenteeism rates by 4-20%. Complex interventions that combine hand disinfection, handwashing, and hygiene education reduce absenteeism due to infections with 30- 50% in school children (age 5 to 12 years).
Smith et al., 2015	Community –adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Hand hygiene has a positive effect on reducing the risk of infection. Poor quality data.
Teasdale et al., 2014	Community behavioural aspects (16 studies)	Infections	Hand hygiene is considered a familiar and socially responsible action.
Wong et al., 2014	Community (10 RCTs)	LCI and ILI	Hand hygiene combined with medical facemask had a significant effect (RR 0.73 (0.53 to 0.99) compared to hand hygiene only (RR 0.90 (0.67-1.20).
Tooher et al., 2013	Community (46 studies)	Influenza A(H1N1)pdm09	The proportion of study subjects that reported washing hands more frequently, ranged from 28% to 90%.
Warren-Gash et al., 2013	Community	Influenza	Hand washing can reduce transmission of influenza and acute respiratory tract infections, but effectiveness varies depending on setting, context and compliance.
Lee et al., 2012	Various community settings-Children	Influenza	Hand washing is an important adjunct but improving compliance, standardizing regimens and quantifying its impact remain challenging.
Jefferson et al., 2011	Various community settings	Respiratory viruses	Frequent handwashing was considered effective especially around young children. Effectiveness of adding virucidals or antiseptics to normal handwashing to decrease respiratory disease transmission

			remains uncertain.
Jefferson et al., 2010	Various community settings (3 RCTs in children; 7 case-control studies)	Respiratory viruses	Frequent handwashing effective against respiratory infections (OR 0.54, 0.44 – 0.67) especially around young children.
Carlson et al., 2010	HCSs	Influenza	Data on physical interventions to prevent influenza transmission support the use of hand hygiene, gowns, gloves, face shields and respiratory protection.
Aiello et al., 2010	Various settings (6 studies)	Influenza	Hand hygiene and alcohol-based sanitisers and combined approaches with facemask use are effective in reducing ILI rates.
Jefferson et al., 2009	Various settings (6 RCTs)	Influenza and SARS	Highly effective in preventing the spread of severe acute respiratory syndrome: handwashing more than 10 times daily (OR 0.45, 95% CI 0.36-0.57), and handwashing, masks, gloves, and gowns combined (OR 0.09, 95% CI 0.02-0.35). Combination of measures were effective in preventing influenza in households. The incremental effect of adding virucidals or antiseptics to handwashing remains uncertain.

Respiratory etiquette

Respiratory etiquette refers to covering mouth and nose when coughing and sneezing for example with the use of tissue paper or cloth.

Objective: Use of a respiratory etiquette, also referred to as cough etiquette, aims to reduce the person-to-person transmission through droplets.

Rationale: Influenza transmission can be reduced by covering nose and mouth when coughing or sneezing. As a virus, influenza particles are extremely small, measuring 0.08–0.12 μm in diameter [141], and can easily be carried in small droplets expelled during coughs and sneezes.

Evidence of effectiveness: A recent review found no data on the effectiveness of respiratory etiquette and effectiveness of the measure was therefore considered questionable [73]. A recent study that evaluated the effectiveness of cough etiquette in blocking aerosol particles, found that it did not block the release or dispersion of aerosol droplets, particularly those smaller than one micron in size [82]. Although evidence of effectiveness is unavailable, use of a cough etiquette is traditionally supported [41,142-148]. One randomized trial observed strong effects of oral care performed by a professional dentist compared to standard oral care in reducing the

oral load of influenza virus [86].

Operational considerations: Improper disposal of tissues may increase the risk of virus transmission and spread. There will be small direct costs. Proper disposal bins should be installed. The only major costs are the purchase or tissues and the disposal of significant amounts of contaminated paper to appropriate disposal containers.

Likely acceptability: Respiratory hygiene would be expected and probably well accepted in a pandemic. Based on a systematic review of public perceptions of NPCs for reducing transmission of respiratory infections, respiratory hygiene measures were viewed as familiar and socially responsible actions to take [69]. they will empower people and give them a practical measure to enact.

Expert opinion: Although the evidence base is limited, respiratory etiquette use is widely recommended in public health guidelines for all community settings (home, schools, workplaces, HCSs etc.) at all times due to their mode of action and evidence of protection against other infectious diseases. Supplies of materials (e.g. tissues, no-touch bins, covered sputum pots) will need to be ensured. Educational programmes can be implemented during ordinary seasonal influenza seasons and pandemics. Proper disposal of the tissues is important, immediately after the use of the respiratory etiquette, followed by hand hygiene measures.

Table 3. Summary of reviews and meta-analyses on respiratory etiquette

Respiratory etiquette - Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Kumar et al., 2017	Various settings (children)	Influenza	Respiratory etiquette, use of facemasks and hand hygiene are considered by the authors the most important measures to reduce risk of infection transmission from person to person.
Saunders-Hasting et al., 2017	Community (2 RCTs, 8 case-control studies, 4 cohort studies, 2 cross-sectional surveys)	Pandemic influenza 2009 infections	Found no data on the effectiveness of cough etiquette.
Smith et al., 2015	Community –adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Some evidence of effectiveness of oral hygiene (tooth brushing and use of oral solutions).

Use of facemasks and respirators

This measure refers to using surgical/medical masks or respirators.

Types

Types of masks range from the simplest, even home-made masks, to cloth, surgical/medical masks and complex respirators which need 'fit testing' and are produced in many different sizes to fit all. Some types of respirators are not appropriate for children and people with facial hair. They usually have three available sizes (small, medium or large) to cover the anatomical differences of the individuals. After the 2009 pandemic, several studies have focused on assessing the effectiveness of the different types of facemasks. Surgical masks can protect users from large respiratory droplets (89). They vary in thickness and permeability and are not certified to protect users from airborne infection. Respirators are specifically designed to protect users from small airborne particles, including aerosols [87,149]. European standard (EN 149:2001+A1:2009) defines classes for respirators entirely or substantially constructed of filtering material (FFP1-3) [150], while the US National Institute for Occupational Safety and Health (NIOSH) classifies respirators according to their ability to filter airborne particles (N95,N99,N100). FFP2 respirators are equivalent to N95 respirators, filtering >94% of particles smaller than 0.6 micrometers, and FFP3 respirators are equivalent to N99 respirators, filtering >99% of particles [150]. There are studies that compare the effectiveness of the different types of masks [75,87,149,151]. Cloth/gauze masks should be avoided as they induce moisture retention and poor filtration and it is unclear whether they confer clinical protection [152].

Facemasks can be used:

- in healthcare settings;
- in other high-exposure situations;
- outside home;
- by people outside of healthcare and patients with respiratory symptoms.

Facemask use in healthcare settings

At least since the 17th century use of a beak-like mask when treating plague cases, physicians have used various types of masks in order to prevent transmission of illness. Here we refer to mask-wearing by people who are at higher risk through possible or probable exposure to infectious patients in healthcare settings. Mask-wearing can be recommended for patients and for health care workers (HCWs). The emergence of novel respiratory pathogens, such as SARS-Coronavirus (SARS-CoV) and pandemic A(H1N1) influenza in 2009 highlighted the vulnerability of HCWs to respiratory infections. Similar considerations will apply for situations when people are caring for ill persons in domestic settings.

Objective: To reduce transmission in HCSs and allow HCWs to continue with their activities, while they are protected from infection.

Rationale: Masks and respirators will act as a physical barrier to protect individuals from droplets and/or aerosols, reducing the exposure to the virus and the individual risk of infection.

Evidence of effectiveness: Recent systematic reviews and meta-analyses to quantify the effectiveness of PPMs in preventing pandemic influenza and other respiratory virus transmission overall demonstrated mixed results regarding facemask use. Some studies suggesting facemask use is significantly protective, especially in HCSs, while others suggesting the opposite [73,83,87,96,99,118,127,128,153-156].

There is evidence for a protective effect of facemasks and respirators against clinical and laboratory-confirmed respiratory infection among HCWs [75]. Evaluating the different types of masks, some studies have shown that compared to surgical masks, respirators provided greater protection against clinical or bacterial respiratory infection, but the studies may have been underpowered to detect a superior protective effect of respirators against influenza [75,87,157]. Compared to surgical masks, respirators have been shown to confer significant protection against self-reported ILI, but evidence of superiority was again limited [75,87] and some studies supported that surgical masks were not inferior to respirators [118,128]. Wearing surgical masks or N95 respirators (with no significant difference between the two in terms of effectiveness) [118] both reduced the risk of SARS-CoV infection by approximately 80%, except when exposed to patients during non-invasive positive-pressure ventilation [75]. Generally, the findings for the comparative effectiveness of surgical masks and respirators are often inconsistent within and across studies leading to variability in current guidance documents [75,152,157-161]. No protective effect against SARS was reported for disposable, cotton, or paper masks [75].

It is unclear what constitutes a sufficient "threshold" for proactive facemask use to ensure its effectiveness; this may vary depending on several factors such as susceptibility of the host, level of exposure and risk of severe outcomes [73]. The frequency of use is an important factor that will influence the intervention effectiveness [73,149]. It is unclear what each study considers as regular, irregular, continuous facemask use in a quantitative manner [73]. Regarding the frequency of facemask use, the risk of influenza infection among HCWs was shown to be decreased for each 10% increase in adherence to facial protection guidelines. Continuous mask use in children was shown to confer a significant protective effect relative to non-users in one cross-sectional study, while another reported a non-significant risk increase associated with frequent use of surgical masks and respirators relative to infrequent use, but was based on a small sample size [162]. Wearing a surgical mask or respirator continuously throughout the work shift was shown to confer significant protection against self-reported clinical respiratory illness and ILI [75]. Wearing a mask when ill and in close contact with other individuals has been shown to reduce airborne transmission [163].

Compliance with the measure will also affect its effectiveness; preliminary results related to influenza infections showed poor compliance with the measure [96,102,164]. Patients usually will wear such masks to protect themselves from further infection, not to protect their surroundings [71,102].

A combined layered approach may increase the effectiveness of the measures [68,99,149]. Results suggest that campaigns to increase the use of facemasks and the frequency of hand washing in situations with a high risk of exposure will likely contribute to preventing pandemic influenza infection [73]. An optimal intervention strategy may be a combined approach, were frequent hand washing is combined with targeted facemask use [99,165], especially among high-risk populations (HCWs, schools-aged children, the elderly).

Education of the users in proper use and disposal of the facemasks is essential and the evidence is that, though people can be supplied with masks and respirators, they will often use them improperly, especially in the case of the more demanding respirators [157,166,167]. Facemasks need to be worn closely fitting and be replaced with new clean and dry masks as soon as they become soiled or moist/humid. The effectiveness of masks and respirators is likely linked to early, consistent and correct usage [149,165].

Conclusively, there is evidence to support universal mask use in hospital settings as part of infection control measures to reduce the risk of clinical respiratory infection and ILI amongst HCWs during a pandemic. Overall, respirators may convey greater protection when aerosol-generating procedures are performed [147,152,168-171], although superiority was not shown in all of the studies and universal use throughout the work shift is

likely to be less acceptable due to greater discomfort [75,86,127,149].

Operational considerations: Some studies have suggested that there could be adverse effects, as mask-wearing may increase indirect transmission; they may allow symptomatic patients to feel confident that they can continue with their everyday routine, causing a higher risk to further transmit the virus, especially if the mask is not worn properly [167]. Another argument is that the constant touching and adjusting of masks with the hands may actually increase influenza transmission. Improper mask disposal may also increase the risk of transmission. Combination with hand hygiene measures after mask disposal may increase effectiveness. Issues of supply and storage of facemasks may rise. Moderate costs will be due to facemask supply, disposal and training, with respirators having increased cost compared with surgical masks [172].

Likely acceptability: This measure will likely be highly acceptable, as there is a tradition of mask wearing in HCSs in the EU. It is quite likely that HCW associations would request or insist that their members have higher level of protection in all circumstances. On the other hand, operational studies in the EU have shown that people wearing respirators find it considerably harder to carry our practical tasks [173,174]. Perceived susceptibility to infection will increase intervention effectiveness [72].

Expert opinion: Facemasks may be used in severe epidemics or pandemics to reduce transmission and current policies mandating standard and droplet precautions when performing routine care for influenza patients are considered reasonable. Single-use surgical masks are preferable to cloth masks, for which there is no evidence of protection and which might facilitate transmission of pathogens when used repeatedly without adequate sterilization. Respirators could be considered in high risk settings by HCWs when aerosol generating procedures are performed [20,47,149,152,167]. Combined measures are also supported, as they seem to increase the effectiveness of the individual measures. Training and monitoring proper use of facemasks will be needed, but these can be implemented during ordinary seasonal influenza seasons [167].

Facemask use in other high-exposure situations

This refers to mask wearing by people who are at higher risk through possible or probable exposure to infectious persons. The following groups may be considered:

- care-providers for ill people with presumed pandemic influenza (please refer to previous section);
- people in public places;
- people in occupations with face-to-face contact with the public.

Objective: To reduce transmission in higher risk settings and allow persons in key activities to continue to work, while being protected from infection.

Rationale: Please look at the previous 'Facemask use in HCSs' chapter.

Evidence of effectiveness: The evidence for effectiveness of mask use in other high-exposure situations is limited. A meta-analysis showed that facemask use was beneficial against certain respiratory infections at mass gatherings. However, its effectiveness against specific infections (i.e. influenza) remained unproven [154]. Several reviews from data obtained at the yearly Hajj mass gatherings have shown that combined facemask use with hand hygiene and vaccination might offer protection from infection, though there is a limited evidence and compliance was considered low [175]. Data about the effectiveness of facemask use exist but are limited, and results are contradictory, highlighting the need for future large-scale studies [154,155,175,176]. See previous

'facemask use in HCSs' chapter on evidence of effectiveness.

Operational considerations: Moderate costs will be due to supply and training. Please also see previous 'facemask' chapter on operational considerations.

Likely acceptability: This is unknown, as there is no tradition of wearing facemasks outside HCS or other occupational settings in Europe. During and following the 2009 pandemic labour representatives (e.g. trade unions) have requested or insisted that their members have protection in certain circumstances. A meta-analysis, not restricted to Europe, showed that about half of the attendees of mass gatherings used facemasks [154], while others suggest that compliance was low [175]. Please also see previous 'facemask use in HCSs' chapter on likely acceptability.

Expert opinion: Use of facemasks by people likely to be exposed to infected persons during a pandemic and by infected persons when they have contact with other individuals is supported by the limited evidence. Facemask use by healthy individuals is supported when caring for ill persons, when the carers belong to high-risk groups or if there are other high-risk circumstances (e.g. due to occupation). A risk-based approach should be considered, identifying people at special risk (e.g. workers with high frequency of face-to-face contact with unselected public) or higher risk settings (e.g. public transport). Issues in communication, training and proper disposal of used masks will need to be addressed.

Facemask use outside the home

This refers to people in the community widely wearing masks outside the home.

Objective: To reduce influenza transmission in public places, workplaces and schools.

Rationale: Please look at previous 'Facemask use' chapters. Although facemask-wearing in public is a common social action in some societies in Asia, this is not the case in Europe.

Evidence of effectiveness: No reviews were identified assessing the effectiveness of public use of facemasks in decreasing influenza or respiratory virus transmission. Please see previous 'Facemask use' chapters for evidence of effectiveness.

Operational considerations: The costs will be substantial. Even though the unit cost is low, considering two or more masks per citizen per day for their outside activities, over the three to five month period of a pandemic the supply costs are highly increased [172]. There would also need to be considerable planning to ensure adequate supplies. Two meta-analyses suggested that masks and respirators may be cost-effective, though there is insufficient data to inform more specific interventions [9,172] and there is a need for more comprehensive economic evaluations to compare the relative costs and benefits of these interventions in situations and settings where alternative options are potentially applicable [172]. Please also see previous 'Facemask use' chapters on operational considerations.

Likely acceptability: This is unknown, as there is little tradition of routine facemask wearing in the community in Europe. Compliance with facemask use was low in some studies [96]. A review of the evidence from the 2009 pandemic showed that masks were not used unless there was a perception of high risk, which is in line with evidence from the SARS epidemic [71,72]. Perceived susceptibility and perceived benefits of mask-wearing appeared to be the most significant factors determining compliance [72]. Perceived barriers included experience

or perception of personal discomfort and sense of embarrassment [72].

Expert opinion: There is lack of evidence on effectiveness of facemasks in community settings. For high/exposure situations please refer to the 'Facemask use in other high-exposure situations' chapter. Wider use of facemasks in the community may be considered in severe pandemic scenarios due to their mechanical mode of action, although there is lack of direct evidence of effectiveness to mitigate the pandemic. There are implications for training and communication, because proper use and disposal of masks needs to be ensured. Combining facemask use with hand hygiene will increase the effectiveness of the interventions.

Facemask use by people and patients with respiratory symptoms

This refers to mask wearing by people (presumably infected) and confirmed patients with respiratory symptoms.

Objective: To reduce transmission from people known or presumed to be infected and infectious.

Rationale: Please look at previous 'Facemask use' chapters.

Evidence of effectiveness: There is some evidence to support the mask or respirator wearing during illness to protect others, and public health emphasis on mask-wearing during illness may help to reduce influenza virus transmission. There are fewer data to support the use of masks or respirators to prevent becoming infected [156] and for transmission in households [85]. Please see previous 'facemask' chapters on evidence of effectiveness.

Operational considerations: Some authorities have suggested adverse effects could result if mask wearing was perceived as an alternative to early self-isolation of ill people. Moderate costs will be due to the supplies required per person [172]; these would be considerable, as the masks would presumably be contaminated very quickly and require frequent changing. Please also see previous 'Facemask use' chapters on operational considerations.

Likely acceptability: This may be better accepted than mask wearing by the general population outside home, and is understandable to the patients and their households and is already a common practice in some healthcare settings [55]. It may also make early self-isolation in home settings more acceptable. People with severe illness find it hard to wear masks, but it is more acceptable by people with mild illness. If exclusively ill people are recommended masks, some social stigma may be attached to it.

Expert opinion: Depending on the severity of the pandemic, facemask use by infected persons when in contact with other individuals is supported [167]. Symptomatic people in the community and patients in HCSs should consider using facemasks as per recommended practice in healthcare settings. This may be the best use of resources when there are limited amounts of facemasks available.

1 **Table 4. Summary of recent reviews and meta-analyses on facemask use effectiveness**

Facemask use- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Chao et al., 2017	HCSs	Droplet-borne infections	Evidence suggested that N95 respirators were more effective in preventing viral and bacterial infections in HCWs compared with surgical masks (several limitations and results to be interpreted with caution).
Offeddu et al., 2017	HCSs (6 RCTs, 23 observational studies)	Respiratory illness (ILI, bacterial, SARS, other viral infections)	RCTs showed a protective effect of masks and respirators against clinical respiratory illness (RR 0.59, 95% CI 0.46-0.77) and ILI (RR 0.34, 95% CI 0.14-0.82). Compared to masks, N95 respirators conferred superior protection against CRI (RR 0.47, 95% CI 0.36-0.62) and laboratory-confirmed bacterial (RR = 0.46; 95% CI: 0.34-0.62), but not viral infections or ILI. Observational studies provided evidence of a protective effect of masks (OR 0.13, 95% CI 0.03-0.62) and respirators (OR 0.12, 95% CI 0.06-0.26) against SARS.
Saunders-Hasting et al., 2017	Community (2 RCTs, 8 case-control studies, 4 cohort studies, 2 cross-sectional surveys)	Pandemic influenza 2009 infections	Facemask use provided a statistically non-significant protective effect.
Smith et al., 2016	Comparison of masks versus respirators (6 studies)	Lab-confirmed respiratory infection, ILI, workplace absenteeism	N95 respirators showed a protective advantage over masks in laboratory settings. Evidence in clinical settings was not convincing. No significant differences were observed between respirators and masks.
Barasheed et al., 2016	Mass gatherings (12 cross sectional, 10 cohort, 2 case studies, 1 RCT)	Respiratory infections	Pooled estimate showed significant protectiveness against respiratory infections, not specific to influenza (RR 0.89, 95% CI: 0.84-0.94).
Bunyan et al., 2016	HCSs	Respiratory infections	Respiratory and facial protection to reduce transmission via the droplet and/or airborne routes or when airborne particles have been created during aerosol-generating procedures

			(AGPs). Not strong evidence on superiority of respirators and the list of AGPs needs to be determined.
Wei et al., 2016	Various settings	Respiratory infections	Short-range airborne route is potentially very important and may be controlled by masks and personalized ventilation.
MacIntyre et al., 2015	Community and HCSs	Influenza and other respiratory infections	Limited evidence of effectiveness of cloth masks, conflicting evidence on superiority of respirators compared to surgical masks.
Smith et al., 2015	Community –adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Evidence supporting facemask use in clinical settings, non-superiority of N95 respirators.
Sim et al., 2014	Community	Respiratory infection	Perceived susceptibility and perceived benefits of mask-wearing appeared to be the most significant factors determining compliance and in turn effectiveness. Perceived barriers included experience or perception of personal discomfort and sense of embarrassment.
Wong et al., 2014	Community (10 RCTs)	LCI and ILI	Hand hygiene combined with facemask use had a significant effect (RR 0.73, 95% CI 0.53 to 0.99).
Benkouiten et al., 2014	Community (mass gatherings, 17 studies)	Respiratory tract infections	Contradictory results on effectiveness and low compliance.
Rainwater-Lovett et al., 2014	LTCFs (37 observational studies)	ILI, influenza	Moderate protective effect of PPE but not statistically significant (OR 0.63, 95% CI 0.33 - 1.19) for influenza A/B outbreaks.
Tooher et al., 2013	Community (46 studies)	Influenza A(H1N1)pdm09	Masks were not used unless there was a perception of high risk.
Coia et al., 2013	HCSs	Various pathogens	Risk assessment based approach for choosing equipment. For most cases surgical masks are sufficient, in aerosol-generating procedures respirators may be required.

Haworth et al., 2013	Community (mass gatherings)		Observational studies failed to demonstrate any clear benefit of using facemasks among Hajj pilgrims, but no large trial had yet been conducted so lack of sufficient evidence.
Al-Tawfiq et al., 2013	Mass gatherings (review on available Hajj pilgrimage literature)	Influenza and other respiratory infections	Mask use may reduce exposure to (inhalation of) droplet nuclei.
Roberge et al., 2011	Community (68 studies)	Infectious diseases	Surgical masks and respirators have shown efficacy in attenuating the dispersal of infectious agents by adults and children. Limited data on the imposed physiological and psychological burden, tolerance, and proper use by children.
Bin-Reza et al., 2011	Community and HC (8 RCTs, 9 observational studies)	Influenza and other respiratory infections	In 6/8 RCTs no difference between control and intervention. 8/9 observational studies masks/respirators independently associated with reduced risk of SARS.
Jefferson et al., 2011	Physical interventions (6 RCTs, 7 case control, 4 cohort, 1 before-after)	Respiratory viruses	Surgical masks or N95 respirators were the most consistent and comprehensive supportive measures. N95 respirators non-inferior to surgical masks.
Aiello et al., 2010	Various settings (4 studies)	Influenza	Effectiveness of facemask use and of combined approaches with hand hygiene.
Cowling et al., 2010	Various settings (6 studies in HC)	Influenza	Limited evidence that masks may reduce infectiousness if worn by infected persons.
Carlson et al., 2010	HCSs (4 studies on N95 respirators, 2 studies on combined approaches with hand washing)	Influenza	Evidence from one trial that surgical masks are non-inferior to N95 respirators in preventing infection, but data are limited. Significant protective effects when combined with hand hygiene.
Jefferson et al., 2010	Physical interventions (3 RCTs, 5 case-control, 2 cohort studies)	Respiratory viruses	Protective effect of mask-wearing, some evidence that N95 respirators were superior to surgical masks for high-risk situations.

Jefferson et al., 2009	Various settings (6 RCTs)	Influenza and SARS	Highly effective in preventing the spread of SARS: wearing masks (OR 0.32, 95% CI 0.25-0.40), wearing N95 masks OR (0.09, 95% CI 0.03-0.30) and handwashing, masks, gloves, and gowns combined (OR 0.09, 95% CI 0.02-0.35). The combination was also effective in interrupting the spread of influenza within households. Limited evidence that respirators superior to simple surgical masks.

Other personal protective equipment used in health care settings

Other personal protective equipment (PPE) refers to gloves, gowns and eye protection (goggles or shields) use in special settings for protection against infection. A range of PPE that provides facial and respiratory protection is available [113,125,126].

Objectives: Other PPE aim to reduce the possibility of exposure to respiratory pathogens and the risk of transmission especially to health-care workers and people in high-risk situations and in close contact with infected individuals.

Rationale: Other PPE create a barrier between the infectious agent and the skin and mucous membranes of the healthcare worker reducing contact, droplet, and aerosol transmission depending upon the PPE selected. Eye protection (goggles or shields) may be used to act as a physical barrier to protect conjunctivae. In most clinical scenarios where other PPE are required, they will comprise either a surgical mask or a respirator, with or without eye protection [47,149]. The use of PPE such as gowns, gloves and protective eye covers are suggested mainly for use in HCSs or caring for patients at home or at long-term care facilities [54,55,86,118].

When there is contact with blood and other body fluids, including respiratory secretions, gloves made of latex, vinyl, nitrile or other synthetic materials are considered appropriate. Gloves should be removed and discarded after patient care and should not be washed or reused. Hand hygiene should follow glove removal.

Evidence of effectiveness: Routine care of influenza infected patients should not necessitate the use of goggles or face shields. Bronchoscopy, respiratory and airway suctioning, and other medical procedures that cause aerosol formation likely facilitate virus dispersal by increasing the risk of splashing/spraying to the eyes. Therefore, face and eye protection are likely to be beneficial [149,177].

The reviews suggest that HCWs should wear an isolation gown when there is a risk that soiling with blood or other body fluids (e.g. respiratory secretions) may occur.

Overall, data on physical interventions to prevent transmission of communicable diseases support the use of hand hygiene, gowns, gloves, face shields and respiratory protection in HCSs [118,178]. A meta-analysis suggested that physical measures are highly effective in preventing the spread of SARS: handwashing more than 10 times daily, wearing masks, wearing gloves, wearing gowns [127,129]. A combination of handwashing, masks, gloves, and gowns was also effective in interrupting the spread of influenza also within households [127,129]. A literature review on the influenza outbreak control practices and the effectiveness of interventions

in long-term care facilities, showed that PPEs may produce modest protective effects [179]. Another review suggested that all means combined (handwashing, masks, gloves and gowns) achieved very high effectiveness [128].

Operational considerations: Additional costs due to the purchase of such equipment will incur in HCSs. Training in proper use and disposal of the PPE will be needed as improper use of PPE may result in increased risk of infection. Proper disinfection/sterilisation of reusable eyewear/gowns is essential after use. Gloves should not be used as a substitute for hand hygiene.

Most routine pandemic influenza patient encounters will not necessitate the use of gowns, but it is recommended during procedures such as intubation or when in close contact with a paediatric patient. Isolation gowns can be disposable and made of synthetic material or reusable and made of washable cloth. Gowns should be the appropriate size to fully cover the areas requiring protection. After patient care is performed, the gown should be removed and placed in a laundry room or waste container. Hand hygiene should follow gown removal. While some studies show no benefit of the routine use of isolation gowns, others demonstrate that its use is associated with reduced infection rates [78]. Various parameters, such as fabrics used, gown design and interfaces, as well as critical parameters that affect microorganism and liquid transmission through fabrics need to be considered [78].

Likely acceptability: Such measures will be likely highly acceptable in HCSs, as they are already common practice.

Expert opinion: Different means may be used depending on a risk assessment-based approach, the procedure/task to be performed and the pandemic virus transmissibility in HCSs, or when caring for patients at home or at long-term care facilities [149]. The selection and use of respiratory and facial protection equipment must be highlighted by appropriate staff education and training, while the requirement for eye protection will largely be determined by the risk of splashing/spraying body fluids to the eyes/face [149]. PPE should be used in combination with proper hand hygiene measures and proper equipment disinfection or disposal.

Table 5. Summary of recent reviews and meta-analyses on other personal protective equipment (gloves, gowns, facial/eye protection) effectiveness

PPE (glove, gown, facial/eye protection)- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Bunyan et al., 2016	HCSs	Respiratory infections	Respiratory and facial protection used to protect from transmission via the droplet and/or airborne routes or when airborne particles have been created during AGPs. The list of AGPs need to be determined.
Kilinc et al., 2015	HCSs	Infectious diseases	While some studies show no benefit of the routine use of isolation gowns, others demonstrate that their use is associated with a reduced infection rate.
Rainwater-Lovett et al., 2014	LTCFs (37 observational studies)	ILI	Moderate protective effect of PPE but not statistically significant (OR 0.63 (0.33 - 1.19) for influenza A/B outbreaks.
Coia et al., 2013	HCSs	Various pathogens	Risk assessment based approach for choosing equipment.
Jefferson et al., 2011	Various settings and study designs, case-control studies	Not specifically influenza – many SARS studies	Barriers (combined masks, gloves, gowns) OR 0.09 (0.02 – 0.25) – 2 studies.
Jefferson et al., 2010	Physical interventions (4 case-control, 1 cohort, 1 before-after studies)	Respiratory viruses	Effective in paediatric ward or combined with isolation.
Carlson et al., 2010	HCSs	Influenza	Data support the use of hand hygiene, gowns, gloves, face shields and respiratory protection.
Weber et al., 2010	HCSs	Influenza	Proper use of personal protective equipment such as masks, N95 respirators, eye protection, and gowns when caring for patients with potentially communicable diseases is proposed by the authors for effective infection control program.
Jefferson et al.,	Various settings (6	Respiratory	Highly effective in preventing the spread of severe acute respiratory syndrome: wearing masks (OR

2009	RCTs)	viruses	0.32, 95% CI 0.25-0.40), wearing N95 masks (OR 0.09, 95% CI 0.03-0.30), wearing gloves (OR 0.43, 95% CI 0.29-0.65), wearing gowns (OR 0.23, 95% CI 0.14-0.37), and handwashing, masks, gloves, and gowns combined (OR 0.09, 95% CI 0.02-0.35). The combination was also effective in interrupting the spread of influenza within households.

Environmental measures

Environmental countermeasures include routine cleaning of frequently used surfaces and objects and minimize sharing of routinely touched objects. They are especially important in settings where people gather regularly. Room air ventilation, the use of UV light sources and antimicrobial surfaces (such as copper-alloy surfaces) are also considered as environmental measures.

Objective: To enhance protection, reduce the risk of infection and the spread and impact of the pandemic.

Rationale: Hand mediated transfer of influenza virus from contaminated surfaces/objects to the mouth or nose is a known route of virus transmission and spread [116,180]. Disinfection of surfaces and objects may therefore reduce the risk of transmission through hand mediated transfer of influenza viruses. Room air ventilation (natural or mechanical) moves outdoor air into a building or a room, and distributes the air within the building or room [181]. The general purpose of ventilation in buildings is to provide healthy air for breathing by both diluting the pollutants originating in the building and removing the pollutants from it [181]. It may therefore assist in the refreshment of air to dissolve aerosolised influenza particles that cause infection through inhalation or contaminate surfaces and objects.

Evidence of effectiveness: Studies have shown that disinfection of surfaces and objects reduces the risk of infection and the spread of influenza and other respiratory viruses [86,182-185]. There is indirect evidence that elimination of viruses from surfaces can have a significant impact on contact transmission. Influenza viruses can remain viable on hard, nonporous materials (for example stainless steel) for two weeks and on porous materials (for example microfiber and cotton) for one week, during which time they can spread from those surfaces to human hands [186]. If porous materials dry within 15 minutes, influenza virus becomes undetectable and can remain viable to transfer to hands up to 12 hours. Influenza viruses have been detected on handles, telephones, TV controllers, and kitchen surfaces [183]. Reduced sharing of such objects is presumed to be beneficial. Influenza viruses survive on hands for only 3-5 minutes, but touching contaminated surfaces and then the eyes, mouth, or nose can result in self-inoculation [182].

Although direct evidence of effectiveness is limited, the routine surface cleaning measures are considered to reduce the spread of viruses, like SARS and influenza and HC associated infections [180,187-190]. Influenza viruses are sensitive to disinfection. Influenza viruses can be removed from surfaces by routine cleaning using detergent-based cleaners (e.g. regular soap) or bleach. Common disinfectants and heat have been found effective at inactivating influenza viruses [191]. Phenolic compounds and glutaraldehyde were found to be effective against viruses [187]. Other means for inactivation of influenza viruses include heat treatments or

ethylene oxide (used in HCSs), quaternary ammonium compounds (used in poultry farms), triethylene glycol, glucoprotamin-containing disinfectants (used in HCSs), although these methods may not be appropriate for most households and other community settings. Hydrogen peroxide vapour that is used in HCSs is found to have virucidal properties also for viruses dried on surfaces [190,192,193]. Vapour concentrations of 10 parts per million hydrogen peroxide or 2 parts per million triethylene glycol can provide effective surface disinfection [194]. Formaldehyde, hydrogen peroxide, and alcohol were considered effective against pathogens and they are compatible with aircraft components [195]. On the other hand, surface-dried viruses were found to resist glucoprotamin-based disinfection [196]. In addition, it has been shown that solely the exposure of surfaces to disinfectants might be insufficient for virus inactivation and mechanical action should be applied to bring attached viruses into contact with virucidal compounds [196]. Self-disinfecting surfaces are under active investigation and could be proven useful especially in HCSs [197]. They can be created by coating surfaces with heavy metals (e.g. silver or copper), germicides (e.g. triclosan), or using other methods (e.g. light-activated antimicrobials) [197]. Copper alloy surfaces have been considered effective in reducing the microbial load, although their effectiveness specifically against influenza viruses has not been studied [198-203].

To help prevent airborne infections, adequate ventilation in HC facilities in all patient-care areas is necessary [181,204,205]. It has been suggested that room ventilation and improving airflow in the living space by opening windows three-four times daily for 10 minutes each time, would be sufficient to dissolve virus particles and maintain the appropriate humidity levels in the air [206]. The ventilation rate, airflow pattern and flow direction impacts the effectiveness [204]. Increasing ventilation rate may effectively reduce the risk of long-range airborne transmission, while it may be of little usefulness in preventing the droplet-borne transmission [204]. Fresh air natural ventilation and sunlight has been shown to reduce the risk of infection [207,208]. Evidence on the effectiveness of different ventilation measures are limited [209]. Other light sources have been also considered; continuous very low dose-rate far-ultra-violet C (UVC) light in indoor public locations is a promising, safe and inexpensive tool to reduce the spread of airborne-mediated microbial diseases [190,210]. Violet-blue light, particularly 405 nm light, has significant antimicrobial properties against a wide range of bacterial and fungal pathogens and, although efficacy is lower than UV light, it is considered safer for continuous use in occupied environments [197,211,212]. As influenza virus prefers low humidity levels, humidification is another measure that has been proposed [213]. The use of novel disinfectants and no-touch decontamination technologies to improve disinfection of surfaces in healthcare is supported by some studies [212,214]. There is, however lack of epidemiological evidence to support the use of the above measures (such as UV light and humidification) and decisions to implement them should be made with caution due to safety concerns.

Operational considerations: There are implications of incorrect use of the disinfectants, with consequences related to the safety of individuals (e.g. triggering asthma attacks) and appropriate disinfection. Most disinfectants (e.g., bleach) require a pre-cleaning step before applying the disinfectant. Regardless of the product, it is important to follow the manufacturer instructions to ensure safety and effective usage. Depending on the extent of implementation of the measure, there will be increased direct costs, due to material and staff costs that will need to be provided for disinfection. Exposure to UV light may increase the risk of skin cancer and eye conditions. Alternative methods, e.g. use of copper-alloy surfaces, increase building costs and their effectiveness specifically against influenza viruses is yet to be studied.

Likely acceptability: The likely acceptability of environmental measures in Europe will be high. Everyday actions will engage and empower the public.

Expert opinion: Evidence indirectly supports the use of environmental measures (object and surface cleaning, minimal sharing of objects and natural air ventilation) during epidemics and pandemics due to the transmission modes of influenza viruses and the potential of these measures to reduce transmission. There is lack of direct evidence on effectiveness against LCI and effectiveness on mitigating the pandemic. Evidence to support use of UV-light and air humidification as a disinfection measure against influenza is not sufficient.

Table 6. Summary of recent reviews and meta-analyses on effectiveness of environmental measures

Environmental measures- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Qian et al., 2018	HCSs	Respiratory viruses	Properly used ventilation systems can reduce the risk of airborne infection significantly.
Rajakaruna et al., 2017	HCSs	SARS, Ebola, MERS	Use of quarantine and ventilation functions supported.
Boyce et al., 2016	HCSs	Various pathogens	Newer disinfectants and no-touch decontamination technologies will improve disinfection of surfaces.
Cook et al., 2016	-	Noroviruses	Copper alloy surfaces may inactivate norovirus by damaging viral capsids. Effective disinfection was achieved by chlorine, calcium or sodium hypochlorite, chlorine dioxide, high hydrostatic pressure, high temperatures, pH values >8.0, freeze-drying, and UV radiation.
Klaus et al., 2016	Aircraft	Various pathogens	Formaldehyde, hydrogen peroxide, and alcohol allow the varying techniques of standard disinfection of surfaces.
Muller et al., 2016	HCSs	Various pathogens	Copper alloy surfaces have antimicrobial properties and are effective against HCAI. Limited information on viruses.
Otter et a., 2016	HCSs	SARS, MERS CoV, Influenza	Importance of indirect contact transmission (involving contamination of inanimate surfaces) in HCSs is uncertain compared with other transmission routes, principally direct contact transmission (independent of surface contamination), droplet, and airborne routes.
Thomas et al., 2016	HCSs	Influenza	The literature on cleaning surfaces shows influenza can be effectively removed with correct chemicals and techniques. Clean rooms with hydrogen peroxide vapour is effective against influenza and clean the areas that cleaners do not reach.

Lidal et al., 2015	Day-care centres	Respiratory and other infections	The effectiveness of initiatives concerning physical conditions (occupation density, time spent indoors/outdoors, space, ventilation, etc.) is uncertain, due to limited high quality evidence.
Smith et al., 2015	Community –adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Limited information on effectiveness of surface disinfection effectiveness.
McLean et al., 2014	-	Bacteria, fungi	Violet-blue light, particularly 405 nm light, has significant antimicrobial properties against a wide range of bacterial and fungal pathogens and, although germicidal efficacy is lower than UV light, this limitation is offset by its facility for safe, continuous use in occupied environments.
Serra et al., 2014	Day-care centres	Respiratory infections	Appropriate cleaning of the environment have been uniformly recommended by different guidelines as non-specific prevention measures against respiratory infections. The evidence on the usefulness of these measures in this setting is limited.
Hobday et al., 2013	Community	Influenza	There is recent evidence and historical data to support the effects of natural ventilation but no evidence for sunlight.
Rutala et al., 2013	HCSs	HCAI	Room decontamination units (such as UVC and hydrogen peroxide systems) aid in reducing environmental contamination after terminal room cleaning and disinfection.
Weber et al., 2013	HCSs	Various pathogens	Improved cleaning and disinfection of room surfaces decreases the risk of HCAI. Self-disinfecting surfaces can be created by impregnating or coating surfaces with heavy metals (e.g. silver or copper), germicides (e.g. triclosan), or miscellaneous methods (e.g. light-activated antimicrobials).
O'Gorman et al., 2012	HCSs	HCAI	Promising but lack of consensus on: minimum percentage copper alloys required for effectiveness, impact of organic soiling on the biocidal effect of copper, and best approach to routine cleaning of such surfaces.

Grass et al., 2011	Various settings	Microbes	Effectiveness of metallic copper surfaces.

Social distancing measures

Social distancing measures refer to measures, such as school closures, voluntary quarantine of exposed persons, voluntary home isolation of patients and other measures in workplaces, schools or mass gatherings.

Objective: Social (interpersonal) distancing policies aim to minimize illness and transmission of infection within the various community settings such as home, workplace, pre-school, school, university, childcare centre, long-term care facility, HCSs etc.

Rationale: Increasing the physical distance between individuals by various means will reduce the spread and transmission of influenza.

Evidence of effectiveness: Various measures exist within this category. Some are considered to be effective and others of uncertain effectiveness. They are often expensive, unpopular and difficult to implement, although social distancing measures have been a recent focus of investigation and some of these measures were implemented during SARS outbreak and the 2009 A(H1N1) influenza pandemic [76,95,215-219]. Results from simulation exercises suggested a critical role of social distancing in the potential control of a future pandemic and indicated that such interventions are capable of arresting influenza epidemic development, if they are used in combination with other measures, activated without delay and maintained for a relatively long period [68,220]. For the implementation of social distancing measures, consideration of asymptomatic infections and individuals that are infected but do not have fever is important, as fever is not always present in influenza infections; there are studies that show that only half of the influenza cases are presented with fever [21,221]. Individual social distancing measures are considered separately in the following chapters.

Operational considerations: Depending on the measure, social distancing measures may have societal, ethical, legal and economic implications.

Likely acceptability: Based on a systematic review of the public perceptions of NPCs for reducing transmission of respiratory infection, there was hesitation about adopting interpersonal distancing behaviours due to their perceived adverse impact and potential of social stigma [69]. Common perceived barriers included beliefs about personal susceptibility, transmission of infection and concerns about self-diagnosis in emerging respiratory infections [69]. Limited information is available to develop policies and procedures on some of the social distancing measures. Additional research is needed to assess the feasibility and effectiveness of practices to promote social distancing [222].

Expert opinion: A layered approach of social distancing measures should be considered, depending on the severity level and the impact of the pandemic [9,68]. Such measures may potentially have a high societal impact, so they would be mostly applicable in more severe pandemics.

Voluntary isolation of cases not requiring hospitalisation

This measure refers to ill persons likely infected by influenza but with no need for hospital care, requested to voluntarily remain in a single, dedicated room through the duration of symptoms (usually 5-7 days).

Objective: To reduce transmission by reducing contact between uninfected and infected persons.

Rationale: Typically, the virus can transmit from an ill person to another person via direct or indirect contact, between one day before the onset of symptoms and 5-7 days after the onset of symptoms. Isolation of infected individuals should reduce the likelihood of transmission and spread of the virus.

Evidence of effectiveness: The amount of influenza virus shed by symptomatic individuals is greater than in the asymptomatic phase, but viral shedding typically begins shortly after infection and before the onset of symptoms [223]. This limits the efficacy of isolation, with maximum effectiveness if individuals are completely quarantined almost immediately after contact with an infected person [41]. Generally, the measure is considered effective, although there is an increased risk of intra-household transmission from index cases to contacts [95]. A small proportion of infected cases will have a very high likelihood of transmission, either due to shedding patterns or contact patterns. The possibility of such "super spreaders" needs also to be considered [224]. In the case of young children and immunocompromised patients, viral shedding and its duration will likely be prolonged. However, more recent studies report that when numbers are small, isolation in hospitals using appropriate infection control measures may be effective [41].

Most of the evidence originates from modelling studies and they suggested that cumulative attack rates would be reduced by this measure [225-227]. However, modelling studies have low strength of evidence. Voluntary home isolation is effective and acceptable, but there is an increased risk of intra-household transmission from index cases to contacts; such risk is increased with longer duration of isolation [95] and can be reduced by appropriate information and behaviour by household members. Antiviral prophylaxis of household members reduces the risk of intra-household transmission during voluntary isolation.

Operational considerations: There may be moderate secondary effects, as other healthy individuals in the same house may be exposed to the risk of infection. Unless carefully managed, the isolated person may not receive adequate care and support, especially if being elderly or living alone. There would be issues of people not being available for work, including caregivers. There can be moderate financial and practical disincentives, job or income insecurity or the need to care for others.

Likely acceptability: Acceptability is considered high as this is an extension of advice given during seasonal influenza. However, acceptability will vary by circumstance. Based on a systematic review of the public perceptions of NPCs for reducing transmission of respiratory infection, there were concerns about adopting isolation due to the perceived adverse impact and social stigma [69]. In five studies, between 50% and 96% of respondents reported intending to stay home from work with symptoms of A(H1N1)pdm09, whereas in six studies, the proportion ranged from <1% to 26% [71].

Expert opinion: Voluntary isolation of infected individuals is supported at all times during epidemics and pandemics. Prompt recognition of illness will be important in order to ensure rapid isolation and antiviral prophylaxis of household members should be considered for the duration of isolation. Support for financial, social, physical, and other needs of the patients and caregivers, e.g. ensuring job security and income replacement for ill persons and caregivers, will need to be carefully planned [228]. Training and supplies will be essential for infection control for household members providing care for the ill person. A combination with personal protective and environmental measures will increase the intervention effectiveness.

Voluntary quarantine of exposed household members

Quarantine, or the sequestration of potentially infectious individuals, was first used in the mid – 14th century in Southern European cities such as Reggio in Italy and Ragusa in Croatia as a countermeasure to slow the introduction of plaque into these cities.

Voluntary quarantine of household contacts of a person with proven or suspected influenza refers to remaining at home for a defined period (e.g. one incubation period, three days) after the last exposure. If symptoms of illness occur, they would then self-isolate and seek medical advice.

Objective: To reduce transmission by decreasing the spread of the influenza virus from household settings.

Rationale: The people at highest risk of acquiring influenza are the household contacts of a case. Since infectivity early in the infection is high, voluntary quarantine of household contacts before they become ill may help prevent further transmission of the virus to the community.

Evidence of effectiveness: Most of the evidence originates from modelling studies and they suggest that cumulative attack rates would be reduced by this measure though less than might be thought intuitively [225,226]. Household quarantine alone reduced overall AR by 10% and peak AR by 20%, whereas combination of school and workplace closure, antiviral treatment and prophylaxis, and household quarantine reduced overall AR by more than 60% and peak AR by more than 80% [226]. Based on the A(H1N1) 2009 experience, a review concluded that strategies like quarantine may have been beneficial in reducing transmission at the individual level at home, although secondary attack rates during the pandemic were similar to those with seasonal influenza [229]. Severity is an important determining factor in the definition of a pandemic when considering to undertake such social distancing measures [230]. Please also see the chapter on evidence of effectiveness for 'Voluntary isolation of cases not requiring hospitalisation'.

Operational considerations: There will be substantial cost, mainly due to a significant number of people being off work. Social, legal and ethical issues may rise due to the restriction in the freedom of movement of individuals. A clear distinction will need to be made between mandatory exclusions and voluntary stay-at-home policies.

Likely acceptability: The acceptability may be low and compliance may be difficult with a measure for which no personal benefit is perceived and the community benefit is unclear [228]. There might be lack of compliance or abuse (real or perceived) by some people undermined confidence in the measure and particular problems with special groups in the population [228]. Experience from previous pandemics and the SARS epidemic is variable but often negative in communities with cultural similarities to Europe [100,231]. National laws and regulations will need to be considered.

Expert opinion: Voluntary quarantine may be considered during a severe pandemic, especially at the early stages to delay the start of local transmission. It is recommended especially when dealing with a small and manageable number of localised cases [24,51,52]. Antiviral prophylaxis will decrease the risk of infection among exposed persons, at least in household settings. Rapid and effective identification of cases in the household, followed by voluntary compliance by household contacts and an ability to provide support to households that are secluded will be essential. Training/education on infection control in the home would be necessary.

Table 7. Summary of recent reviews and meta-analyses on the effectiveness of isolation of cases and voluntary quarantine of exposed persons

Isolation of cases/voluntary quarantine of exposed persons- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Rashid et al., 2015	Community	Pandemic influenza	Voluntary home isolation and quarantine are effective and acceptable measures but there is an increased risk of intra-household transmission from index cases to contacts.
Tooher et al., 2013	Community (46 studies)	Pandemic Influenza	Five studies reported between 50% and 96% of respondents reported intending to stay home from work with symptoms of A(H1N1)pdm09, whereas six studies, <1% to 26%.
Jefferson et al., 2011 (5 cohort, 6 before-after)	Various settings	Respiratory viruses	Case-control studies suggested implementing transmission barriers, isolation and hygienic measures are effective at containing respiratory virus epidemics. Cohorting in paediatric wards, early identification of cases and isolation of close contacts were effective.
Jefferson et al., 2010 (2 cohort, 6 before-after)	Various settings	Respiratory viruses	Limited evidence for social distancing being effective, especially if related to risk of exposure. Early identification of cases and isolation was effective.
Lee et al., 2009	Community	Pandemic influenza	Isolation of cases and quarantine of close contacts are considered by the authors as important interventions during containment phase. Combined approaches (also with pharmaceutical interventions will increase effectiveness).

Interventions in educational and child care settings

School closure policies as an example of interpersonal distancing measures have been considered as a policy to mitigate influenza epidemics and pandemics spread [232]. Respiratory infections spread easily in day care and school settings, and children are considered to be the main drivers of influenza transmission in the community. During previous pandemics, schools have closed reactively due to widespread transmission and increased absenteeism of children and employees, instead of a more proactive controlled manner before extensive viral spread [232]. Schools and day care institutions should have an operational plan for closure and reopening triggers in a crisis, and parents and carers would need to be involved in order to make the necessary

arrangements. Other measures, such as student distancing, division of classes in smaller groups, division of school activities in morning/afternoon groups, open-air classes/activities, shortened day/week duration, e-learning opportunities and cessation of transportation with school buses may be alternative solutions, when the situation does not justify school closures.

Several difficulties arise in implementing this policy: the need to define and measure the triggers and level of severity and transmissibility in children to justify closures; the secondary effects that will probably be major and the transmission of the virus outside school [41]. In many settings, schools additionally perform special social functions providing social care, HC and meals [233].

Other, less disruptive, non pharmaceutical measures may also be applied in educational settings to mitigate the impact of the pandemic. Those are: hand and respiratory hygiene, voluntary isolation at home, isolation of staff and students when they become ill during school hours, reducing crowding at schools and school buses, proper environmental cleaning and ventilation, dissemination of public health messages, ensuring essential services and supplies [227].

Proactive school and day care closures

Proactive closures refer to the early and planned closure of schools prior to the start of local transmission of the virus.

Objective: To prevent the amplification and spread of influenza transmission in schools and the community.

Rationale: School children are considered to be the main drivers of influenza transmission and contact transmission occurs extensively at educational settings. School closures will reduce the extensive influenza virus transmission and spread that occurs in schools and its further spread to the community.

Evidence of effectiveness: Reviews and simulation studies suggest that school closures can be a useful control measure during an influenza pandemic, particularly for reducing peak demand on health services [9,95,218,219]. There are some observational analyses that suggest a decrease in virus transmission when seasonal influenza outbreaks or pandemics coincide with school holidays [100,106,234,235]. However, the effects are smaller than it might be predicted by modelling studies, perhaps because children also mix outside schools [164,233,236-239]. Contradicting evidence and uncertainty regarding the effectiveness of school closure [240,241] may have limited its implementation over the course of the past pandemics [242,243]. During the 2009 A(H1N1) pandemic, school closures were shown to have caused a contact rate reduction and lower number of influenza cases in school-aged children [9,233,244]. Modelling studies generally support school closures and confinement in the home as an effective measure for reducing overall attack rates within communities [239], especially when coupled with antiviral prophylaxis [68].

From the experience from the 2009 A(H1N1) pandemic shared during a WHO consultation, countries suggested that school closures were effective in mitigating the spread of influenza and reducing within school transmission, especially in the early phases of an outbreak [232], although they were not necessarily effective (or measurable) for reducing overall community transmission [232].

A recent meta-analysis also investigated the impact of school closure and the optimal duration of closure [245]. It concluded that implementing school closure before or after the epidemic reaches its peak, reduced the overall influenza epidemic, by a mean reduction of 29.65%. A more pronounced effect was observed if the measure was

implemented earlier during the pandemic and the longer the duration of closure the more the epidemic peak would be delayed [245]. These findings suggest that policy makers could consider school closure policies more diffusely as a response strategy to influenza epidemics and pandemics, depending on the feasibility and the cost [81,245,246].

The advantage of proactive closures is that they can be performed before any transmission has taken place in schools. The disadvantage is the difficulty of identifying the optimal triggers, so that the intervention is not implemented too early, in which case it will be costly and difficult to sustain. School closures appear to have the potential to reduce influenza transmission, but the heterogeneity in the data available means that the optimum strategy (e.g. the ideal timing and duration of closure) remains unclear [217]. In Hong Kong, where day-cares and primary schools were closed when local transmission of A(H1N1)pdm09 was identified and secondary schools closed for summer vacation shortly afterwards, it was estimated that transmission was reduced by approximately 25% [244]. Please see 'Reactive school closure' chapter for evidence of effectiveness.

Operational considerations: There can be financial and practical disincentives [232] and major secondary effects from job or income insecurity or the need to care for others. Consideration of a public policy to permit a paid leave of absence from work for parents during school closures may be beneficial to mitigate some of the secondary effects. A significant proportion of healthcare workers that have school-aged children might also need to refrain from their duties in order to care for their children [233]. School closures have the potential to cause adverse consequences, which may likely disproportionately affect students, families and the communities [247,248]. There will be disruption of education, as well as other services provided by the schools (e.g. school meals, doctor visits). Legal issues will need to be closely monitored [232]. The disruption caused by school closures will be significant, especially for west European societies that have little tradition of school closures outside holiday seasons. A greater understanding of age-dependent behaviours, during school closures as a consequence of a pandemic, is required [249]. Moderate costs will be due to the planning and logistics of school closures. The cost-effectiveness of this measure should be assessed in future studies [249]. Existing studies suggest that school closures may not be cost effective for mild pandemics, although they might be for more severe situations [250].

Likely acceptability: EU countries have implemented school-related measures during seasonal epidemics and the 2009 A(H1N1) pandemic. The fact that some countries already have experience of gradual or regional closures for seasonal or pandemic influenza outbreaks demonstrates that logistic and feasibility challenges of school closure strategies can be to some extent bypassed [81,219,251].

Expert opinion: Proactive school closures should be considered in severe epidemics and pandemics, as they can be associated with significant societal and economic costs. The extent of proactive school closures will depend on the severity level of the pandemic and should be considered after evaluating the adverse effects on the community. Whole-of-society plans to mitigate secondary effects should be considered. Policy makers may also consider intermediate options, such as partial school closures, which might provide ways to gain from the benefits of school closures [247]. The optimal timing and duration of the implementation of the measure will need to be carefully considered on a case-by-case basis. Planning to mitigate transmission within schools, while children continue attending, is always advisable.

Reactive school and day care closures

Reactive closures of schools have been implemented when widespread virus transmission was observed in the

school. A distinction can be made between school closures and class dismissal (when a school remains open but the students are dismissed). The latter might be preferable in some instances, as it makes re-opening and support of vulnerable children and families easier [233,252].

Objective: To reduce the anticipated amplification and spread of influenza transmission in schools, as well as reduce the indirect impact on the community.

Rationale: Please see 'Proactive school closure' chapter above.

Evidence of effectiveness:

A review of modelling studies suggested that reactive school and workplace closures alone did not impact on overall attack rate, but reduced peak attack rate by about 40% [68,226], while combination approaches (antiviral treatment and prophylaxis, school closure and pre-pandemic vaccination with 20% coverage) reduced overall AR by more than 60% and peak AR by more than 75% [226]. A model-based analysis categorised four types of school closures: reactive gradual closure, starting from class-by-class, then grades and finally the whole school [81]. Four closure strategies were considered: nationwide, countywide, reactive school-by-school, reactive gradual and their potential impact was assessed. Policies were considered based on triggers that are feasible to monitor, such as school absenteeism and national ILI surveillance system. This study found that, under specific constraints on the average number of weeks lost per student, reactive school-by-school, gradual, and county-wide closure gave comparable outcomes in terms of optimal infection attack rate reduction, peak incidence reduction or peak delay. Optimal implementations generally required short closures of one week each; this duration was long enough to break the transmission chain without leading to unnecessarily long periods of class interruption. Gradual and county closures were less sensitive to variations in school absenteeism and thus were slightly more feasible in practice [81].

During the 2009 A(H1N1) pandemic, closures occurred in schools that reported significant illness and were likely motivated by excessive absenteeism, rather than done proactively [253].

Operational considerations: Please see 'Proactive school closure' chapter above.

Likely acceptability: Please see 'Proactive school closure' chapter above.

Expert opinion: Depending on the severity of the pandemic, reactive school closures might be necessary to plan for, due to high absenteeism and operational issues. Like in proactive school closures, the timing and duration of the closures will need to be carefully considered on a case-by-case basis to avoid unnecessary societal disruption. Planning to mitigate transmission within schools, while children continue attending, is always advisable. Whole-of-society plans to mitigate secondary effects should be considered.

Table 8. Summary of recent reviews and meta-analyses on school closure effectiveness

School closures- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Bin Nafisah et al., 2018	Educational settings	Influenza	Implementing school closure before or after the epidemic reaches its peak, reduced the overall peak of the influenza epidemic, by a mean reduction of 29.65%. Early implementation and long duration increased the effectiveness.
Uscher Pines et al., 2018	Educational settings (16 articles)	Influenza	Limited information available on effectiveness and to develop policies and procedures on social distancing. Most frequently identified school practices were cancelling or postponing after-school activities, cancelling classes or activities with a high rate of mixing/contact that occur within the school day, and reducing mixing during transport.
Rashid et al., 2015	Educational and other community settings	Pandemic influenza	School closure, whether proactive or reactive, appears to be moderately effective and acceptable in reducing the transmission of influenza and in delaying the peak of an epidemic but is associated with very high secondary costs.
Jackson et al., 2014	Educational settings (45 modelling studies)	Influenza	Most modelling analyses indicated that school closures would lead to reductions in the peak incidence and cumulative attack rate. Predictions of the reduction in the peak incidence were in most studies between 20–60%.
Jackson et al., 2013	Educational settings (79 epidemiological studies)	Influenza	Effective to reduce influenza transmission, but due to heterogeneity in the available data optimum strategy remains unclear (e.g. ideal length and timing of closure).
Lee et al., 2009	Educational settings	Influenza	Effective if done early, decisively, and for prolonged periods.

Measures in the workplace and public places

These measures refer to a variety of means to reduce risk of infection in the workplace, on the way to and from work and in public places. These measures include: flexible working schedules/shifts for employees, the opportunity to distance working/teleworking, encouraging social distancing measures within the workspace,

increased use of emails, teleconferences to reduce close contact, reduced contact between employees and customers, reduced contact between employees, adoption of flexible leave policies and promotion of use of other personal protective countermeasures in combination [68].

Objective: To reduce workplace and community transmission, delaying the spread and slowing the peak of the pandemic.

Rationale: Influenza can easily transmit from person-to-person in work and other public places where people gather in contained spaces for long periods. Viral transmission will be reduced by decreasing the frequency and length of social interactions and the physical contact between individuals.

Evidence of effectiveness: There is some evidence of influenza attack rates in working-age adults (aged 18-64 years) that have been reported to be as high as 15.5% over an influenza season [24]. Measures at work, like home working, are considered modestly effective [95]. A modelling study showed that alternative intervention (e.g. flu leave days) aimed at increasing time spent away from work when ill, would reduce infections in the workplace by 25.33% (1 flu leave day) or 39.22% (2 flu leave days) compared with baseline [254]. Modelling studies suggest that workplace closures resulted in a small reduction in cumulative attack rates or peak attack rates, although there is a decrease when assessing the effect of combining interventions [70,226,255,256]; most modelling studies assessed workplace closure in combination with school closures or other measures. A recent review of modelling studies suggests that workplace closures in combination with other measures may be effective, although will have marked implications [68]. Workplace closures in combination with home working were found to be modestly effective and were acceptable, but likely to be economically disruptive [95]. A decision for workplace closures is difficult because of the lack of objective information on the level of influenza transmission that takes place in the workplace, on transport going to and from work and in other public places. Modelling studies suggest proportions of transmission in such settings, however there are few empirical data to support these suggestions [100,106]. A recent review of epidemiological and modelling studies showed that social distancing in workplaces was associated with a reduction in influenza-like illness and seroconversion to A(H1N1)pdm09 [257]. However, the overall risk of bias in the epidemiological studies was high. The modelling studies estimated that workplace social distancing measures alone produced a median reduction of 23% in the cumulative influenza AR in the general population [257]. It also delayed and reduced the peak influenza attack rate [257]. The reduction in the cumulative attack rate was more pronounced when workplace social distancing was combined with other non-pharmaceutical or pharmaceutical interventions. However, the effectiveness was estimated to decline with higher basic reproduction number values, delayed triggering of workplace social distancing, or lower compliance [257].

Multiple factors, such as guilt associated with missing work, inability to complete tasks, security and access to paid leave days, affect employees' decision to stay home when experiencing ILI symptoms [254]. An estimated 42% of workers in Pennsylvania, USA would not get paid if they stayed home when ill [254]. Their willingness to stay home when ill may thus be associated with access to paid leave days. Other measures that would enable them to fulfil their tasks would be more acceptable, increasing the effectiveness of this intervention.

Operational considerations: There will be variable to moderate secondary effects that will depend on the extent of the measures. There will be significant secondary societal and economic effects from workplace closures in the highly interdependent societies of Europe.

Likely acceptability: Some organisations are used to closing, or at least scaling activities down, during holiday

seasons but not for extended periods. Employees will accept workplace closures if there is no anxiety regarding job security and income replacement. It would be convenient for parents if they need to care for their children during school closures. There will be moderate costs that will depend on the extent of the measures. Costs of full workplace closures for any period of time will be significant. Other workplace measures will be more acceptable.

Expert opinion: Measures at workplaces (e.g. teleworking, social distancing) are considered effective and feasible during all phases of a moderate to severe epidemic or pandemic. The selection of which measures will be applied will depend on the company and the type of work. Other personal protective and environmental measures should be applied in combination with workplace measures. Workplace closures may be necessary to reduce transmission in severe pandemics. Business continuity plans should include pandemic scenarios.

Table 9. Summary of recent reviews and meta-analyses on effectiveness of measures at workplaces and public places

Workplace/Public place measures- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Ahmed et al., 2018	Workplaces (12 modelling studies, 3 epidemiological)	Pandemic Influenza	Reduction in ILI and seroconversion to 2009 influenza A (H1N1). Modelling studies estimated a median reduction of 23% in the cumulative influenza attack rate in the general population and delayed and reduced the peak influenza attack rate. Combination with other measures increased effectiveness. Effectiveness was estimated to decline with higher basic reproduction number values, delayed triggering of workplace social distancing, or lower compliance.
Hansen et al., 2018	Workplaces	Infectious eases	Workplace strategies to prevent and control infectious illness transmission may reduce costs and productivity losses experienced by businesses related to infectious illness absenteeism.
Rashid et al., 2015	Community	Pandemic influenza	Work closure and home working are also modestly effective and are acceptable, but likely to be economically disruptive.
Jefferson et al., 2011 (5 cohort, 6 before-after)	Various settings	Respiratory viruses	Insufficient evidence to support screening at entry ports and social distancing (spatial separation of at least one metre between those infected and those non-infected).
Jefferson et al., 2010 (2 cohort, 6 before-after)	Various settings	Respiratory viruses	Limited evidence for social distancing being effective, especially if related to risk of exposure. Early identification of cases and isolation was effective.
Lee et al., 2009	Workplaces	Influenza	Workplace closures in combination with other measures may be effective, although will have marked implications.

Measures related to mass gatherings

This refers to interpersonal distancing measures implemented during mass gatherings to avoid crowding, as well as organisational measures, such as postponing or cancelling an event. It also refers to other NPCs, such as hand and respiratory hygiene that will need to be applied.

Objective: This measure will aim to reduce transmission and dissemination of influenza through large gatherings.

Rationale: Mass gatherings increase the close contact of people for long periods of time in contained spaces, increase influenza virus transmission and spread, assist in the introduction of the virus to the community hosting the event, and increase influenza virus spread in the gathering and to healthy household members after attending the event. Restricting, modifying, postponing, or cancelling large gatherings may slow virus spread [258-263]. Combined use of other NPCs will aim to reduce the person to person viral transmission.

Evidence of effectiveness: Large meetings, conferences, religious pilgrimages, sports events and other national and international events play an important role in spreading infectious diseases [258,262-268]. In the case of gastrointestinal and respiratory illnesses, the explosive spread following small or large gatherings is commonly reported. Several reviews from data obtained at the yearly Hajj mass gatherings have shown that infections are a common cause of hospital admission, which often occurs in the home country of pilgrims [155,265,266]. The most common outbreaks at these mass gatherings involved respiratory infections and vaccine preventable diseases, mainly influenza and measles [80,154,155].

Restricting mass gatherings, in combination with other social distancing measures, may help reduce transmission, but conclusive evidence on the individual effect of mass gathering restriction alone could not be identified [155]. Models suggest that cancellation of non-essential public gatherings might help to decrease rates of transmission and overall morbidity, but the effectiveness of the interventions has not been quantified [41,258]. Evidence suggests that event duration and extent may be the key factors that determine the risk of influenza transmission, along with whether the venue is indoors or outdoors [269]. Modelling studies have shown that monitoring, postponing, or cancelling large public gatherings may be warranted close to the epidemic peak, but not earlier or later during the epidemic [270]. From the experience of the 2009 pandemic shared during a WHO consultation on 24 June 2009, 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 [232].

Regarding the other NPCs that could be implemented during such events to mitigate the impact of the pandemic, it is often difficult to assess the effect of a single NPC independently from other NPCs or factors in infection control, such as environmental hygiene, crowding and education [155]. There is lack of evidence regarding adherence to NPCs and vaccination. One review suggested that a modest proportion of attendees was shown to adhere to facemask use [154], while others suggested that adherence was low [155,175]. Facemask use seems to be beneficial against certain respiratory infections at mass gatherings, although evidence is lacking regarding the effectiveness against specific respiratory infections [154,155,175,176].

Operational considerations: There might be secondary societal and economic effects on organisers, attendees and employees and considerable costs; any decision to cancel all events over a period would be controversial and costly, so therefore will need to be considered with a risk-based approach. The issue of financial liability and meeting insurance would need to be considered.

Likely acceptability: The public likely expects cancellation, postponements and re-arrangements of mass

gatherings, so acceptability would be probably high. The use of other NPCs will also be likely acceptable.

Expert opinion: Implementation of actions related to mass gatherings should depend on the risk assessment; the severity of the pandemic, the local pandemic situation, the timing, duration and extent of the event and the area from and to which the attendees are commuting (affected or non-affected). During severe pandemics, early and sustained avoidance of crowding may be considered as an action to limit virus transmission. Instead of cancellation, the postponement or re-scheduling of the event might be sufficient. Event planners should evaluate the situation after liaising with local and national public health authorities and taking individual rights into consideration. Other personal protective and environmental measures should be considered in combination.

Table 10. Summary of recent reviews and meta-analyses on mass gathering measure effectiveness

Mass gatherings- Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Hoang et al., 2018	Mass gatherings	Various pathogens	The most commonly acquired respiratory viruses were human rhinovirus, followed by human coronaviruses and influenza A virus. Vaccination, use of facemasks, disposable handkerchiefs and hand hygiene may be recommended, but the effectiveness of these measures has been poorly investigated in the context of MGs.
Barasheed et al., 2016	Mass gatherings (12 cross sectional, 10 cohort, 2 case studies, 1 RCT)	Respiratory infections	Pooled estimate showed significant protectiveness against respiratory infections, not specific to influenza (RR=0.89, 95% CI: 0.84-0.94), modest proportion of attendees used facemasks.
Benkouiten et al., 2014	Mass gatherings (17 studies)	Respiratory tract infections	Contradictory results for effectiveness of hand washing, respiratory etiquette and facemasks. Issues of low compliance, especially with facemask use.
Al Tawfiq et al., 2013	Mass gatherings	Respiratory tract infections	The use of masks may reduce exposure to droplet nuclei. The practice of social distancing, hand hygiene, and contact avoidance was associated with reduced risk of respiratory illness.
Haworth et al., 2013	Mass gatherings		Observational studies failed to demonstrate any clear benefit of using facemasks or hand washing among Hajj pilgrims.
Ishole et al., 2011	Mass gatherings	Influenza	Evidence suggests that event duration and crowdedness may be the key factors that determine the risk of influenza transmission, and possibly the type of venue (indoor/outdoor).

Travel-related measures

Travel-related measures include provision of travel advice and recommendations, screening of travellers and travel restrictions. Evidence for the effectiveness of some of those measures is limited and their implementation would depend on the risk assessment and resultant risk/ benefit analysis of the actions being considered [35].

International and domestic travel advice

Travel advice (or travel recommendations) can refer to official government advice, which has legal and economic implications or measures that travellers should consider to minimise risk of infection. Travel and trade restrictions are regulated under Internal Health Regulations (IHR) part III.

Objective: Through advising against travel during the pandemic, to reduce the number of people who are infected during a trip to areas/ countries where transmission is higher, and reduce the risk of importation from countries with high transmission. A secondary objective is to reduce transmission among people who are travelling (in airports queues, on planes, etc.). Travel recommendations may also be given on the use of preventative measures during traveling to minimise the risk of developing influenza and complications.

Rationale: Travelling facilitates the spread of influenza from infected to uninfected areas. Close contact of people increases transmission and spread of the virus during the actual travels. Reduced travelling and using other measures while travelling may therefore delay the spread of the pandemic.

Evidence of effectiveness: In the case of a pandemic, the net number of influenza infections that are likely to be prevented is small compared to the total number of infections. Modelling studies suggest in order to have a small delaying effect, adherence to international advice should be 100% [271]. Although border control is considered impractical and ineffective (see next chapters), travel advice, even at border entry points will likely be a more effective approach to the international control of communicable diseases [272,273]. Advice may promote the use of preventative measures for travellers especially those at high-risk for developing complications among crew members and passengers, as well as those participating in mass gatherings [273]. Providing advice and information on isolation, health monitoring and hygiene measures has been suggested to be more effective than travel restrictions [44]. There is, however no evidence to quantify the effectiveness of travel advice during an influenza pandemic. During the SARS epidemic in 2003, international travel to affected areas declined steeply, before formal travel advice was issued.

Operational considerations: The costs related to issuing the advice will be limited, but indirect, secondary societal and economic effects will be significant, as the advice may have considerable impact on the travel industry and commerce. Complex issues of liability may arise and be costly to resolve, irrespective if costs are borne by individuals, companies, insurance or the public.

Likely acceptability: Travel advice will likely be anticipated by the public. There are considerable concerns that European residents abroad will attempt to return to their home countries despite the advice and perhaps put themselves at greater risk, than if they stayed at their current location. Additionally, people may try to leave EU Member States for other EU countries or non-European countries with better perceived public health protection or medical services.

Expert opinion: Although there is lack of evidence to quantify the effectiveness of travel advice to mitigate a pandemic, issuing relative travel advice, consistent with IHR, is supported during epidemics or pandemics at any

level of severity. Information campaigns and health information at the ports of entry/exit and travel recommendations for travellers concerning use of other NPCs are also supported.

Entry and exit screening at national borders

This measure refers to the use of devices and other means for entry and exit screening at national borders.

Objective: To reduce the number of infectious people entering or leaving a country, focusing on those coming from countries that are first experiencing the pandemic wave [272,274].

Rationale: With the use of measures such as active screening, non-contact infrared thermometers (NCITs) or encouraging reporting of infection, the number of infectious people entering/leaving a country with infection may be reduced, in this way reducing viral spread.

Evidence of effectiveness: Experience from the SARS outbreak and influenza 2009 pandemic showed that both entry and exit screening were ineffective in preventing spread [272,275]. There is no evidence to compare the effectiveness of entry versus exit screening, although exit screening would be more logical and was recommended in the past. Application of what we know about the natural history of influenza suggests that attempts to screen out infected persons will be equally unsuccessful because many infectious people may be pre-symptomatic or asymptomatic or may even hide their symptoms before the screening point [276]. That is also the conclusion of modelling exercises [271]. Reviews suggested that there is insufficient evidence to support screening at entry/exit points [44,127-129].

Screening methods include the use of NCITs in airports to detect infected passengers [276]. Studies from the 2009 pandemic found that the positive predictive value of detecting a laboratory-confirmed pandemic influenza ranged from 0.9% to 76.0%, and was likely to be too low to effectively detect and contain pandemic infection. Other studies suggest limited efficacy of NCITs to detect symptomatic passengers at the early stages of a pandemic influenza [276]. A study of entry screening for pandemic A(H1N1) influenza at the Auckland International Airport, which focused on encouraging infection reporting suggested a screening sensitivity of 5.8%, which the authors concluded to be insufficient to delay the spread of pandemic influenza. Molecular diagnostics or point of care antigen detection tests may be considered, but will be expensive and resource intensive if used in a large population [277]. Border screening using self-reported symptoms and temperature testing also showed limitations for preventing pandemic influenza from entering a country. Using "any symptom" or cough would lead to many uninfected people being investigated, yet some infected people would remain undetected. If more specific criteria such as fever were used, most infected people would enter the country despite screening [21,22,278]. The high prevalence of other respiratory virus infections also had important implications for the prediction of influenza in airline travellers [279].

Overall, modelling and observational studies support low efficacy associated with such border control measures [272] and insufficient evidence to support their use. The general consensus appears to be that even rigorous and extensive border control measures will likely delay the spread of pandemic influenza by few days [9,280]. It has been suggested that travel advice and outbreak related communication for travellers at border entry points, together with effective communication with clinicians and more effective disease control measures in the community, may be a more effective approach to the international control of communicable diseases [272].

Operational considerations: Widespread and sustained screening of travellers would ultimately be impractical and inefficient as long as detecting asymptomatic shedding is not feasible. On the other hand, difficulties with

the rapid diagnosis of influenza patients increase the risk of detaining and restricting travel of a large number of symptomatic persons who will not be infected by influenza.

There will be moderate secondary societal and economic effects, especially with regards to dealing with people who are considered possibly infectious on entry, their investigation, diagnosis and care [281]. Direct costs for equipment and employees will be considerable. Healthcare staff would be occupied at the entry and exit points, although their expertise would be more essential in other settings [281]. Screening should be conducted with caution and informed consent according to the IHR should be obtained from the travellers in case of specimen collection.

Likely acceptability: Following from the previous experience, there is likely to be an expectation among the public, the media and decision-makers that there will be entry screening. This requires preparation, e.g. with simulation exercises, to explain to decision-makers why this is not desirable and anticipated to be ineffective.

Expert opinion: The existing evidence does not support the notion that entry/exit screening border control measures can delay or mitigate an influenza pandemic due to lack of sensitivity to detect symptomatic, pre-symptomatic and asymptomatic infections.

Domestic travel restrictions

This measure refers to travel restrictions (e.g. airport and train station closures) implemented within a country or region.

Objective: Domestic travel restrictions aim to prevent or limit the geographic extent of virus transmission. Through restricting travel during the pandemic, to reduce the number of people who are infected during a trip to areas where transmission is higher. Another objective is to reduce transmission among people who are travelling (in airports queues, on planes, etc.).

Rationale: Travelling facilitates the spread of influenza from infected to uninfected areas. Close contact of people increases transmission and spread of the virus during the actual travel. Reduced travelling may therefore delay the spread of the pandemic.

Evidence of effectiveness: This measure will possibly have a minor delaying effect depending on the timing and extent of its implementation. Some observations concluded that this measure was successful in a few settings during previous pandemics. However, these were rare instances and in rather isolated settings in which there was very limited travel anyway [94,95]. Internal mobility restriction is considered effective only if prohibitively high (50% of travel) restrictions are applied [95]. Models suggest that restrictions on long-distance travel might help to decrease rates of transmission and overall morbidity, but the effectiveness of the interventions has not been quantified [41,258]. A systematic review has concluded that internal travel restrictions could delay the spread of influenza epidemics by one week [77]. Travel restrictions reduced the incidence of new cases by less than 3%, while impact was reduced when restrictions were implemented more than six weeks after the notification of epidemics or when the level of transmissibility was high [77]. Overall, travel restrictions would have minimal impact in urban centres with dense populations and travel networks. There was no evidence that travel restrictions would contain influenza within a defined geographical area [70,77], although combined approaches (antiviral treatment and prophylaxis, household quarantine, school and workplace closure, as well as effective border control) have been shown to reduce overall attack rates by more than 70% and peak attack rates by more than 90% [226]. During the 2009 pandemic WHO did not recommend

travel restrictions, as it would have very little effect on stopping the virus from spreading, but would be highly disruptive to the global community [53,282].

Operational considerations: There will be important secondary effects. In most European settings, this measure would result in large social and economic effects as many functions, like food distribution and fuel supply, may be impacted. There will be major costs to the transport system. Costs through loss of revenue will be considerable though internal travel is likely to decline anyway. Other direct costs on travel-dependent industry and trade will need to be considered.

Likely acceptability: Acceptability is unknown in Europe although a reduction in non-essential travel is likely to be accomplished relatively easily. Voluntary measures and guidelines would likely be more acceptable and thus more effective. Efforts to forcibly limit public assembly or movement could have legal and ethical implications, especially when there is limited scientific evidence supporting such restrictions. There are also important practical and logistical limitations to mandatory long-term community restrictions, in addition to the problem of likely public opposition to such measures [41].

Expert opinion: Domestic travel restrictions might be considered only in high impact situations, as they can be associated with significant societal and economic costs. Such community restrictions may have legal and ethical considerations and should be considered on a case-by-case basis.

Border closures

This measure refers to the closure of international borders due to an influenza pandemic, which is regulated under the IHR.

Objective: To reduce the risk of importation from countries with high transmission, through travel restrictions to or from an affected area. Through restricting travel during the pandemic, to reduce the number of people who are infected during a trip to areas/countries where transmission is higher and to reduce transmission among people who are travelling (in airports queues, on planes, etc.).

Rationale: Please see 'International and domestic travel restrictions' chapter.

Evidence of effectiveness: There will be limited effectiveness from border closures [44], unless almost complete and rapidly implemented in the early pandemic phases. A systematic review has concluded that international border restrictions could delay the spread and peak of influenza epidemics by two months, ranging from a few days to four months [68,77]. Travel restrictions reduced the incidence of new cases by less than 3%, while impact was reduced when restrictions were implemented more than six weeks after the notification of epidemics or when the level of transmissibility was high [77].

Overall, travel restrictions are considered to have minimal impact and no evidence was found that such travel restrictions would contain influenza within a defined geographical area [77]. The experience is that, unless there is almost complete cessation of travel to a country, the attempts of border closure will be unsuccessful in preventing entry. That is also the suggestion of modelling exercises [271]. International border control measures are unlikely to delay the spread of pandemic influenza by more than a few days [77,281]. Such aggressive measures to attempt to stop or slow an emerging pandemic in its early stages were previously considered possible based on modelling studies; experience from the 2009 pandemic has resulted in a general agreement that such attempts are impractical [37]. A study has shown that complete suspension of 99.9% of air travel can only delay individual national epidemics by up to four months, while a combination with other strategies (e.g.

vaccination) can reduce influenza transmission by 40% and delay pandemic spread by up to 10 months [68]. A combination of pharmaceutical and non-pharmaceutical strategies, including border control measures, may have substantial impact in reducing the global spread of viruses [226]. Overall, efficient border closures may decelerate the pandemic.

Operational considerations: There will be massive secondary effects within Europe due to the high extent of essential day-to-day travel across borders. There will be a strong need for international coordination, as well as close collaboration between the governments with airline companies. For most settings in Europe, the direct costs of trying to close borders would be very high.

Likely acceptability: Despite the above considerations, the public and decision-makers may wish to close borders during a pandemic.

Expert opinion: International border closures are not very effective and create large secondary effects, with significant societal and economic disruption. Border closures may be considered in very specific situations (e.g. in small island nations) depending on the pandemic severity and on the risk assessment. Border closures due to public health risks are regulated under the IHR.

Table 11. Summary of recent reviews and meta-analyses on travel-related measure effectiveness

Travel-related measures – Evidence of effectiveness			
Study	**Setting**	**Infection type**	**Conclusions**
Huizer et al., 2015	Community (100 papers)	Infectious diseases	Travel advice, isolation of ill travellers, health monitoring of affected travellers and hygiene measures are applicable measures which can be effective to prevent disease spread. Contact tracing, although frequently practiced, is less applicable, and experiences are less positive. Exit and entry screening, quarantine and travel restrictions are unlikely to be effective, and require extensive resources.
Rashid et al., 2015	Community	Pandemic influenza	Internal mobility restriction is effective only if prohibitively high (50% of travel) restrictions are applied.
Selvey et al., 2015	Airports	Infectious diseases (including influenza and SARS)	Entry/exit screening was not effective. Travel advice at border entry points and more effective disease control measures in the community are more effective.
Mateus et al., 2014	Community (23 studies)	Influenza	Internal travel restrictions and international border restrictions delayed the spread by one week and two months, respectively. International travel restrictions delayed the spread and peak by few days-four months. Travel restrictions reduced the incidence of new cases by less than 3%. Impact reduced when restrictions were implemented late (>six weeks after notification of epidemic) or when the level of transmissibility was high. Travel restrictions had minimal impact in urban centres with dense populations and travel networks. No evidence that travel restrictions would contain influenza within a defined geographical area.
Jefferson et al.,	Various settings	Influenza	Insufficient evidence to support screening at

2011			entry/exit points.
Cowling et al., 2010	Community	Influenza	Entry/exit screening may lead to short-term delays in local transmission: 7-12 day delays compared to nations that did not implement it, with lower bounds of 95% CI consistent with no additional delays and upper bounds extending to 20-30 day additional delays.
Jefferson et al., 2010	Various settings	Respiratory viruses	Insufficient evidence to support screening at entry/exit points.
Bitar et al., 2009	Airport	Pandemic influenza	Limited efficacy of NCIT to detect symptomatic passengers at the early stages of a pandemic influenza. External factors can also impair the screening strategy.
Jefferson et al., 2009	Airport	Influenza	Insufficient evidence to support screening at entry/exit points.
Lee et al., 2009	Community	Pandemic influenza	Most modelling studies found that travel restrictions alone did not impact overall AR. Reducing air travel restrictions has been modelled to be effective in delaying pandemic spread if nearly 100% reduction can be achieved, which is difficult or impossible to achieve. Combination approaches are more effective.

1

2

4. Discussion and conclusions

Prerequisites for NPC implementation

Risk communication

Risk communication, including community engagement and social mobilisation, is a core capacity for emergency response that all countries should establish to respond to an influenza pandemic [34,283-285]. Communication is a key element of all preparedness and response plans, and can directly influence the success of the response against epidemics and pandemics at any severity level. Communication needs to be tailored to the audience, accurate, timely and honest. Messages need to be clear and unambiguous – otherwise this can generate uncertainty and more questions. Recent experiences with MERS-CoV, avian influenza, Ebola virus disease, Zika virus disease, and yellow fever have shown that communicating risk in health emergencies is essential and can have a serious impact on the epidemic response. A structured schedule of briefings can help manage requests for information. Well-trained, confident and trustworthy spokespeople are essential to delivery of messages. Building relationships with media organizations – press, radio, internet and TV – in advance of an incident can help with relationships during a response. Risk communication strategies should clarify locations and situations where exposure to the virus is likely, emphasizing the value of engaging in protective behaviours during and immediately following exposure to these environments. Social media also need to be increasingly considered, and the role of pseudo-experts, as well as hoax or wilfully false messages.

Education and training

A well-trained and educated workforce is essential to a successful response. This will instill self-confidence in the staff themselves, and can reduce the need for rapid training in a response. There is a challenge with when to do training and maintaining competencies and capabilities, however regular refresher training can be a useful approach. Additionally, training and education could be given to members of the public – for example around self-care, accessing healthcare and community cohesion. A variety of mechanisms can be used to provide training, including face to face or on-line, group lectures or one to one. Training should be tailored to the subject being taught and the recipients. Written guidance documents will aid the response and the necessary knowledge acquisition. It is crucial upon employers to educate employees about the hazards to which they are exposed and to provide the necessary means to avoid them. This is particularly important in healthcare settings.

ECDC and WHO provide on-line 5.1.2e and on-line material to enhance knowledge about different aspects of pandemic preparedness and response [286-288].

5. Implications for public health research

The evidence base on public health measures to mitigate the impact of pandemic influenza is limited. Research on innovative approaches to environmental control, social distancing, travel related measures and PPMs should be encouraged and funded; sleeping contracts, with pre-approved protocols, in advance of a future pandemic that can be activated when needed would be an option. WHO has published in 2017 an update on the public health research agenda for influenza [289,290]. Moreover, evaluation of effectiveness and appropriate monitoring after the implementation of the measures will provide valuable evidence for the next pandemics.

Understanding the effectiveness and optimal implementation of public health measures is important for public health decision makers in planning interventions and targeting limited resources. Many studies have focused on the evaluation of the effectiveness of both personal and community-level public health measures since 2009. However, the relative effectiveness of one public health measure compared to another and across the different population groups is still unclear. There is a limited number of observational studies and large well designed RCTs to assess the actual impact of public health measures in the different settings [289,290]. Research could focus on the effectiveness, adherence, acceptability and new ways of reducing the risk of infection during a pandemic.

The lack of quantitative data on effectiveness supports the role of mathematical modelling in understanding pandemic virus transmission and evaluating NPCs under conditions of uncertainty. It would be useful to extend modelling concepts through the application of alternative approaches, including cost effectiveness [291].

The variability in pandemic situations, including the degree of infectiousness, timing, population demographics and susceptibility, and availability of pharmaceutical and NPCs, inhibit the ability to draw general conclusions for the effectiveness of the measures reported from a small number of studies, to other settings and future pandemics [75]. An important avenue for primary research is the prospective study of intervention effectiveness in infectious disease emergency situations.

Influenza transmission

Enhancing knowledge in the area of influenza transmission and shedding is crucial to informing recommendations on the use of individual protective measures during future influenza pandemics. Future studies are needed to evaluate the relative impact of different modes of influenza transmission, and how this may shift between seasonal and pandemic settings. Studies should investigate the relative importance of droplet, contact and airborne transmission in seasonal and pandemic influenza in relation to the effectiveness of various interventions to reduce transmission; furthermore, studies should investigate the details of aerosol transmission including the infectious dose, survival of the virus in aerosols and aerosol generating procedures in clinical settings [290]. Virus survival on hands and on the different types of surfaces should also be determined. Limited reviews have quantified the effectiveness of PPE against different pathogens, although their effectiveness may differ against viral and bacterial agents or pathogens with potentially different transmission modes. The role (prevalence and impact) of heterogeneity in influenza infectiousness and transmission, i.e. of asymptomatic infections and super spreaders, in the transmission chain should be clarified [21,290]. Mathematical models for virus transmission in the various community settings would be helpful [292].

Influenza diagnosis

Adequate diagnostic algorithms for case detection and case definitions for surveillance are essential. Research could focus on the development of sensitive and specific influenza rapid tests for community-based studies and early rapid diagnosis of influenza viruses. The clinical implications of influenza viral load are still undetermined.

Hand hygiene

Research could focus on the effect of increased frequency and quality of hand washing on influenza virus transmission, aiming to identify the optimal threshold for advising guidelines. A comparison of various hand hygiene methods would be useful.

Respiratory hygiene and other PPEs

Data about the effectiveness of facemask use in the different settings are limited, and results are contradictory, highlighting the need for future studies. The efficacy of the different types of masks for reducing transmission and spread of influenza in the general community needs to be determined. Large, well-designed studies would also enable investigation of the role of facemask and respirator use specifically against laboratory confirmed influenza infections and clarify the circumstances under which individual PPE use is most warranted. The inclusion of relevant controls would be important [75]. There is lack of evidence on effectiveness of respiratory etiquette.

Environmental measures

Research could aid in understanding surface contamination issues and identifying situations in which surface cleaning should be emphasized. Research should focus on identifying the best practice guidelines (dosage, duration, frequency) and evaluate the different products. There are limited RCTs on the effect of surface and object cleaning on influenza prevention in the different settings. Novel techniques (e.g. far-UV-C light) for safe and effective surface and air disinfection for use in the different settings should be studied. Research should also focus on the efficacy of ventilation in reducing influenza transmission. The role of humidification still needs to be assessed.

Social distancing measures

Though there is evidence for the use of social distancing measures, research could focus on gathering data on social mixing patterns in schools and the various community settings. Studies should focus on the timing and duration of school closures and other social distancing and environmental measures in schools [290]. An important aspect is to provide evidence base for assessing societal and economic secondary effects of the measures for individuals, families and communities. Depending on the age of school children, there will be different consequences from school-closures that need to be determined. Most of the current evidence on effectiveness of voluntary isolation and voluntary quarantine practises originates from modelling studies; more robust experimental data should be produced. The role of asymptomatic infections and super-spreaders need to be clarified in relation to these measures.

Border control

Sensitive and specific novel screening tools for identifying infected travelers at international borders should be investigated. There are limited data on the possible differences in effectiveness of exit compared to entry screening.

Social behaviour, ethical and legal aspects

The public knowledge, perception and behavioral aspects related to the use of NPCs across the different populations need to be assessed, as is the role of cultural and demographic factors on NPC common practices, in relation to NPC effectiveness. Prospective studies could aid in the verification of behaviour and would enhance understanding of intervention effectiveness. Studies should focus on the role of social science research in establishing social, ethical and legal standards in the application of public health policy, and address the public perception of influenza and its impact on societies, particularly in under-resourced populations [289,290]. Research could focus on determining effective risk communication strategies for enhancing compliance and adherence to NPCs and the extent of barriers to NPC implementation [293].

References

1. Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet. 2017 Dec 14.
2. Guan Y, Vijaykrishna D, Bahl J, Zhu H, Wang J, Smith GJ. The emergence of pandemic influenza viruses. Protein Cell. 2010 Jan;1(1):9-13.
3. Henderson DA, Courtney B, Inglesby TV, Toner E, Nuzzo JB. Public health and medical responses to the 1957-58 influenza pandemic. Biosecur Bioterror. 2009 Sep;7(3):265-73.
4. Simonsen L, Spreeuwenberg P, Lustig R, Taylor RJ, Fleming DM, Kroneman M, et al. Global mortality estimates for the 2009 Influenza Pandemic from the GLaMOR project: a modeling study. PLoS Med. 2013 Nov;10(11):e1001558.
5. Breteler JK, Tam JS, Jit M, Ket JC, De Boer MR. Efficacy and effectiveness of seasonal and pandemic A (H1N1) 2009 influenza vaccines in low and middle income countries: a systematic review and meta-analysis. Vaccine. 2013 Oct 25;31(45):5168-77.
6. Demicheli V, Jefferson T, Ferroni E, Rivetti A, Di Pietrantonj C. Vaccines for preventing influenza in healthy adults. Cochrane Database Syst Rev. 2018 Feb 1;2:Cd001269.
7. Manzoli L, De Vito C, Salanti G, D'Addario M, Villari P, Ioannidis JP. Meta-analysis of the immunogenicity and tolerability of pandemic influenza A 2009 (H1N1) vaccines. PLoS One. 2011;6(9):e24384.
8. Yin JK, Chow MY, Khandaker G, King C, Richmond P, Heron L, et al. Impacts on influenza A(H1N1)pdm09 infection from cross-protection of seasonal trivalent influenza vaccines and A(H1N1)pdm09 vaccines: systematic review and meta-analyses. Vaccine. 2012 May 2;30(21):3209-22.
9. Saunders-Hastings PR, Krewski D. Reviewing the History of Pandemic Influenza: Understanding Patterns of Emergence and Transmission. Pathogens. 2016 Dec 6;5(4).
10. Lansbury LE, Smith S, Beyer W, Karamehic E, Pasic-Juhas E, Sikira H, et al. Effectiveness of 2009 pandemic influenza A(H1N1) vaccines: A systematic review and meta-analysis. Vaccine. 2017 Apr 11;35(16):1996-2006.
11. European Centre for Disease Prevention and Control(ECDC). Influenza vaccine effectiveness [cited 2018]. Available from: https://ecdc.europa.eu/en/seasonal-influenza/prevention-and-control/vaccine-effectiveness.
12. World Health Organisation(WHO). WHO recommendations on the composition of influenza virus vaccines. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/en/.
13. European Centre for Disease Prevention and Control(ECDC). Expert opinion on neuraminidase inhibitors for the prevention and treatment of influenza 2017. Available from: https://ecdc.europa.eu/sites/portal/files/documents/Scientific-advice-neuraminidase-inhibitors-2017.pdf.
14. Halloran ME, Hayden FG, Yang Y, 5.1.2e IM, Jr., Monto AS. Antiviral effects on influenza viral transmission and pathogenicity: observations from household-based trials. Am J Epidemiol. 2007 Jan 15;165(2):212-21.
15. European Centre for Disease Prevention and Control(ECDC). Public health use of influenza antivirals during influenza pandemics 2009. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/0907_GUI_Public_Health_use_of_Influenza_Antivirals_during_Influenza_Pandemic.pdf.
16. Kutter JS, Spronken M, Fraaij PL, Fouchier R, Herfst S. Transmission routes of respiratory viruses among humans. Current Opinion in Virology. 2018;28.
17. Killingley B, Nguyen-Van-Tam J. Routes of influenza transmission. Influenza Other Respir Viruses. 2013 Sep;7 Suppl 2:42-51.
18. Biggerstaff M, Cauchemez S, Reed C, Gambhir M, Finelli L. Estimates of the reproduction number for seasonal, pandemic, and zoonotic influenza: a systematic review of the literature. BMC Infect Dis. 2014 Sep 4;14:480.
19. Cowling BJ, Ip DK, Fang VJ, Suntarattiwong P, Olsen SJ, Levy J, et al. Aerosol transmission is an important mode of influenza A virus spread. Nat Commun. 2013;4:1935.
20. Bischoff WE, Swett K, Leng I, Peters TR. Exposure to influenza virus aerosols during routine patient care. J Infect Dis. 2013 Apr;207(7):1037-46.
21. Ip DK, Lau LL, Leung NH, Fang VJ, Chan KH, Chu DK, et al. Viral Shedding and Transmission Potential of Asymptomatic and Paucisymptomatic Influenza Virus Infections in the Community. Clin Infect Dis. 2017 Mar 15;64(6):736-42.
22. Ip DKM, Lau LLH, Chan KH, Fang VJ, Leung GM, Peiris MJS, et al. The Dynamic Relationship Between Clinical Symptomatology and Viral Shedding in Naturally Acquired Seasonal and Pandemic Influenza Virus Infections. Clin Infect Dis. 2016 Feb 15;62(4):431-7.

23. Thomas Y, Boquete-Suter P, Koch D, Pittet D, Kaiser L. Survival of influenza virus on human fingers. Clin Microbiol Infect. 2014 Jan;20(1):O58-64.
24. Centre for Disease Control and Prevention(CDC). Community Mitigation Guidelines to Prevent Pandemic Influenza – United States, 2017 2017. Available from: https://www.cdc.gov/media/dpk/cdc-24-7/preventing-pandemic-influenza/community-mitigation-guidelines-for-preventing-pandemic-flu.html.
25. Dorigatti I, Cauchemez S, Ferguson NM. Increased transmissibility explains the third wave of infection by the 2009 H1N1 pandemic virus in England. Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13422-7.
26. Kuo PC, Huang JH, Liu MD. Avian influenza risk perception and preventive behavior among traditional market workers and shoppers in Taiwan: practical implications for prevention. PLoS One. 2011;6(9):e24157.
27. Bean B, Moore BM, Sterner B, Peterson LR, Gerding DN, Balfour HH, Jr. Survival of influenza viruses on environmental surfaces. J Infect Dis. 1982 Jul;146(1):47-51.
28. Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. Lancet Infect Dis. 2007 Apr;7(4):257-65.
29. Bridges CB, Kuehnert MJ, Hall CB. Transmission of influenza: implications for control in health care settings. Clin Infect Dis. 2003 Oct 15;37(8):1094-101.
30. Poulson RL, Tompkins SM, Berghaus RD, Brown JD, Stallknecht DE. Environmental Stability of Swine and Human Pandemic Influenza Viruses in Water under Variable Conditions of Temperature, Salinity, and pH. Appl Environ Microbiol. 2016 Jul 1;82(13):3721-6.
31. Lowen A, Palese P. Transmission of influenza virus in temperate zones is predominantly by aerosol, in the tropics by contact: a hypothesis. PLoS Curr. 2009 Aug 17;1:Rrn1002.
32. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. Proc Natl Acad Sci U S A. 2009 Mar 3;106(9):3243-8.
33. World Health Organisation(WHO). Global Influenza Programme.
34. Cordova-Villalobos JA, Macias AE, Hernandez-Avila M, Dominguez-Cherit G, Lopez-Gatell H, Alpuche-Aranda C, et al. The 2009 pandemic in Mexico: Experience and lessons regarding national preparedness policies for seasonal and epidemic influenza. Gac Med Mex. 2017 Jan-Feb;153(1):102-10.
35. Nguyen-Van-Tam JS, Sellwood C. Intervention strategies for emerging respiratory virus infections: policy and public health considerations. Curr Opin Virol. 2013 Apr;3(2):192-8.
36. Mizumoto K, 5.1.2e, Yamamoto T. Effectiveness of antiviral prophylaxis coupled with contact tracing in reducing the transmission of the influenza A (H1N1-2009): a systematic review. Theor Biol Med Model. 2013 Jan 16;10:4.
37. Pan-Canadian Public Health Sector. Canadian pandemic influenza preparedness: Planning Guidance for the Health Sector. 2015.
38. Enanoria WT, Crawley AW, Tseng W, Furnish J, Balido J, Aragon TJ. The epidemiology and surveillance response to pandemic influenza A (H1N1) among local health departments in the San Francisco Bay Area. BMC Public Health. 2013 Mar 27;13:276.
39. Holloway R, Rasmussen SA, Zaza S, Cox NJ, Jernigan DB. Updated preparedness and response framework for influenza pandemics. MMWR Recomm Rep. 2014 Sep 26;63(Rr-06):1-18.
40. World Health Organisation(WHO). WHO guidance for surveillance during an influenza pandemic. 2017.
41. Aledort JE, Lurie N, Wasserman J, Bozzette SA. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. BMC Public Health. 2007 Aug 15;7:208.
42. European Centre for Disease Prevention and Control(ECDC). Risk assessment guidelines for diseases transmitted on aircraft(RAGIDA) 2010. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/1012_GUI_RAGIDA_2.pdf.
43. Control(ECDC) ECfDPa. Risk assessment guidelines for infectious diseases transmitted on aircraft (RAGIDA) - Influenza. 2014.
44. Huizer YL, Swaan CM, Leitmeyer KC, 5.1.2e. Usefulness and applicability of infectious disease control measures in air travel: a review. Travel Med Infect Dis. 2015 Jan-Feb;13(1):19-30.
45. Browne A, Ahmad SS, Beck CR, Nguyen-Van-Tam JS. The roles of transportation and transportation hubs in the propagation of influenza and coronaviruses: a systematic review. J Travel Med. 2016 Jan;23(1).
46. Weber DJ, Rutala WA, Fischer WA, Kanamori H, Sickbert-Bennett EE. Emerging infectious diseases: Focus on infection control issues for novel coronaviruses (Severe Acute Respiratory Syndrome-CoV and Middle East Respiratory Syndrome-CoV), hemorrhagic fever viruses (Lassa and Ebola), and highly pathogenic avian influenza viruses, A(H5N1) and A(H7N9). Am J Infect Control. 2016 May 2;44(5 Suppl):e91-e100.
47. World Health Organisation(WHO). Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care 2014. Available from: https://ecdcevtclu.ecdcnet.europa.eu/EnterpriseVault/Search/htmlview.aspx?VaultId=1A6178B738C995E42A4F12A94C54AE3771110000ecdcevtclu&SavesetId=201808224954187~20180518154228000~Z~A102A926DB0E9339A9FBDB1204A7EDD1&AttachmentId=1.
48. World Health Organisation(WHO). Recommended composition of influenza virus vaccines for use in the 2019-2020 northern hemisphere influenza season. 2019.
49. World Health Organisation(WHO). Hospital preparedness checklist for pandemic influenza. 2009.
50. Ministry of Health Singapore. MOH pandemic readiness and response plan for influenza and other acute respiratory diseases. 2014.

51. World Health Organisation(WHO). WHO global influenza preparedness plan 2005. Available from: http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5.pdf.
52. World Health Organisation(WHO). WHO Global Influenza Preparedness Plan. 2005 Annex One Recommendations for non-pharmaceutical public health measures (p42-46) 2005. Available from: http://www.who.indae34t/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5.pdf.
53. World Health Organisation(WHO). Pandemic influenza preparedness and response. WHO guidance document April 2009 2009. Available from: http://www.who.int/csr/disease/influenza/pipguidance2009/en/index.html.
54. World Health Organisation(WHO). Prevention and control of outbreaks of seasonal influenza in long-term care facilities: a review of the evidence and best-practice guidance 2017. Available from: http://www.euro.who.int/__data/assets/pdf_file/0015/330225/LTCF-best-practice-guidance.pdf.
55. Lansbury LE, Brown CS, Nguyen-Van-Tam JS. Influenza in long-term care facilities. Influenza Other Respir Viruses. 2017 Sep;11(5):356-66.
56. World Health Organisation(WHO). WHO guidance for surveillance during an influenza pandemic. 2017.
57. World Health Organisation(WHO). A checklist for pandemic influenza risk and impact management: building capacity for pandemic response. 2018.
58. European Centre for Disease Prevention and Control(ECDC). Guide to public health measures to reduce the impact of influenza pandemics in Europe: 'The ECDC Menu' 2009. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/0906_TER_Public_Health_Measures_for_Influenza_Pandemics.pdf.
59. European Centre for Disease Prevention and Control(ECDC). Personal protective measures (non-pharmaceutical) for reducing the risk of acquiring or transmitting human influenza. Available from: https://ecdc.europa.eu/en/seasonal-influenza/prevention-and-control/personal-protective-measures.
60. Public Health England. Pandemic Influenza Response Plan. 2014.
61. National Health Service UK. Health and Social Care Influenza Pandemic Preparedness and Response 2012. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213696/dh_133656.pdf.
62. UK Department of Health. UK influenza pandemic preparedness strategy 2011 2011. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/215666/dh_125333.pdf.
63. Robert Koch Institut. Nationaler Pandemieplan Teil II 2016. Available from: https://www.rki.de/DE/Content/InfAZ/I/Influenza/Pandemieplanung/Downloads/Pandemieplan_Teil_II_gesamt.pdf?__blob=publicationFile.
64. Ministry of Health Singapore. MOH pandemic readiness and response plan for influenza and other acute respiratory diseases. 2014. Available from: https://www.moh.gov.sg/content/dam/moh_web/Diseases%20and%20Conditions/DORSCON%202013/Interim%20Pandemic%20Plan%20Public%20Ver%20_April%202014.pdf.
65. Government of New Zealand. New Zealand influenza pandemic plan: a framework for action. 2017. Available from: https://www.health.govt.nz/publication/new-zealand-influenza-pandemic-plan-framework-action.
66. Australian government Department of Health. Australian Health Management Plan for Pandemic Influenza. 2014.
67. Royal Australian College of General Practitioners. Infection prevention and control standards for general practices and other office-based and community-based practices (5th edition) 2014. Available from: https://www.dermcoll.edu.au/wp-content/uploads/RACGP-Infection-Prevention-and-Control-Standards.pdf.
68. Lee VJ, Lye DC, Wilder-Smith A. Combination strategies for pandemic influenza response - a systematic review of mathematical modeling studies. BMC Med. 2009 Dec 10;7:76.
69. Teasdale E, Santer M, Geraghty AW, Little P, Yardley L. Public perceptions of non-pharmaceutical interventions for reducing transmission of respiratory infection: systematic review and synthesis of qualitative studies. BMC Public Health. 2014 Jun 11;14:589.
70. Mao L. Evaluating the combined effectiveness of influenza control strategies and human preventive behavior. PLoS One. 2011;6(10):e24706.
71. Tooher R, Collins JE, Street JM, Braunack-Mayer A, Marshall H. Community knowledge, behaviours and attitudes about the 2009 H1N1 Influenza pandemic: a systematic review. Influenza Other Respir Viruses. 2013 Nov;7(6):1316-27.
72. Sim SW, Moey KS, Tan NC. The use of facemasks to prevent respiratory infection: a literature review in the context of the Health Belief Model. Singapore Med J. 2014 Mar;55(3):160-7.
73. Saunders-Hastings P, Crispo JAG, Sikora L, Krewski D. Effectiveness of personal protective measures in reducing pandemic influenza transmission: A systematic review and meta-analysis. Epidemics. 2017 Sep;20:1-20.
74. Qualls N, Levitt A, Kanade N, Wright-Jegede N, Dopson S, Biggerstaff M, et al. Community Mitigation Guidelines to Prevent Pandemic Influenza - United States, 2017. MMWR Recomm Rep. 2017 Apr 21;66(1):1-34.
75. Offeddu V, Yung CF, Low MSF, Tam CC. Effectiveness of Masks and Respirators Against Respiratory Infections in Healthcare Workers: A Systematic Review and Meta-Analysis. Clin Infect Dis. 2017 Nov 13;65(11):1934-42.

76. Moghadas SM, Haworth-Brockman M, Isfeld-Kiely H, Kettner J. Improving public health policy through infection transmission modelling: Guidelines for creating a Community of Practice. Can J Infect Dis Med Microbiol. 2015 Jul-Aug;26(4):191-5.
77. Mateus AL, Otete HE, Beck CR, Dolan GP, Nguyen-Van-Tam JS. Effectiveness of travel restrictions in the rapid containment of human influenza: a systematic review. Bull World Health Organ. 2014 Dec 1;92(12):868-80d.
78. Kilinc FS. A Review of Isolation Gowns in Healthcare: Fabric and Gown Properties. J Eng Fiber Fabr. 2015 Sep;10(3):180-90.
79. Godoy P, Castilla J, Delgado-Rodriguez M, Martin V, Soldevila N, Alonso J, et al. Effectiveness of hand hygiene and provision of information in preventing influenza cases requiring hospitalization. Prev Med. 2012 Jun;54(6):434-9.
80. Gautret P, Steffen R. Communicable diseases as health risks at mass gatherings other than Hajj: what is the evidence? Int J Infect Dis. 2016 Jun;47:46-52.
81. Fumanelli L, Ajelli M, Merler S, Ferguson NM, Cauchemez S. Model-Based Comprehensive Analysis of School Closure Policies for Mitigating Influenza Epidemics and Pandemics. PLoS Comput Biol. 2016 Jan;12(1):e1004681.
82. Zayas G, Chiang MC, Wong E, MacDonald F, Lange CF, Senthilselvan A, et al. Effectiveness of cough etiquette maneuvers in disrupting the chain of transmission of infectious respiratory diseases. BMC Public Health. 2013 Sep 8;13:811.
83. Wong VW, Cowling BJ, Aiello AE. Hand hygiene and risk of influenza virus infections in the community: a systematic review and meta-analysis. Epidemiol Infect. 2014 May;142(5):922-32.
84. Talaat M, Afifi S, Dueger E, El-Ashry N, Marfin A, Kandeel A, et al. Effects of hand hygiene campaigns on incidence of laboratory-confirmed influenza and absenteeism in schoolchildren, Cairo, Egypt. Emerg Infect Dis. 2011 Apr;17(4):619-25.
85. Suess T, Remschmidt C, Schink SB, Schweiger B, Nitsche A, Schroeder K, et al. The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009-2011. BMC Infect Dis. 2012 Jan 26;12:26.
86. Smith SM, Sonego S, Wallen GR, Waterer G, Cheng AC, Thompson P. Use of non-pharmaceutical interventions to reduce the transmission of influenza in adults: A systematic review. Respirology. 2015 Aug;20(6):896-903.
87. Smith JD, MacDougall CC, Johnstone J, Copes RA, Schwartz B, Garber GE. Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. Cmaj. 2016 May 17;188(8):567-74.
88. World Health Organisation(WHO). Pandemic influenza risk management: WHO interim guidance. 2013.
89. World Health Organisation(WHO). Pandemic influenza risk management. 2017.
90. World Health Organisation(WHO). WHO Guidelines on Hand Hygiene in Health Care 2009. Available from: http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf.
91. Centre for Disease Control and Prevention(CDC). Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States 2007. Available from: https://www.cdc.gov/flu/pandemic-resources/pdf/community_mitigation-sm.pdf.
92. Cox NJ, Tamblyn SE, Tam T. Influenza pandemic planning. Vaccine. 2003 May 1;21(16):1801-3.
93. Kilbourne ED. Influenza pandemics of the 20th century. Emerg Infect Dis. 2006 Jan;12(1):9-14.
94. Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic. Jama. 2007 Aug 8;298(6):644-54.
95. Rashid H, Ridda I, King C, Begun M, Tekin H, Wood JG, et al. Evidence compendium and advice on social distancing and other related measures for response to an influenza pandemic. Paediatr Respir Rev. 2015 Mar;16(2):119-26.
96. Aiello AE, Coulborn RM, Aragon TJ, Baker MG, Burrus BB, Cowling BJ, et al. Research findings from nonpharmaceutical intervention studies for pandemic influenza and current gaps in the research. Am J Infect Control. 2010 May;38(4):251-8.
97. van der Weerd W, Timmermans DR, Beaujean DJ, Oudhoff J, van Steenbergen JE. Monitoring the level of government trust, risk perception and intention of the general public to adopt protective measures during the influenza A (H1N1) pandemic in The Netherlands. BMC Public Health. 2011 Jul 19;11:575.
98. Barrios LC, Koonin LM, Kohl KS, Cetron M. Selecting nonpharmaceutical strategies to minimize influenza spread: the 2009 influenza A (H1N1) pandemic and beyond. Public Health Rep. 2012 Nov-Dec;127(6):565-71.
99. Aiello AE, Murray GF, Perez V, Coulborn RM, Davis BM, Uddin M, et al. Mask use, hand hygiene, and seasonal influenza-like illness among young adults: a randomized intervention trial. J Infect Dis. 2010 Feb 15;201(4):491-8.
100. Bell D, Nicoll A, Fukuda K, Horby P, Monto A, Hayden F, et al. Non-pharmaceutical interventions for pandemic influenza, national and community measures. Emerg Infect Dis. 2006 Jan;12(1):88-94.
101. Canini L, Andreoletti L, Ferrari P, D'Angelo R, Blanchon T, Lemaitre M, et al. Surgical mask to prevent influenza transmission in households: a cluster randomized trial. PLoS One. 2010 Nov 17;5(11):e13998.
102. MacIntyre CR, Cauchemez S, Dwyer DE, Seale H, Cheung P, Browne G, et al. Face mask use and control of respiratory virus transmission in households. Emerg Infect Dis. 2009 Feb;15(2):233-41.

103. Cowling BJ, Chan KH, Fang VJ, Cheng CK, Fung RO, Wai W, et al. Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. Ann Intern Med. 2009 Oct 6;151(7):437-46.
104. Roberts L, Smith W, Jorm L, Patel M, Douglas RM, McGilchrist C. Effect of infection control measures on the frequency of upper respiratory infection in child care: a randomized, controlled trial. Pediatrics. 2000 Apr;105(4 Pt 1):738-42.
105. Ryan MA, Christian RS, Wohlrabe J. Handwashing and respiratory illness among young adults in military training. Am J Prev Med. 2001 Aug;21(2):79-83.
106. Bell D, Nicoll A, Fukuda K, Horby P, Monto A, Hayden F, et al. Non-pharmaceutical interventions for pandemic influenza, international measures. Emerg Infect Dis. 2006 Jan;12(1):81-7.
107. Institute of Medicine Forum on Microbial T. The National Academies Collection: Reports funded by National Institutes of Health. The Domestic and International Impacts of the 2009-H1N1 Influenza A Pandemic: Global Challenges, Global Solutions: Workshop Summary. Washington (DC): National Academies Press (US) National Academy of Sciences.; 2010.
108. Nicoll A. Personal (non-pharmaceutical) protective measures for reducing transmission of influenza--ECDC interim recommendations. Euro Surveill. 2006 Oct 12;11(10):E061012.1.
109. Rabie T, Curtis V. Handwashing and risk of respiratory infections: a quantitative systematic review. Trop Med Int Health. 2006 Mar;11(3):258-67.
110. Azor-Martinez E, Gonzalez-Jimenez Y, Seijas-Vazquez ML, Cobos-Carrascosa E, Santisteban-Martinez J, Martinez-Lopez JM, et al. The impact of common infections on school absenteeism during an academic year. Am J Infect Control. 2014 Jun;42(6):632-7.
111. Torner N, Soldevila N, Garcia JJ, Launes C, Godoy P, Castilla J, et al. Effectiveness of non-pharmaceutical measures in preventing pediatric influenza: a case-control study. BMC Public Health. 2015 Jun 9;15:543.
112. Cheng VC, Tai JW, Wong LM, Chan JF, Li IW, To KK, et al. Prevention of nosocomial transmission of swine-origin pandemic influenza virus A/H1N1 by infection control bundle. J Hosp Infect. 2010 Mar;74(3):271-7.
113. Kuster SP, Coleman BL, Raboud J, McNeil S, De Serres G, Gubbay J, et al. Risk factors for influenza among health care workers during 2009 pandemic, Toronto, Ontario, Canada. Emerg Infect Dis. 2013 Apr;19(4):606-15.
114. Deng Y, Zhang Y, Wang XL, Liu WT, Duan W, Yang P, et al. [Pandemic influenza A (H1N1) virus infection factors among healthcare workers - a case-control study]. Zhonghua Yu Fang Yi Xue Za Zhi. 2010 Dec;44(12):1075-8.
115. Zhang Y, Seale H, Yang P, MacIntyre CR, Blackwell B, Tang S, et al. Factors associated with the transmission of pandemic (H1N1) 2009 among hospital healthcare workers in Beijing, China. Influenza Other Respir Viruses. 2013 May;7(3):466-71.
116. Levy JW, Suntarattiwong P, Simmerman JM, Jarman RG, Johnson K, Olsen SJ, et al. Increased hand washing reduces influenza virus surface contamination in Bangkok households, 2009-2010. Influenza Other Respir Viruses. 2014 Jan;8(1):13-6.
117. Grayson ML, Melvani S, Druce J, Barr IG, Ballard SA, Johnson PD, et al. Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers. Clin Infect Dis. 2009 Feb 1;48(3):285-91.
118. Carlson AL, Budd AP, Perl TM. Control of influenza in healthcare settings: early lessons from the 2009 pandemic. Curr Opin Infect Dis. 2010 Aug;23(4):293-9.
119. Willmott M, Nicholson A, Busse H, MacArthur GJ, Brookes S, Campbell R. Effectiveness of hand hygiene interventions in reducing illness absence among children in educational settings: a systematic review and meta-analysis. Arch Dis Child. 2016 Jan;101(1):42-50.
120. Hansen S, Zimmerman PA, van de Mortel TF. Infectious illness prevention and control methods and their effectiveness in non-health workplaces: an integrated literature review. J Infect Prev. 2018 Sep;19(5):212-8.
121. Lee BY, Shah M. Prevention of influenza in healthy children. Expert Rev Anti Infect Ther. 2012 Oct;10(10):1139-52.
122. Warren-Gash C, Fragaszy E, Hayward AC. Hand hygiene to reduce community transmission of influenza and acute respiratory tract infection: a systematic review. Influenza Other Respir Viruses. 2013 Sep;7(5):738-49.
123. Hocine MN, Temime L. Impact of hand hygiene on the infectious risk in nursing home residents: A systematic review. Am J Infect Control. 2015 Sep 1;43(9):e47-52.
124. Zivich PN, Gancz AS, Aiello AE. Effect of hand hygiene on infectious diseases in the office workplace: A systematic review. Am J Infect Control. 2018 Apr;46(4):448-55.
125. Mbakaya BC, Lee PH, Lee RL. Hand Hygiene Intervention Strategies to Reduce Diarrhoea and Respiratory Infections among Schoolchildren in Developing Countries: A Systematic Review. Int J Environ Res Public Health. 2017 Apr 1;14(4).
126. McCloskey B, Dar O, Zumla A, Heymann DL. Emerging infectious diseases and pandemic potential: status quo and reducing risk of global spread. Lancet Infect Dis. 2014 Oct;14(10):1001-10.
127. Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev. 2010 Jan 20(1):Cd006207.
128. Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev. 2011 Jul 6(7):Cd006207.

129. Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. Bmj. 2009 Sep 21;339:b3675.
130. McGuinness SL, Barker SF, O'Toole J, Cheng AC, Forbes AB, Sinclair M, et al. Effect of hygiene interventions on acute respiratory infections in childcare, school and domestic settings in low- and middle-income countries: a systematic review. Trop Med Int Health. 2018 Aug;23(8):816-33.
131. Ajelli M, Poletti P, Melegaro A, Merler S. The role of different social contexts in shaping influenza transmission during the 2009 pandemic. Sci Rep. 2014 Nov 27;4:7218.
132. Widmer AF. Surgical hand hygiene: scrub or rub? J Hosp Infect. 2013 Feb;83 Suppl 1:S35-9.
133. Stebbins S, Cummings DA, Stark JH, Vukotich C, Mitruka K, Thompson W, et al. Reduction in the incidence of influenza A but not influenza B associated with use of hand sanitizer and cough hygiene in schools: a randomized controlled trial. Pediatr Infect Dis J. 2011 Nov;30(11):921-6.
134. World Health Organisation(WHO), Unicef. Behavioural interventions for reducing the transmission and impact of influenza A(H1N1) virus: a framework for communication strategies. 2009. Available from: http://www.who.int/csr/resources/publications/swineflu/framework/en/.
135. Price L, Melone L, McLarnon N, Bunyan D, Kilpatrick C, Flowers P, et al. A systematic review to evaluate the evidence base for the World Health Organization's adopted hand hygiene technique for reducing the microbial load on the hands of healthcare workers. Am J Infect Control. 2018 Jul;46(7):814-23.
136. Kingston L, O'Connell NH, Dunne CP. Hand hygiene-related clinical trials reported since 2010: a systematic review. J Hosp Infect. 2016 Apr;92(4):309-20.
137. Huis A, van Achterberg T, de Bruin M, Grol R, Schoonhoven L, Hulscher M. A systematic review of hand hygiene improvement strategies: a behavioural approach. Implement Sci. 2012 Sep 14;7:92.
138. Cookson B, Mathai E, Allegranzi B, Pessoa-Silva CL, Bagheri Nejad S, Schneider A, et al. Comparison of national and subnational guidelines for hand hygiene. J Hosp Infect. 2009 Jul;72(3):202-10.
139. Pittet D, Allegranzi B, Boyce J. The World Health Organization Guidelines on Hand Hygiene in Health Care and their consensus recommendations. Infect Control Hosp Epidemiol. 2009 Jul;30(7):611-22.
140. Lau CH, Springston EE, Sohn MW, Mason I, Gadola E, Damitz M, et al. Hand hygiene instruction decreases illness-related absenteeism in elementary schools: a prospective cohort study. BMC Pediatr. 2012 May 15;12:52.
141. Stanley WM. The size of influenza virus. J Exp Med. 1944 Mar 1;79(3):267-83.
142. Kumar V. Influenza in Children. Indian J Pediatr. 2017 Feb;84(2):139-43.
143. Brouqui P, Puro V, Fusco FM, Bannister B, Schilling S, Follin P, et al. Infection control in the management of highly pathogenic infectious diseases: consensus of the European Network of Infectious Disease. Lancet Infect Dis. 2009 May;9(5):301-11.
144. Collignon PJ, Carnie JA. Infection control and pandemic influenza. Med J Aust. 2006 Nov 20;185(10 Suppl):S54-7.
145. Sebastian MR, Lodha R, Kabra SK. Swine origin influenza (swine flu). Indian J Pediatr. 2009 Aug;76(8):833-41.
146. Rathore MH, Jackson MA. Infection Prevention and Control in Pediatric Ambulatory Settings. Pediatrics. 2017 Nov;140(5).
147. Bartlett JG, Borio L. Healthcare epidemiology: the current status of planning for pandemic influenza and implications for health care planning in the United States. Clin Infect Dis. 2008 Mar 15;46(6):919-25.
148. Narain JP, Kumar R, Bhatia R. Pandemic (H1N1) 2009: epidemiological, clinical and prevention aspects. Natl Med J India. 2009 Sep-Oct;22(5):242-7.
149. Coia JE, Ritchie L, Adisesh A, Makison Booth C, Bradley C, Bunyan D, et al. Guidance on the use of respiratory and facial protection equipment. J Hosp Infect. 2013 Nov;85(3):170-82.
150. European Committee for Standardization. Respiratory protective devices - Filtering half masks to protect against particles - Requirements, testing, marking 2009. Available from: https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:32928&cs=1B0AB06FEB70E43960D46D1198C37CC09.
151. Johnson DF, Druce JD, Birch C, Grayson ML. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. Clin Infect Dis. 2009 Jul 15;49(2):275-7.
152. MacIntyre CR, Chughtai AA. Facemasks for the prevention of infection in healthcare and community settings. Bmj. 2015 Apr 9;350:h694.
153. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Lancet. 2003 May 24;361(9371):1761-6.
154. Barasheed O, Alfelali M, Mushta S, Bokhary H, Alshehri J, Attar AA, et al. Uptake and effectiveness of facemask against respiratory infections at mass gatherings: a systematic review. Int J Infect Dis. 2016 Jun;47:105-11.
155. Benkouiten S, Brouqui P, Gautret P. Non-pharmaceutical interventions for the prevention of respiratory tract infections during Hajj pilgrimage. Travel Med Infect Dis. 2014 Sep-Oct;12(5):429-42.
156. Cowling BJ, Zhou Y, Ip DK, Leung GM, Aiello AE. Face masks to prevent transmission of influenza virus: a systematic review. Epidemiol Infect. 2010 Apr;138(4):449-56.
157. Bunyan D, Ritchie L, Jenkins D, Coia JE. Respiratory and facial protection: a critical review of recent literature. J Hosp Infect. 2013 Nov;85(3):165-9.

158. Maltezou HC. Novel (pandemic) influenza A H1N1 in healthcare facilities: implications for prevention and control. Scand J Infect Dis. 2010 Jul;42(6-7):412-20.
159. Gralton J, McLaws ML. Protecting healthcare workers from pandemic influenza: N95 or surgical masks? Crit Care Med. 2010 Feb;38(2):657-67.
160. Seale H, Dwyer DE, Cowling BJ, Wang Q, Yang P, Macintyre CR. A review of medical masks and respirators for use during an influenza pandemic. Influenza Other Respir Viruses. 2009 Sep;3(5):205-6.
161. Schuchat A, Bell BP, Redd SC. The science behind preparing and responding to pandemic influenza: the lessons and limits of science. Clin Infect Dis. 2011 Jan 1;52 Suppl 1:S8-12.
162. Toyokawa T, Sunagawa T, Yahata Y, Ohyama T, Kodama T, Satoh H, et al. Seroprevalence of antibodies to pandemic (H1N1) 2009 influenza virus among health care workers in two general hospitals after first outbreak in Kobe, Japan. J Infect. 2011 Oct;63(4):281-7.
163. Wei J, Li Y. Airborne spread of infectious agents in the indoor environment. Am J Infect Control. 2016 Sep 2;44(9 Suppl):S102-8.
164. Cowling BJ, Fung RO, Cheng CK, Fang VJ, Chan KH, Seto WH, et al. Preliminary findings of a randomized trial of non-pharmaceutical interventions to prevent influenza transmission in households. PLoS One. 2008 May 7;3(5):e2101.
165. Bin-Reza F, Lopez Chavarrias V, Nicoll A, Chamberland ME. The use of masks and respirators to prevent transmission of influenza: a systematic review of the scientific evidence. Influenza Other Respir Viruses. 2012 Jul;6(4):257-67.
166. Cummings KJ, Cox-Ganser J, Riggs MA, Edwards N, Kreiss K. Respirator donning in post-hurricane New Orleans. Emerg Infect Dis. 2007 May;13(5):700-7.
167. World Health Organisation(WHO). Advice on the use of masks in the community setting in Influenza A (H1N1) outbreaks 2009. Available from: http://www.who.int/csr/resources/publications/Adviceusemaskscommunityrevised.pdf.
168. Chao YS, Spry C. CADTH Rapid Response Reports. The Use of N95 Respirators for Protection against Droplet Borne Illness: A Review of the Clinical Effectiveness and Guidelines. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health
Copyright (c) 2017 Canadian Agency for Drugs and Technologies in Health.; 2017.
169. Seto WH. Airborne transmission and precautions: facts and myths. J Hosp Infect. 2015 Apr;89(4):225-8.
170. CADTH Rapid Response Reports. Respiratory Precautions for Protection from Bioaerosols or Infectious Agents: A Review of the Clinical Effectiveness and Guidelines. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health
Copyright (c) 2014 Canadian Agency for Drugs and Technologies in Health.; 2014.
171. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. PLoS One. 2012;7(4):e35797.
172. Mukerji S, MacIntyre CR, Newall AT. Review of economic evaluations of mask and respirator use for protection against respiratory infection transmission. BMC Infect Dis. 2015 Oct 13;15:413.
173. Health Protection Agency(HPA). The use of facemasks during an influenza pandemic 2007. Available from: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_077781.pdf.
174. Roberge R. Facemask use by children during infectious disease outbreaks. Biosecur Bioterror. 2011 Sep;9(3):225-31.
175. Haworth E, Barasheed O, Memish ZA, Rashid H, Booy R. Prevention of influenza at Hajj: applications for mass gatherings. J R Soc Med. 2013 Jun;106(6):215-23.
176. Al-Tawfiq JA, Zumla A, Memish ZA. Respiratory tract infections during the annual Hajj: potential risks and mitigation strategies. Curr Opin Pulm Med. 2013 May;19(3):192-7.
177. Thompson KA, Pappachan JV, Bennett AM, Mittal H, Macken S, Dove BK, et al. Influenza aerosols in UK hospitals during the H1N1 (2009) pandemic--the risk of aerosol generation during medical procedures. PLoS One. 2013;8(2):e56278.
178. Weber DJ, Rutala WA, Schaffner W. Lessons learned: protection of healthcare workers from infectious disease risks. Crit Care Med. 2010 Aug;38(8 Suppl):S306-14.
179. Rainwater-Lovett K, Chun K, Lessler J. Influenza outbreak control practices and the effectiveness of interventions in long-term care facilities: a systematic review. Influenza Other Respir Viruses. 2014 Jan;8(1):74-82.
180. Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. J Hosp Infect. 2016 Mar;92(3):235-50.
181. World Health Organisation(WHO). Natural Ventilation for Infection Control in Health-Care Settings 2009. Available from: http://www.who.int/water_sanitation_health/publications/natural_ventilation.pdf.
182. Weber TP, Stilianakis NI. Inactivation of influenza A viruses in the environment and modes of transmission: a critical review. J Infect. 2008 Nov;57(5):361-73.
183. Oxford J, Berezin EN, Courvalin P, Dwyer DE, Exner M, Jana LA, et al. The survival of influenza A(H1N1)pdm09 virus on 4 household surfaces. Am J Infect Control. 2014 Apr;42(4):423-5.
184. Boone SA, Gerba CP. The occurrence of influenza A virus on household and day care center fomites. J Infect. 2005 Aug;51(2):103-9.

185. Scott E. Community-based infections and the potential role of common touch surfaces as vectors for the transmission of infectious agents in home and community settings. Am J Infect Control. 2013 Nov;41(11):1087-92.
186. Thompson KA, Bennett AM. Persistence of influenza on surfaces. J Hosp Infect. 2017 Feb;95(2):194-9.
187. Patnayak DP, Prasad AM, Malik YS, Ramakrishnan MA, Goyal SM. Efficacy of disinfectants and hand sanitizers against avian respiratory viruses. Avian Dis. 2008 Jun;52(2):199-202.
188. Serra ME. Prevention of respiratory infections at day care centers: recommendations and systematic review of the evidence. Arch Argent Pediatr. 2014 Aug;112(4):323-31.
189. Weber DJ, Anderson D, Rutala WA. The role of the surface environment in healthcare-associated infections. Curr Opin Infect Dis. 2013 Aug;26(4):338-44.
190. Rutala WA, Weber DJ. Disinfectants used for environmental disinfection and new room decontamination technology. Am J Infect Control. 2013 May;41(5 Suppl):S36-41.
191. Jeong EK, Bae JE, Kim IS. Inactivation of influenza A virus H1N1 by disinfection process. Am J Infect Control. 2010 Jun;38(5):354-60.
192. Goyal SM, Chander Y, Yezli S, Otter JA. Evaluating the virucidal efficacy of hydrogen peroxide vapour. J Hosp Infect. 2014 Apr;86(4):255-9.
193. Thomas RE. Do we have enough evidence how seasonal influenza is transmitted and can be prevented in hospitals to implement a comprehensive policy? Vaccine. 2016 Jun 8;34(27):3014-21.
194. Rudnick SN, McDevitt JJ, First MW, Spengler JD. Inactivating influenza viruses on surfaces using hydrogen peroxide or triethylene glycol at low vapor concentrations. Am J Infect Control. 2009 Dec;37(10):813-9.
195. Klaus J, Gnirs P, Holterhoff S, Wirtz A, Jeglitza M, Gaber W, et al. Disinfection of aircraft : Appropriate disinfectants and standard operating procedures for highly infectious diseases. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2016 Dec;59(12):1544-8.
196. Zeitler B, Rapp I. Surface-Dried Viruses Can Resist Glucoprotamin-Based Disinfection. Appl Environ Microbiol. 2014 Dec;80(23):7169-75.
197. Weber DJ, Rutala WA. Self-disinfecting surfaces: review of current methodologies and future prospects. Am J Infect Control. 2013 May;41(5 Suppl):S31-5.
198. O'Gorman J, Humphreys H. Application of copper to prevent and control infection. Where are we now? J Hosp Infect. 2012 Aug;81(4):217-23.
199. Vincent M, Hartemann P, Engels-Deutsch M. Antimicrobial applications of copper. Int J Hyg Environ Health. 2016 Oct;219(7 Pt A):585-91.
200. Cook N, Knight A, Richards GP. Persistence and Elimination of Human Norovirus in Food and on Food Contact Surfaces: A Critical Review. J Food Prot. 2016 Jul;79(7):1273-94.
201. Muller MP, MacDougall C, Lim M. Antimicrobial surfaces to prevent healthcare-associated infections: a systematic review. J Hosp Infect. 2016 Jan;92(1):7-13.
202. Grass G, Rensing C, Solioz M. Metallic copper as an antimicrobial surface. Appl Environ Microbiol. 2011 Mar;77(5):1541-7.
203. Villapun VM, Dover LG, Cross A, Gonzalez S. Antibacterial Metallic Touch Surfaces. Materials (Basel). 2016 Aug 29;9(9).
204. Qian H, Zheng X. Ventilation control for airborne transmission of human exhaled bio-aerosols in buildings. J Thorac Dis. 2018 Jul;10(Suppl 19):S2295-s304.
205. Rajakaruna SJ, Liu WB, Ding YB, Cao GW. Strategy and technology to prevent hospital-acquired infections: Lessons from SARS, Ebola, and MERS in Asia and West Africa. Mil Med Res. 2017 Oct 27;4(1):32.
206. Institute RK. Tipps und Informationen zur Neuen Grippe A/H1N1, Robert Koch Institute, 2009, GrippeWeb 2009. Available from: https://grippeweb.rki.de/.
207. Hobday RA, Dancer SJ. Roles of sunlight and natural ventilation for controlling infection: historical and current perspectives. J Hosp Infect. 2013 Aug;84(4):271-82.
208. Hobday RA, Cason JW. The open-air treatment of pandemic influenza. Am J Public Health. 2009 Oct;99 Suppl 2:S236-42.
209. Lidal IB, Berg RC, Austvoll-Dahlgren A, Hval Straumann G, Vist GE. NIPH Systematic Reviews: Executive Summaries. Infection Control in Day-Care Facilities: Effect of Handhygiene, Training and Physical Interventions. Oslo, Norway: Knowledge Centre for the Health Services at The Norwegian Institute of Public Health (NIPH) Copyright (c)2015 by The Norwegian Institute of Public Health (NIPH). 2015.
210. Welch D, Buonanno M, Grilj V, Shuryak I, Crickmore C, Bigelow AW, et al. Far-UVC light: A new tool to control the spread of airborne-mediated microbial diseases. Sci Rep. 2018 Feb 9;8(1):2752.
211. Maclean M, McKenzie K, Anderson JG, Gettinby G, MacGregor SJ. 405 nm light technology for the inactivation of pathogens and its potential role for environmental disinfection and infection control. J Hosp Infect. 2014 Sep;88(1):1-11.
212. Boyce JM. Modern technologies for improving cleaning and disinfection of environmental surfaces in hospitals. Antimicrob Resist Infect Control. 2016;5:10.
213. Reiman JM, Das B. Humidity as a non-pharmaceutical intervention for influenza A. 2018;13(9):e0204337.
214. Han JH, Sullivan N, Leas BF, Pegues DA, Kaczmarek JL, Umscheid CA. Cleaning Hospital Room Surfaces to Prevent Health Care-Associated Infections: A Technical Brief. Ann Intern Med. 2015 Oct 20;163(8):598-607.

215. Perez Velasco R, Praditsitthikorn N, Wichmann K, Mohara A, Kotirum S, Tantivess S, et al. Systematic review of economic evaluations of preparedness strategies and interventions against influenza pandemics. PLoS One. 2012;7(2):e30333.
216. Borse RH, Behravesh CB, Dumanovsky T, Zucker JR, Swerdlow D, Edelson P, et al. Closing schools in response to the 2009 pandemic influenza A H1N1 virus in New York City: economic impact on households. Clin Infect Dis. 2011 Jan 1;52 Suppl 1:S168-72.
217. Jackson C, Vynnycky E, Hawker J, Olowokure B, Mangtani P. School closures and influenza: systematic review of epidemiological studies. BMJ Open. 2013;3(2).
218. Jackson C, Mangtani P, Hawker J, Olowokure B, Vynnycky E. The effects of school closures on influenza outbreaks and pandemics: systematic review of simulation studies. PLoS One. 2014;9(5):e97297.
219. Cauchemez S, Van Kerkhove MD, Archer BN, Cetron M, Cowling BJ, Grove P, et al. School closures during the 2009 influenza pandemic: national and local experiences. BMC Infect Dis. 2014 Apr 16;14:207.
220. Kelso JK, Milne GJ, Kelly H. Simulation suggests that rapid activation of social distancing can arrest epidemic development due to a novel strain of influenza. BMC Public Health. 2009 Apr 29;9:117.
221. Lau LL, 5.1.2e, Kelly H, Ip DK, Leung GM, Cowling BJ. Household transmission of 2009 pandemic influenza A (H1N1): a systematic review and meta-analysis. Epidemiology. 2012 Jul;23(4):531-42.
222. Uscher-Pines L, Schwartz HL, Ahmed F, Zheteyeva Y, Meza E, Baker G, et al. School practices to promote social distancing in K-12 schools: review of influenza pandemic policies and practices. BMC Public Health. 2018 Mar 27;18(1):406.
223. Lessler J, Reich NG, Brookmeyer R, Perl TM, Nelson KE, Cummings DA. Incubation periods of acute respiratory viral infections: a systematic review. Lancet Infect Dis. 2009 May;9(5):291-300.
224. Killingley B, Greatorex J, Digard P, Wise H, Garcia F, Varsani H, et al. The environmental deposition of influenza virus from patients infected with influenza A(H1N1)pdm09: Implications for infection prevention and control. J Infect Public Health. 2016 May-Jun;9(3):278-88.
225. Germann TC, Kadau K, 5.1.2e IM, Jr., Macken CA. Mitigation strategies for pandemic influenza in the United States. Proc Natl Acad Sci U S A. 2006 Apr 11;103(15):5935-40.
226. Ferguson NM, Cummings DA, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. Nature. 2006 Jul 27;442(7101):448-52.
227. World Health Organisation(WHO). Reducing transmission of pandemic (H1N1) 2009 in school settings 2009. Available from: http://www.who.int/csr/resources/publications/reducing_transmission_h1n1_2009.pdf.
228. Rothstein MA, Talbott MK. Encouraging compliance with quarantine: a proposal to provide job security and income replacement. Am J Public Health. 2007 Apr;97 Suppl 1:S49-56.
229. Leung GM, Nicoll A. Reflections on pandemic (H1N1) 2009 and the international response. PLoS Med. 2010 Oct 5;7(10).
230. Pada S, Tambyah PA. Overview/reflections on the 2009 H1N1 pandemic. Microbes Infect. 2011 May;13(5):470-8.
231. DiGiovanni C, Conley J, Chiu D, Zaborski J. Factors influencing compliance with quarantine in Toronto during the 2003 SARS outbreak. Biosecur Bioterror. 2004;2(4):265-72.
232. World Health Organisation(WHO). WHO Consultation on suspension of classes and restriction of mass gatherings to mitigate the impact of epidemics caused by the new influenza A (H1N1); Summary of the third scientific teleconference on influenza A (H1N1). 2009.
233. Cauchemez S, Valleron AJ, Boelle PY, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. Nature. 2008 Apr 10;452(7188):750-4.
234. Copeland DL, Basurto-Davila R, Chung W, Kurian A, Fishbein DB, Szymanowski P, et al. Effectiveness of a school district closure for pandemic influenza A (H1N1) on acute respiratory illnesses in the community: a natural experiment. Clin Infect Dis. 2013 Feb;56(4):509-16.
235. Jackson C, Vynnycky E, Mangtani P. The Relationship Between School Holidays and Transmission of Influenza in England and Wales. Am J Epidemiol. 2016 Nov 1;184(9):644-51.
236. Cowling BJ, Ip DK, Fang VJ, Suntarattiwong P, Olsen SJ, Levy J, et al. Modes of transmission of influenza B virus in households. PLoS One. 2014;9(9):e108850.
237. Inglesby TV, Nuzzo JB, O'Toole T, Henderson DA. Disease mitigation measures in the control of pandemic influenza. Biosecur Bioterror. 2006;4(4):366-75.
238. Guclu H, Read J, Vukotich CJ, Jr., Galloway DD, Gao H, Rainey JJ, et al. Social Contact Networks and Mixing among Students in K-12 Schools in Pittsburgh, PA. PLoS One. 2016;11(3):e0151139.
239. Hens N, Ayele GM, Goeyvaerts N, Aerts M, Mossong J, Edmunds JW, et al. Estimating the impact of school closure on social mixing behaviour and the transmission of close contact infections in eight European countries. BMC Infect Dis. 2009 Nov 27;9:187.
240. Russell ES, Zheteyeva Y, Gao H, Shi J, Rainey JJ, Thoroughman D, et al. Reactive School Closure During Increased Influenza-Like Illness (ILI) Activity in Western Kentucky, 2013: A Field Evaluation of Effect on ILI Incidence and Economic and Social Consequences for Families. Open Forum Infect Dis. 2016 Sep;3(3):ofw113.
241. Davis BM, Markel H, Navarro A, Wells E, Monto AS, Aiello AE. The effect of reactive school closure on community influenza-like illness counts in the state of Michigan during the 2009 H1N1 pandemic. Clin Infect Dis. 2015 Jun 15;60(12):e90-7.
242. Trotter Y, Jr., Dunn FL, Drachman RH, Henderson DA, Pizzi M, Langmuir AD. Asian influenza in the United States, 1957-1958. Am J Hyg. 1959 Jul;70(1):34-50.

243. Earn DJ, He D, Loeb MB, Fonseca K, Lee BE, Dushoff J. Effects of school closure on incidence of pandemic influenza in Alberta, Canada. Ann Intern Med. 2012 Feb 7;156(3):173-81.
244. Wu JT, Cowling BJ, Lau EH, Ip DK, Ho LM, Tsang T, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. Emerg Infect Dis. 2010 Mar;16(3):538-41.
245. Bin Nafisah S, Alamery AH, Al Nafesa A, Aleid B, Brazanji NA. School closure during novel influenza: A systematic review. J Infect Public Health. 2018 Jan 30.
246. Centre for Disease Control and Prevention(CDC). CDC guidance for state and local public health officials and school administrators for school (K–12) responses to influenza during the 2009–2010 school year 2010. Available from: https://www.cdc.gov/h1n1flu/schools/schoolguidance.htm.
247. Berkman BE. Mitigating pandemic influenza: the ethics of implementing a school closure policy. J Public Health Manag Pract. 2008 Jul-Aug;14(4):372-8.
248. Centre for Disease Control and Prevention(CDC). Parental attitudes and experiences during school dismissals related to 2009 influenza A (H1N1) --- United States, 2009. MMWR Morb Mortal Wkly Rep. 2010 Sep 10;59(35):1131-4.
249. Mizumoto K, Yamamoto T, 5.1.2e. Contact behaviour of children and parental employment behaviour during school closures against the pandemic influenza A (H1N1-2009) in Japan. J Int Med Res. 2013 Jun;41(3):716-24.
250. Pasquini-Descomps H, Brender N, Maradan D. Value for Money in H1N1 Influenza: A Systematic Review of the Cost-Effectiveness of Pandemic Interventions. Value Health. 2017 Jun;20(6):819-27.
251. Kann L, Kinchen S, Modzelski B, Sullivan M, Carr D, Zaza S, et al. ILI-related school dismissal monitoring system: an overview and assessment. Disaster Med Public Health Prep. 2012 Jun;6(2):104-12.
252. Potter MA, Brown ST, Cooley PC, Sweeney PM, Hershey TB, Gleason SM, et al. School closure as an influenza mitigation strategy: how variations in legal authority and plan criteria can alter the impact. BMC Public Health. 2012 Nov 14;12:977.
253. Dooyema CA, Copeland D, Sinclair JR, Shi J, Wilkins M, Wells E, et al. Factors influencing school closure and dismissal decisions: influenza A (H1N1), Michigan 2009. J Sch Health. 2014 Jan;84(1):56-62.
254. Kumar S, Grefenstette JJ, Galloway D, Albert SM, Burke DS. Policies to reduce influenza in the workplace: impact assessments using an agent-based model. Am J Public Health. 2013 Aug;103(8):1406-11.
255. Carrat F, Luong J, Lao H, Salle AV, Lajaunie C, Wackernagel H. A 'small-world-like' model for comparing interventions aimed at preventing and controlling influenza pandemics. BMC Med. 2006 Oct 23;4:26.
256. Xia H, Nagaraj K, Chen J, Marathe MV. Synthesis of a high resolution social contact network for Delhi with application to pandemic planning. Artif Intell Med. 2015 Oct;65(2):113-30.
257. Ahmed F, Zviedrite N, Uzicanin A. Effectiveness of workplace social distancing measures in reducing influenza transmission: a systematic review. BMC Public Health. 2018 Apr 18;18(1):518.
258. World Health Organisation(WHO). Public health for mass gatherings-key considerations 2015. Available from: http://apps.who.int/iris/bitstream/handle/10665/162109/WHO_HSE_GCR_2015.5_eng.pdf?sequence=1.
259. Abubakar I, Gautret P, Brunette GW, Blumberg L, Johnson D, Poumerol G, et al. Global perspectives for prevention of infectious diseases associated with mass gatherings. Lancet Infect Dis. 2012 Jan;12(1):66-74.
260. Gutierrez I, Litzroth A, Hammadi S, Van Oyen H, Gerard C, Robesyn E, et al. Community transmission of influenza A (H1N1)v virus at a rock festival in Belgium, 2-5 July 2009. Euro Surveill. 2009 Aug 6;14(31).
261. Rashid H, Haworth E, Shafi S, Memish ZA, Booy R. Pandemic influenza: mass gatherings and mass infection. Lancet Infect Dis. 2008 Sep;8(9):526-7.
262. Rainey JJ, Phelps T, Shi J. Mass Gatherings and Respiratory Disease Outbreaks in the United States - Should We Be Worried? Results from a Systematic Literature Review and Analysis of the National Outbreak Reporting System. PLoS One. 2016;11(8):e0160378.
263. World Health Organisation(WHO). WHO Consultation on suspension of classes and restriction of mass gatherings to mitigate the impact of epidemics caused by the new influenza A (H1N1) 2009. Available from: https://ecdcevtclu.ecdcnet.europa.eu/EnterpriseVault/Search/htmlview.aspx?VaultId=1A6178B738C995E42A4F12A94C54AE3771110000ecdcevtclu&SavesetId=201808224954183~20180518153909000O~Z~A102A351B046590940A79BF0F2C3DF11&AttachmentId=1.
264. World Health Organisation(WHO). Interim planning considerations for mass gatherings in the context of pandemic (H1N1) 2009 influenza. 2009.
265. Hoang VT, Gautret P. Infectious Diseases and Mass Gatherings. Curr Infect Dis Rep. 2018 Aug 28;20(11):44.
266. Salmon-Rousseau A, Piednoir E, Cattoir V, de La Blanchardiere A. Hajj-associated infections. Med Mal Infect. 2016 Oct;46(7):346-54.
267. Botelho-Nevers E, Gautret P. Outbreaks associated to large open air festivals, including music festivals, 1980 to 2012. Euro Surveill. 2013 Mar 14;18(11):20426.
268. Al-Tawfiq JA, Benkouiten S, Memish ZA. A systematic review of emerging respiratory viruses at the Hajj and possible coinfection with Streptococcus pneumoniae. Travel Med Infect Dis. 2018 May - Jun;23:6-13.
269. Ishola DA, Phin N. Could influenza transmission be reduced by restricting mass gatherings? Towards an evidence-based policy framework. J Epidemiol Glob Health. 2011 Dec;1(1):33-60.
270. Shi P, Keskinocak P, Swann JL, Lee BY. The impact of mass gatherings and holiday traveling on the course of an influenza pandemic: a computational model. BMC Public Health. 2010 Dec 21;10:778.

271. Cooper BS, Pitman RJ, Edmunds WJ, Gay NJ. Delaying the international spread of pandemic influenza. PLoS Med. 2006 Jun;3(6):e212.
272. Selvey LA, Antao C, Hall R. Entry screening for infectious diseases in humans. Emerg Infect Dis. 2015 Feb;21(2):197-201.
273. Goeijenbier M, van Genderen P, Ward BJ, Wilder-Smith A, Steffen R, Osterhaus AD. Travellers and influenza: risks and prevention. J Travel Med. 2017 Jan;24(1).
274. European Centre for Disease Prevention and Control(ECDC). Infection prevention and control measures for Ebola virus disease: Entry and exit screening measures 2014. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Ebola-outbreak-technicalreport-exit-entry-screening-13Oct2014.pdf.
275. Bell DM. Public health interventions and SARS spread, 2003. Emerg Infect Dis. 2004 Nov;10(11):1900-6.
276. Bitar D, Goubar A, Desenclos JC. International travels and fever screening during epidemics: a literature review on the effectiveness and potential use of non-contact infrared thermometers. Euro Surveill. 2009 Feb 12;14(6).
277. Chen J, Yang K, Zhang M, Shen C, Chen J, Wang G, et al. Rapid identification of imported influenza viruses at Xiamen International Airport via an active surveillance program. Clin Microbiol Infect. 2018 Mar;24(3):289-94.
278. Priest PC, Jennings LC, Duncan AR, Brunton CR, Baker MG. Effectiveness of border screening for detecting influenza in arriving airline travelers. Am J Public Health. 2015 Oct;105 Suppl 4:S607-13, s0-6.
279. Jennings LC, Priest PC, Psutka RA, Duncan AR, Anderson T, Mahagamasekera P, et al. Respiratory viruses in airline travellers with influenza symptoms: Results of an airport screening study. J Clin Virol. 2015 Jun;67:8-13.
280. Cowling BJ, Lau LL, Wu P, Wong HW, Fang VJ, Riley S, et al. Entry screening to delay local transmission of 2009 pandemic influenza A (H1N1). BMC Infect Dis. 2010 Mar 30;10:82.
281. Health Canada. Learning from SARS. Renewal of public health in Canada. A report of the National Advisory Committee on SARS and Public Health, October 2003 2003. Available from: http://www.phac-aspc.gc.ca/publicat/sars-sras/pdf/sars-e.pdf.
282. World Health Organisation(WHO). No rationale for travel restrictions. 2009.
283. World Health Organisation(WHO). Communicating risk in public health emergencies. A WHO guideline for emergency risk communication (ERC) policy and practice. 2017.
284. Centre for Disease Control and Prevention(CDC). NIOSH-Approved Particulate Filtering Facepiece Respirators. Available from: https://www.cdc.gov/niosh/npptl/topics/respirators/disp_part/default.html.
285. Centre for Disease Control and Prevention(CDC). Crisis & Emergency Risk Communication (CERC) [cited 2018]. Available from: https://emergency.cdc.gov/cerc/index.asp.
286. European Centre for Disease Prevention and Control(ECDC). ECDC Virtual Academy [cited 2018]. Available from: https://eva.ecdc.europa.eu/.
287. World Health Organisation(WHO). Infection prevention and control:Tools for training and education [cited 2018]. Available from: https://www.who.int/infection-prevention/tools/hand-hygiene/slides/en/.
288. World Health Organisation(WHO). Report prepared for the WHO annual consultation on the composition of influenza vaccine for the Northern Hemisphere 2019-2020. 2019.
289. World Health Organisation(WHO). WHO public health research agenda for influenza: limiting the spread of pandemic, zoonotic and seasonal epidemic influenza, 2017 update 2017. Available from: http://apps.who.int/iris/handle/10665/259892.
290. World Health Organisation(WHO). WHO public health research agenda for influenza 2017. Available from: http://www.who.int/influenza/resources/research/en/.
291. Postma MJ, Milne G, Nelson EA, Pyenson B, Basili M, Coker R, et al. Pharmaceutical interventions for mitigating an influenza pandemic: modeling the risks and health-economic impacts. Expert Rev Anti Infect Ther. 2010 Dec;8(12):1431-9.
292. Killingley B, Enstone J, Booy R, Hayward A, Oxford J, Ferguson N, et al. Potential role of human challenge studies for investigation of influenza transmission. Lancet Infect Dis. 2011 Nov;11(11):879-86.
293. Vukotich CJ, Jr., Coulborn RM, Aragon TJ, Baker MG, Burrus BB, Aiello AE, et al. Findings, gaps, and future direction for research in nonpharmaceutical interventions for pandemic influenza. Emerg Infect Dis. 2010 Apr;16(4):e2.

Annex. PubMed search strategy

PubMed searches were performed until 18 December 2018. The key terms: influenza', 'pandemic', 'respiratory infection', 'respiratory tract infection', 'respiratory virus', 'non-pharmaceutical measures', 'public health measures', 'non-pharmaceutical interventions', 'personal protective measures', 'personal protective equipment', 'environmental', 'cleaning', 'surface', 'humidification', 'ventilation', 'disinfectants', 'disinfection', 'copper', 'alloy', 'sunlight', 'hand hygiene', 'mask', 'respirator', 'hand disinfection', 'social distancing', 'voluntary isolation',

'workplace', 'quarantine', 'mass gatherings', 'Hajj', 'school closure', 'entry screening', 'exit screening', 'border closure', 'travel advice', 'travel measures', were used in the following combinations:

Measure	Search terms
Non-pharmaceutical countermeasures	(non[All Fields] AND ("pharmacy"[MeSH Terms] OR "pharmacy"[All Fields] OR "pharmaceutical"[All Fields] OR "dosage forms"[MeSH Terms] AND "forms"[All Fields]) [All Fields]) AND interventions[All Fields] AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp] (non[All Fields] AND ("pharmacy"[MeSH Terms] OR "pharmacy"[All Fields] OR "pharmaceutical"[All Fields][All Fields]) AND ("measures"[All Fields]) AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp] (non[All Fields] AND ("pharmacy"[MeSH Terms] OR "pharmacy"[All Fields] OR "pharmaceutical"[All Fields] AND "measures"[All Fields]) OR "weights and measures"[All Fields] OR "measures"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp] (non[All Fields] AND ("pharmacy"[MeSH Terms] OR "pharmacy"[All Fields] OR "pharmaceutical"[All Fields]) AND interventions[All Fields] AND effectiveness[All Fields]) AND Review[ptyp]
Hand hygiene	(("hand hygiene"[MeSH Terms] OR ("hand"[All Fields] AND "hygiene"[All Fields]) OR "hand hygiene"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp] (("hand disinfection"[MeSH Terms] OR ("hand"[All Fields] AND "disinfection"[All Fields]) OR "hand disinfection"[All Fields] OR ("hand"[All Fields] AND "washing"[All Fields]) OR "hand washing"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp] (("hand disinfection"[MeSH Terms] OR ("hand"[All Fields] AND "disinfection"[All Fields]) OR "hand disinfection"[All Fields] OR ("hand"[All Fields] AND "washing"[All Fields]) OR "hand washing"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp] (("hand hygiene"[MeSH Terms] OR ("hand"[All Fields] AND "hygiene"[All Fields]) OR "hand hygiene"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp]
Respiratory etiquette	(respiratory[All Fields] AND etiquette[All Fields]) AND Review[ptyp] (("cough"[MeSH Terms] OR "cough"[All Fields]) AND etiquette[All Fields]) AND Review[ptyp] (respiratory[All Fields] AND ("hygiene"[MeSH Terms] OR "hygiene"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp] (respiratory[All Fields] AND ("hygiene"[MeSH Terms] OR "hygiene"[All Fields]) AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infections"[All Fields]) OR "respiratory infections"[All Fields])) AND Review[ptyp]
Facemasks	(facemask[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp] (("face"[MeSH Terms] OR "face"[All Fields]) AND ("masks"[MeSH Terms] OR "masks"[All Fields] OR "mask"[All Fields]) AND ("influenza, human"[MeSH Terms]

	OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(("masks"[MeSH Terms] OR "masks"[All Fields] OR "mask"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(("masks"[MeSH Terms] OR "masks"[All Fields] OR "mask"[All Fields]) AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infection"[All Fields]) OR "respiratory infection"[All Fields])) AND Review[ptyp]
Other personal protective equipment	(("personal protective equipment"[MeSH Terms] OR ("personal"[All Fields] AND "protective"[All Fields] AND "equipment"[All Fields]) OR "personal protective equipment"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(personal[All Fields] AND protective[All Fields] AND ("weights and measures"[MeSH Terms] OR ("weights"[All Fields] AND "measures"[All Fields]) OR "measures"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(personal[All Fields] AND protective[All Fields] AND interventions[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(personal[All Fields] AND protective[All Fields] AND interventions[All Fields] AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp]
Environmental measures	(("environment"[MeSH Terms] OR "environment"[All Fields] OR "environmental"[All Fields]) OR ("weights"[All Fields] AND "measures"[All Fields]) OR "measure"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(surface[All Fields] AND cleaning[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(humidification[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(("ventilation"[MeSH Terms] OR "ventilation"[All Fields] OR "respiration"[MeSH Terms] OR "respiration"[All Fields]) AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infection"[All Fields]) OR "respiratory infection"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp]
	(cleaning[All Fields] AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infection"[All Fields]) OR "respiratory infection"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp]
	(("disinfectants"[Pharmacological Action] OR "disinfectants"[MeSH Terms] OR "disinfectants"[All Fields] OR "disinfectant"[All Fields]) AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND

	"infections"[All Fields]) OR "respiratory tract infections"[All Fields] OR ("respiratory"[All Fields] AND "infection"[All Fields]) OR "respiratory infection"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp]
	(("disinfection"[MeSH Terms] OR "disinfection"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields]) AND effectiveness[All Fields]) AND Review[ptyp]
	(("disinfection"[MeSH Terms] OR "disinfection"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(("disinfectants"[Pharmacological Action] OR "disinfectants"[MeSH Terms] OR "disinfectants"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(("infection"[MeSH Terms] OR "infection"[All Fields]) AND ("sunlight"[MeSH Terms] OR "sunlight"[All Fields]) AND ("ventilation"[MeSH Terms] OR "ventilation"[All Fields] OR "respiration"[MeSH Terms] OR "respiration"[All Fields])) AND Review[ptyp]
	(("copper"[MeSH Terms] OR "copper"[All Fields]) AND ("disinfection"[MeSH Terms] OR "disinfection"[All Fields])) AND Review[ptyp]
Social distancing measures	(social[All Fields] AND distancing[All Fields]) AND Review[ptyp]
	(social[All Fields] AND distancing[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
Isolation of infected individuals	(("quarantine"[MeSH Terms] OR "quarantine"[All Fields]) AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp]
Voluntary quarantine of exposed individuals	voluntary[All Fields] AND ("isolation and purification"[Subheading] OR ("isolation"[All Fields] AND "purification"[All Fields]) OR "isolation and purification"[All Fields] OR "isolation"[All Fields]) AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])
School closure	(("schools"[MeSH Terms] OR "schools"[All Fields] OR "school"[All Fields]) AND closure[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
Workplace closure	("workplace"[MeSH Terms] OR "workplace"[All Fields]) AND closure[All Fields]
	("workplace"[MeSH Terms] OR "workplace"[All Fields]) AND closure[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])
Workplace measures	"workplace"[MeSH Terms] OR "workplace"[All Fields]) AND "measures"[All Fields]) OR "measure"[All Fields]) AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])
Mass gatherings	(("mass"[All Fields]) AND gathering[All Fields] AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp]
	(("mass"[All Fields]) AND gathering[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp]
	(Hajj[All Fields] AND effectiveness[All Fields]) AND Review[ptyp]

	(Hajj[All Fields] AND ("public health"[MeSH Terms] OR ("public"[All Fields] AND "health"[All Fields]) OR "public health"[All Fields]) AND "measures"[All Fields]) OR "measures"[All Fields])) AND Review[ptyp]
Travel advice	(("travel"[MeSH Terms] OR "travel"[All Fields]) AND advice[All Fields] AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp]
Entry and exit screening	(entry[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields]) AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp] (entry[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields] AND ("influenza, human"[MeSH Terms] OR ("influenza"[All Fields] AND "human"[All Fields]) OR "human influenza"[All Fields] OR "influenza"[All Fields])) AND Review[ptyp] (entry[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields]] OR ("early"[All Fields] AND "detection"[All Fields] AND respiratory[All Fields]) AND Review[ptyp]
Internal travel restriction	(("travel"[MeSH Terms] OR "travel"[All Fields]) AND ("weights and measures"[MeSH Terms] OR ("weights"[All Fields] AND "measures"[All Fields]) OR "weights and measures"[All Fields] OR "measures"[All Fields]) AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields])) AND Review[ptyp]
Border closure	(("travel"[MeSH Terms] OR "travel"[All Fields]) AND restrictions[All Fields] AND effectiveness[All Fields]) AND Review[ptyp]