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Expert opinion on non-pharmaceutical countermeasures against pandemic influenza

Document number: AF60/03	Date: 10 February 2020
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 was reviewed in the AF58, and all substantive comments have been taken into account in current version. This document will be opened for a public consultation immediately after the AF opinion.
Action:	The revised Expert Opinion is circulated for information to the AF, prior to public consultation.
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. 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.
5. 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.
6. An international panel of experts reviewed the draft document in May 2018 and the AF58 reviewed it in September 2019. Following substantive comments made in the AF meeting, the Expert Opinion has been revised in order to:
    a. Apply a quality of evidence rating on the identified reviews (AMSTAR2)
    b. Add table 3 "Potential model for combining NPCs according to the pandemic severity assessment"
    c. Strengthen language on recommendations as "ECDC expert opinion"; including a revision of Table 2: "Summary of ECDC expert opinion on non-pharmaceutical countermeasures"
    d. Slightly revise structure of chapter on "Use of facemasks and respirators"
    e. Describe in Methods the role of the EU/EEA MS pandemic planning colleagues in reviewing the draft Expert opinion

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

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Draft for public consultation

ECDC EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

ECDC SCIENTIFIC ADVICE

Expert opinion on non-pharmaceutical countermeasures against pandemic influenza

Acknowledgements

This report was drafted by [redacted] and [redacted] (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. [redacted] drafted 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 that were invited based on their personal expertise and not representing their countries: [redacted] (NL), [redacted] (DE), [redacted] (SE), [redacted] (HK), [redacted] (PL), [redacted] (UK), [redacted] (SE), [redacted] (NO), [redacted] (UK), [redacted] (UK), [redacted] (ES), [redacted] (UK), [redacted] (NL) and [redacted] (US CDC), [redacted] (WHO HQ), [redacted] (European Commission DG SANTE.C3). ECDC experts that participated to the meeting were: [redacted], [redacted], [redacted], [redacted] and [redacted]. The report has been reviewed by [redacted] and [redacted] (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

NHS National Health Service

NPC Non-pharmaceutical countermeasure

OD Odds Ratio

PHE Public Health England

PPE Personal Protective Equipment

PPM Personal Protective Measure

RCT Randomised Controlled Trial

RR Risk Ratio

SARI Sever Acute Respiratory Infections

SARS-CoV Severe Acute Respiratory Syndrome Corona Virus

WHO World Health Organization

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, tens of thousands of hospitalisations and deaths 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 the available 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 with regards to operational feasibility and acceptability. The NPCs are categorised into personal protective, environmental, social distancing and travel-related measures. The document also aims to identify gaps in research and so 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 excluded. The quality of the included reviews was assessed using AMSTAR 2. The information was sorted by intervention type and separated into the relevant chapters.

An expert meeting to discuss the evidence base for effectiveness of NPCs and to revise the draft document accordingly was organised by ECDC in May 2018. The discussion panel consisted of scientific content (social science scientists, experts working on non-pharmaceutical interventions, authors of systematic literature reviews and meta-analyses included in this paper) and policy experts (public health professionals, pandemic planners) from Germany, the Netherlands, Norway, Hong Kong, Poland, Spain, Sweden, the United Kingdom, United States, European Commission DG SANTE.C3, the U.S., WHO HQ and ECDC. The independent expert panel members were selected for their specific expertise, and their input was requested on the basis of that expertise rather than on the basis of policy or practice of their countries or employing organisations. The views of the experts were taken into account to the extent possible, however the final Expert opinion is ECDCs understanding of the best available evidence.

The draft Expert opinion was also shared with EU Member State pandemic preparedness experts participating in three regional workshops in spring of 2019 and ECDCs advisory forum in September 2019 and a public consultation was launched in November 2019. Feedback from these consultations has been incorporated into the document, to the extent possible.

Results in short

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 varied in different countries and settings during the previous pandemics. The number of included reviews for each type of measures and their grading according to the AMSTAR 2 system is shown in Table 1.

Overall, there was a limited evidence base on the effectiveness of NPCs against influenza infection especially in community settings and sometimes the conclusions of the reviews (especially regarding hand washing and facemask effectiveness against influenza infection) were variable. The quality of included reviews was variable ranging from high to critically low quality, usually the main flaw being the lack of quality assessment criteria and grading of their included studies. Graded studies that were included in the moderate/high quality reviews were on the other hand often of low quality and sometimes the evidence-base consisted mainly of simulation studies. A lot of evidence is indirect, i.e. it comes from studies not directly applicable to pandemic influenza, but to other infectious diseases or respiratory viruses or seasonal influenza. Studies focused on laboratory confirmed influenza are rare. For environmental measures, most of the evidence is also indirect, originating from studies that focus on the mechanistic mode of action of these measures to reduce the viral load on surfaces, objects and air.

Effectiveness of the measures will depend on additional factors, for example proper use, frequency and duration of use, combination of measures 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 in some studies difficult to disentangle the effects of specific interventions. In the situation of limited and sometimes conflicting evidence, the expert opinion is based on expert judgement, taking into account theoretical and operational considerations, common practice, feasibility and current guidelines and recommendations of public health organisations.

Personal protective measures (PPMs) (hand hygiene, cough etiquette, facemasks and respirators and other measures, i.e. voluntary home isolation when ill) and environmental measures are commonly recommended and undertaken during seasonal influenza epidemics and pandemics. The evidence of PPM effectiveness to mitigate the pandemic is limited or even absent, 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 use during pandemics depending on the severity level, 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, such as travel restrictions and border closures may delay the viral spread for a short period, but only if they achieve almost complete isolation of the country and at very early pandemic phases, which is generally considered unfeasible and can be done only in specific contexts, such as on small island nations. They are also undesirable due to major societal and economic costs. Border screening was assessed as unlikely to be successful because current screening methods (e.g. thermal scanners) have low sensitivity to identify infection 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 2. The options for implementation of NPCs according to the pandemic severity assessment (using the PISA indicator 'impact') are summarised in Table 3.

Table 1. Number of included reviews on non-pharmaceutical countermeasures by quality (AMSTAR 2 grading)

Countermeasure	Number of systematic reviews	AMSTAR2 grading of systematic reviews				Number of non systematic reviews
		High	Moderate	Low	Critically low	
Hand hygiene	14*	6	4	1	2	5
Cough etiquette	2	1	1			2
Facemasks and respirators	11	6	3		2	9
Other personal protective equipment	3	2			1	4
Environmental measures	4*		3			14
Voluntary isolation of ill	3	2			1**	1
Voluntary quarantine of exposed	3	2			1**	1
School closures	4				4**	2
Workplace measures	5	2	2		1**	1
Measures in mass gatherings	2		2			3
Travel-related measures (domestic and international travel restrictions, exit/entry screening)	5	2	1		2**	6

* One systematic review was not assessed because only a short version was available in English

** A number of these reviews were graded according to AMSTAR 2 as 'critically low' due to lack of description of risk of bias for their included studies, which may however not be appropriate for the included studies.

Table 2. Summary of ECDC expert opinion on non-pharmaceutical countermeasures

Personal Protective Measures	ECDC expert opinion
Hand hygiene	Although the available evidence from the included literature reviews on effectiveness of hand hygiene in reducing influenza infections is contradicting, the use of hand hygiene has been proven effective against other pathogens. Therefore recommending hand hygiene is considered a rational precaution, with limited costs and no associated risks.
Cough etiquette	Although the available evidence base is very limited, cough etiquette is widely recommended in public health guidelines for all community settings (home, schools, workplaces, HCSs etc.) at all times due to their potential mechanical mode of action.
Use of surgical facemasks	Available evidence supports recommending facemask use for infected persons when in contact with other individuals. Surgical facemask use by HCWs in HCS should be recommended in epidemics or pandemics to reduce transmission and current policies mandating standard and droplet precautions when performing routine care for influenza patients are reasonable. Use of surgical 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, although most evidence originates from HCSs. There is lack of evidence on effectiveness of wider use of facemasks in community settings, therefore such recommendations should only be considered in severe pandemic scenarios.
Use of respirators	Respirators should be considered in high risk settings by HCWs especially when aerosol generating procedures are performed.
Other personal protective equipment	Available evidence supports recommending use of PPE in health care settings, when performing aerosol-generating procedures or when the risk of exposure to respiratory secretions is high.
Environmental Measures	
Surface and object cleaning	Available indirect evidence supports recommending the use of environmental measures such as surface cleaning and disinfection at all times during pandemics due to their mechanical action against influenza virus and the potential of these measures to reduce transmission.

Room ventilation	Available limited and mostly indirect evidence supports recommending measures that improve indoor ventilation at all times during pandemics.
Social distancing measures	
Voluntary isolation of ill persons	Available evidence supports recommending voluntary isolation of infected individuals at all times during pandemics.
Voluntary quarantine of exposed persons	Available, limited evidence, originating mainly from modelling studies, support recommending voluntary quarantine based on a situational risk assessment.
Interventions in educational and child care settings	Available evidence which is generally of low quality and based on modelling studies, supports recommending *proactive* closures of schools and day care facilities only during severe epidemics and pandemics, as they can be associated with significant societal and economic costs. Available evidence, does not provide support for *reactive* school and day care closures in order to impact the evolution of a pandemic.
Measures in the workplace and other public places	Available evidence supports recommending measures at workplaces (e.g. teleworking, social distancing), which can be modestly effective and feasible during all phases of a pandemic. Evidence from modelling studies support recommending workplace closures in extraordinarily severe pandemics.
Measures at mass gatherings	Available limited evidence, mainly from modelling studies, supports recommending cancellations of mass gatherings only before the peak of severe pandemics. Available limited evidence base, mainly indirect in describing the extent of transmission that takes place during mass gatherings, supports recommendations for other measures (e.g. facemask use, web-casting, education campaigns, environmental measures) during moderate or more severe pandemics, depending on the type of the event and a risk assessment.
Travel-related measures	
International and domestic travel advice	Although there is lack of evidence to quantify the effectiveness of trave advice to mitigate a pandemic, issuing relative travel advice, consistent with IHR and national law, is recommended during the early stages of epidemics or pandemics at any level of severity.

Entry and exit screening at national borders	The available 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 of current systems to detect symptomatic, pre-symptomatic and asymptomatic infections.
Domestic travel restrictions	Available limited evidence does not support recommending domestic travel restrictions, except for very specific, isolated settings in the early stages of extraordinary severe pandemics.
Border closures	Available, limited evidence, mainly from modelling studies, does not support recommending border closures in Europe, as they will have an impact on the timing of the introduction of the pandemic influenza virus into the countries or on the peak of the local epidemic only if almost complete and at early pandemic phases.

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.

Table 3. Potential model for combining NPCs according to the pandemic severity assessment*

Low	Moderate	High	Extraordinary high
Hand hygiene Cough etiquette Environmental measures Voluntary isolation of ill Travel advice	Hand hygiene Cough etiquette Environmental measures Voluntary isolation of ill Travel advice Workplace measures Measures in mass gatherings Facemask use by symptomatic people in the community	Hand hygiene Cough etiquette Environmental measures Voluntary isolation of ill Travel advice Workplace measures Measures in mass gatherings Facemasks (in wider community) School closures	Hand hygiene Cough etiquette Environmental measures Voluntary isolation of ill Travel advice Workplace measures Measures in mass gatherings Facemasks (in wider community) School closures Quarantine of exposed persons Workplace closures Domestic travel restrictions

* taking into consideration the feasibility of each measure (note also that border closures are generally not recommended unless required by national law in extraordinary circumstances during a severe pandemic, and countries implementing this measure should notify WHO as required by the IHR (2005)).

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 timing and duration need to be carefully considered by measure and according to the pandemic risk assessment due to the high socioeconomic cost and to ensure sustainability. Personal protective and environmental measures are everyday actions with minimal associated risks that are likely to be highly acceptable and undertaken also during seasonal epidemics, whereas social distancing and travel-related measures may be less acceptable and have higher societal, legal, ethical and/or 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 portfolio 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, hospitalizations 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 (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 measures

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 for 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 the timely use of a specific pandemic vaccine 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 polymerase 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].

There are two modes of respiratory transmission: droplet and airborne transmission. This 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 infectious droplets [19,20]. Recommendations to control influenza virus transmission in various community settings include measures that reduce transmission and spread by aerosol and fomite mechanisms. Aerosolised particles are particles of different sizes; the largest droplets (5-10μm aerodianamic diameter) will transmit an infection only to those in the immediate vicinity, they travel typically 1-2 meters from their source and then settle to objects and surfaces thereby causing indirect transmission. Smaller droplets travel a distance determined by their size. Those droplets are <5μm in diameter and may remain suspended in the air for longer periods, travel longer distances, and reach the lower respiratory tract. Inhalation of droplets 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 the 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 most importantly 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 or hosts that don't present the typical Influenza-Like-Illness (ILI) symptoms (e.g. fever) [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, cough 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 May 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].

The Pandemic Influenza Severity Assessment (PISA) tool

The Pandemic Influenza Severity Assessment (PISA) tool was introduced by the WHO to monitor the influenza pandemics [35]. The aims of the influenza severity assessment are to:

- describe the epidemiological situation and assess the severity of an influenza epidemic or pandemic based on all available information
- inform national and global risk assessments
- inform public health preparedness, response and recovery measures as well as resource allocation.

The severity of a pandemic is evaluated through three indicators: transmissibility, seriousness of disease and impact. The tool that aims to aid public health authorities to assess the severity of pandemic influenza, can also be used to inform appropriate decisions on NPC use. The final evaluation of severity may inform the choice of which NPCs to use and when to implement the measures. The pandemic impact level ranges from low to moderate, high or extraordinarily high. Some NPCs may be recommended at all times, while others only in severe or extraordinarily severe pandemics.

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, characterise 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, one of which would be the 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 experiences with SARS and the 2009 pandemic, enhanced level of national and international surveillance has been proven crucial in order to contain the viral spread. 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 [42,43].

Contact tracing for transmission 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 [44,45].

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 [45,46].

Overall, for influenza viruses, 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 [47]. Transmission occurs aboard aeroplanes, at the destination and possibly at airports [47]. Control measures to prevent influenza transmission on cruise ships are needed to reduce morbidity and mortality [47]. The feasibility and cost benefit of contact tracing needs to be carefully assessed.

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. For more information on options for action, it is advisable to refer to the relevant document [45].

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 [48]. 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 [49].

Specimen/patient transport

All human specimens of respiratory secretions and excretions should be considered as potentially infectious [50]. 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 [51]. 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 [49]. Hospital triage procedures are the process of prioritising patients on first contact based on their need for immediate medical care and treatment (e.g. high risk groups) 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. Dedicated waiting and isolation rooms need to be determined.

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]. High risk groups during a pandemic may vary from those during seasonal influenza seasons, due to the uncertain viral characteristics and pre-existing immunity against the pandemic virus. 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 [52].

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 in several guidance documents, including a guide specific for the prevention and control of influenza in long-term care facilities [53-59]. ECDC in 2009 published a technical report that is a guide to public health measures to reduce the impact of influenza pandemics in Europe [44,60,61]. The U.S. Centers for Disease Control and Prevention (CDC) has recently updated the 2007 guide Community Mitigation Guidelines to Prevent Pandemic Influenza [60]. Several other guidance documents that include NPC use are available from national public health institutes and agencies, such as the Public Health England (PHE) [62-64], Public Health Canada (PHAC) [37], Robert Koch Institute [65], Ministry of Health Singapore [66], New Zealand [67], Australia [68], as well as professional organisations, such as The Royal Australian College of General Practitioners (RACGP) [69] and other government-funded bodies, such as the UK National Health Service (NHS) [63].

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 [9,70]. In the early pandemic phases, a layered approach 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 [70]. Despite the anticipated effectiveness of each measure, NPCs are often evaluated in terms of their perceived necessity, 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 stigma associated with some of the interventions [71-74]. Intercountry variability and differences between populations within a single country suggest that one-size-fits-all plans may be less effective [73]. Planned public health actions should therefore be tailored to the pandemic impact, severity and local situation.

The EU decision no 1082/2013/EU on serious cross-border threats to health regulates the risk assessment, communication and coordination of responses due to situations such as influenza pandemics, and ensures risk management measures in EU Member States are taken in consultation with each other and in liaison with the European Commission.

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 and other respiratory virus 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 included systematic reviews were assessed using AMSTAR 2 [75]. The grading system scored the reviews as follows:

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

The information was sorted by intervention type and separated into the relevant chapters. Systematic and non systematic reviews have been designated accordingly in the tables. The ECDC expert opinion on options for action based on the evidence of effectiveness for each measure were summarised. The options for implementation of NPCs according to the pandemic severity assessment were summarised in a table using the PISA indicator 'impact', and taking under consideration the feasibility.

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 [60].

Between 2009 and 2018, a substantial amount of studies, reviews and guidelines have been published [9,64,67,71,76-90]. We examined infection control policies and guidelines from WHO, US 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 [53], more recent WHO documents [58,59,91,92] and WHO's 2009 guidance on NPCs [93], the CDC Interim Pre-pandemic planning guidance 2007 [94] and the Community Mitigation guidelines to prevent pandemic influenza published in 2017 [24,77] provide clear recommendations for national and subnational authorities. In this review, and it's previous version [60], no explicit recommendations are formulated, although an expert opinion on 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 [95]. The independent expert panel members were selected and invited based on their specific expertise, and their input was requested on the basis of that expertise rather than on the basis of policy or practice of their countries or employing organisations. The specific expertise included in the panel were public health professionals, pandemic planners, social science scientists, experts working on non-pharmaceutical interventions, and included some who were authors of systematic literature reviews and meta-analyses included in this paper. The main objectives of this meeting were to present and discuss the evidence base derived from the literature review 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 draft Expert opinion was also shared with EU Member State pandemic preparedness experts participating in three regional workshops in spring of 2019 and ECDC Advisory Forum in September 2019 and a public consultation was launched in November 2019. Feedback from these consultations has been incorporated into the document, to the extent possible.

WHO published in October 2019 a guidance on "Non-pharmaceutical public health measures for mitigating the risk and impact of epidemic and pandemic influenza", based on a systematic literature review [96]. ECDC experts reviewed the WHO guidance and assessed that key recommendations contained within the WHO guidance are consistent and aligned with the ECDC expert opinion.

The following NPCs have been included, categorised as follows:

Personal protective measures

- Hand hygiene
- Respiratory hygiene
    - Cough etiquette

- Facemask use
  - by staff in healthcare settings
  - situations with high exposure risk
  - outside home
  - by people outside of healthcare and patients with respiratory symptoms
- Other personal protective equipment.

Environmental measures

- Surface and object cleaning
- Room air ventilation

Social distancing measures

- Voluntary isolation of ill persons not requiring hospitalisation
- 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 on options for action.

Limitations

Evidence of effectiveness is lacking or is limited for some of the measures and systematic literature reviews are lacking for some of the measures; for those measures, options for action are provided based on the experts' opinion, existing reviews/studies and WHO and other international guidelines. Some evidence is indirect, focusing on the mechanistic mode of action of the measures against influenza viruses and not directly on their effectiveness to mitigate the epidemic. The expert opinion includes only PubMed papers and only in the English language. The paper extraction, selection and quality assessment was performed by one reviewer only. The potential impact of each measure was not quantified or compared to the other measures. AMSTAR 2 was used to assess the quality of systematic reviews, but this tool does not assess the quality of studies included in these reviews; some of the reviews have identified and/or included poor quality studies. The included reviews often include the same studies. The AMSTAR 2 tool is also not equally applicable for grading all of the included reviews and some of the otherwise high quality reviews may be graded as 'critically low' due only to the absence of an assessment of the risk of bias of included 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 and feasibility studies have not been included in this review.

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3. Results and conclusions

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 [41,97-100]. Evidence was stronger for some of the measures (e.g. hand hygiene) and weak (e.g. border closures) or limited (e.g. cough etiquette) for others. PPMs (hand hygiene, cough etiquette), a few social distancing measures (voluntary home isolation when ill) and environmental measures are commonly recommended and undertaken during influenza epidemics. They are generally inexpensive and easy to implement, though their effectiveness during other respiratory virus or 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 use during pandemics, depending on the severity level, include voluntary quarantine of exposed household members, wider use of facemasks in the community and other social distancing measures (e.g. school closures and measures in mass gatherings). The evidence-base does not support entry/exit screening, and travel restrictions are overall considered unfeasible and undesirable.

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 4-13): 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 is presented in Table 1. The expert opinion for the options for action of each measure is presented in Table 2. The options for implementation of NPCs according to the pandemic severity assessment are summarised in Table 3. A summary of included reviews per measure is provided in the table following the respective measure (Tables 4-13).

Overall, there is a limited evidence base on the effectiveness of NPCs against influenza infection especially in community settings and sometimes the conclusions of reviews (especially regarding hand washing and facemask effectiveness against influenza infection) were contradictory. The quality of included reviews is variable ranging from high to critically low quality, usually the main flaw being the lack of quality assessment criteria and grading of their included studies. Furthermore, studies that were included in the moderate/high quality reviews were often assessed by the individual reviews as having increased risk of bias and for some measures the evidence-base consisted mainly of modelling studies (e.g. for border closures, domestic travel restrictions, voluntary isolation when ill, voluntary quarantine) that are considered as evidence of weak strength.

Personal protective measures

PPMs refer to, hand and respiratory hygiene, cough etiquette, and respirator or facemask use; these are commonly recommended and undertaken during influenza outbreaks and they are generally inexpensive and easy to implement [41,101-103]. Their effectiveness during respiratory virus or seasonal influenza epidemics may differ from an influenza pandemic, due to the uncertain characteristics of the pandemic strain and its preferred mode of transmission, while public anxiety may actually increase rates of adherence [104-108]. 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 [73,76].

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 viral transmission from person to person by direct or indirect contact in any community setting. It will also 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: Twenty reviews have been included and the evidence is summarised in Table 4. Of those reviews, 14 were systematic (six 'high', four 'moderate', one 'low' and two 'critically low' AMSTAR 2 score).

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 [23,25]. Several studies and reviews have evaluated hand washing effectiveness against respiratory infections both before [41,104,105,109-114] and after the 2009 pandemic [9,76,82,87-89,103,115-131]. 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 [132-134] and this is especially evident in younger children that are less capable of hygienic behaviour themselves, have longer-lived infections and increased social contact, acting as portals of infection into the household [132,133,135].

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 against infection [76,89,132,133,135], however many studies on the effectiveness of this measure were not focused on LCI. A recent systematic literature review conducted by WHO suggested that hand hygiene has a limited effect in reducing LCIs when combined with facemask use (9%), while hand hygiene alone did not have any effect in six out of seven RCTs [136]. The included studies were heterogeneous and in many cases had a high risk of bias.

The frequency of hand washing is an important factor that may influence the effectiveness of the intervention. 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, individual susceptibility and risk of severe outcomes [76]. Increased frequency of hand washing and motivation by influenza exposure, was found to be significantly protective in several studies, but the quality of those individual studies has not been evaluated by this review [76,82,116,117,119,120,137]. Hand washing may also confer indirect protection, through minimising the influenza virus surface contamination in households [24,89,121,138].

Both soap and water and alcohol based solutions may be used against respiratory viruses. The mechanism of action for alcohol is to denature proteins on the respiratory virus surface and disrupt the lipid envelope, which is required for entry into host cells. Some studies suggest that use of an alcohol-based hand sanitizer is more effective in preventing direct spread of most respiratory 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 [41,138,139]. An evidence based review on the use of soap and water versus alcohol solutions concluded both were effective [122]. 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 [140].

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.

Likely acceptability: Hand hygiene is broadly acceptable and easy to implement, while giving people a practical measure to enact in the case of a pandemic [73]. 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 [71]. Multimodal strategies to enhance hand hygiene compliance were shown to achieve slight to moderate improvements [141]. Compliance with good hand hygiene practices may be higher than that for facemasks, which have been less acceptable in the past [73,107]. 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 [142].

ECDC expert opinion: Although the available evidence from the included literature reviews on effectiveness of hand hygiene in reducing influenza infections is contradictory, the use of hand hygiene has been proven effective against other pathogens. Therefore recommending hand hygiene is considered a rational precaution, with limited costs and no significant associated risks. Hand hygiene should be recommended in all community settings (home, schools, workplaces etc.) at all times as frequently as possible, especially following possible exposure to infectious agents. Effectiveness is likely to increase when used in combination with other measures (e.g. facemasks). Compliance may also increase during a pandemic, increasing effectiveness. It is an essential hygiene measure in HC and long-term care settings, which manage vulnerable individuals. Educational programmes for proper and frequent hand washing will be needed during ordinary seasonal influenza seasons and during pandemics. Sanitising gels may be used if hand-washing with soap and water is not possible; sanitising gel solutions based on 60-85% alcohol content should be preferred [24].

1 **Table 4. Summary of reviews and meta-analyses on hand hygiene effectiveness**

Hand hygiene - Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Hansen et al., 2018 [125]	Moderate	Workplace settings (3 cluster RCTs, 2 prospective interventional, 2 pre-post design)	Infectious diseases	Moderate evidence to support hand hygiene programs.
McGuinness et al., 2018 [135]	High	Childcare, school, domestic settings (14 cluster RCTs)	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 [129]	Low	Workplace settings (8 experimental, 2 observational, 1 simulation)	Infectious diseases	Minimal hand-hygiene interventions effective at reducing the incidence of employee illness.
Kumar et al., 2017 [143]	Not systematic	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 [130]	Moderate	Various settings - children (8 RCTs)	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 [76]	High	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 [141]	Critically low	HCSs (16 RCTs)	HC associated infections	Adopting a multimodal approach to hand hygiene achieved slight to moderate improvements in hand hygiene compliance.

Willmott et al., 2016 [124]	High	Educational settings (18 cluster 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 [128]	Critically low	Nursing homes (22 outbreak reports, 13 observational, 8 before-after, 13 RCTs)	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 infection risk.
Lidal et al., 2015 [144]	N/A*	Day-care centres (18 primary studies)	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 [89]	Moderate	Community –adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Hand hygiene and dental hygiene has a positive effect on reducing the risk of infection. Poor quality data.
Benkouiten et al., 2014 [145]	Not systematic	Community	Respiratory tract infections	Contradictory results on effectiveness of hand hygiene in preventing respiratory infections among Haji and variable compliance.
Wong et al., 2014 [86]	High	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, which did not have a significant effect (RR 0.90 (0.67-1.20).

Haworth et al., 2013 [146]	Not systematic	Community (mass gatherings)	Respiratory tract infections	Supportive of hand hygiene in Haji due to protection against respiratory viruses, not specific influenza.
Warren-Gash et al., 2013 [127]	Moderate	Community (3 RCTs, 1 case-control for LCI and 9 RCTs, 3 non randomised for ARI/ILI)	Influenza (LCI, ARI/ILI)	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 [126]	Not systematic	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 [133]	High	Community and hospital settings (56 RCTs, cluster RCTs, observational studies, case-control)	Respiratory viruses	The highest quality cluster-RCTs suggest respiratory virus spread can be prevented by hygienic measures, such as handwashing, especially in younger children. The effectiveness of adding virucidals or antiseptics to normal handwashing to decrease respiratory disease transmission remains uncertain.
Carlson et al., 2010 [123]	Not systematic	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 [101]	Not systematic	Various settings	Influenza	Hand hygiene and alcohol-based sanitisers and combined approaches with facemask use are effective in reducing ILI rates.
Jefferson et al., 2009 [132,134]	High	Various settings (4 RCTs, 14 cluster RCTs, 7 case-control, 16 prospective cohort, 5 retrospective cohort, 13 before-after)	Respiratory viruses	Frequent handwashing effective against respiratory infections (OR 0.54, 0.44 – 0.67) especially in young children that are less capable of hygienic behaviour themselves and in household members of index cases. Additional benefit from

	reduced transmission from children to other household members is broadly supported in results of other study designs, where the potential for confounding is greater. Combination of measures were effective in preventing influenza in households (OR 0.09, CI 0.02 to 0.35) . The incremental effect of adding virucidals or antiseptics to handwashing remains uncertain.

*Not assessed because only short version was available in English

Cough etiquette

Cough etiquette, as a respiratory hygiene measure, refers to covering mouth and nose when coughing and sneezing for example with the use of tissue paper or cloth.

Objective: 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 [147], and can easily be carried in small droplets expelled during coughs and sneezes.

Evidence of effectiveness: Four reviews have been included and are presented in Table 5. Of those reviews, two were systematic (one 'high' and one 'moderate' AMSTAR 2 score). There is lack of evidence for the effectiveness of cough etiquette.

Recent reviews found no data on the effectiveness of cough etiquette and effectiveness of the measure was therefore considered questionable [76,136]. 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 [85]. Although evidence of effectiveness is unavailable, the use of a cough etiquette is traditionally supported in guidelines and recommendations [41,143,148-153].

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 [71]. They will empower people and give them a practical measure to enact.

ECDC expert opinion: Although the available evidence base is very limited, cough etiquette use is widely recommended in public health guidelines for all community settings (home, schools, workplaces, HCSs etc.) at all times due to their plausible mode of action. If recommended as a measure, supplies of materials (e.g. tissues, no-touch bins, covered sputum pots) will need to be ensured. Proper disposal of the tissues is important, immediately after the use, followed by hand hygiene measures. Educational programmes can be implemented during ordinary seasonal influenza seasons and pandemics.

Table 5. Summary of reviews and meta-analyses on respiratory hygiene and cough etiquette

Cough etiquette - Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Kumar et al., 2017 [143]	Not systematic	Various settings (children)	Influenza	Cough 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 [76]	High	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 [89]	Moderate	Community –adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Some evidence of effectiveness of oral hygiene (tooth brushing and use of oral solutions).
Benkouiten et al., 2014 [145]	Not systematic	Community (mass gatherings, 17 studies)	Respiratory tract infections	Use of disposable handkerchiefs had no significant beneficial effect on the prevalence of either respiratory symptoms among pilgrims during the Hajj or viral pathogens from their nasal samples.

Use of facemasks and respirators

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

Types of facemasks

Types of facemasks range from the simplest, even home-made masks, to cloth and surgical/medical masks. 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. After the 2009 pandemic, several studies have focused on assessing the effectiveness of the different types of facemasks. Cloth/gauze masks may induce moisture retention and poor filtration and it is unclear whether they confer clinical protection [154].

Types of respirators

Respirators are specifically designed to protect users from small airborne particles, including aerosols [90,155]. Complex respirators need 'fit testing' and are produced in many different sizes to fit all. They usually have three available sizes (small, medium or large) to cover the anatomical differences of the individuals. Some types of respirators are not appropriate for children and people with facial hair. European standard (EN 149:2001+A1:2009) defines classes for respirators entirely or substantially constructed of filtering material (FFP1-3) [156], 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 µm, and FFP3 respirators are equivalent to N99 respirators, filtering >99% of particles [156]. There are studies that compare the effectiveness of the different types of masks [78,90,155,157].

Use of facemasks or respirators:

- by staff in healthcare settings;

Use of facemasks:

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

Facemask or respirator use by staff 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 with the objective of preventing transmission of illness. At the end of 19th century, following the realisation of the potential role of human exhalation as a cause of surgical wound sepsis, Huebner recommended the use of a mask made out of two layers of gauze to be used during operations. Here we refer to facemask-wearing by people who are at higher risk through possible or probable exposure to infectious patients in HCSs. 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 to provide protection from infection to HCWs to enable them to continue with their activities.

Rationale: Facemasks 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: Twenty-one reviews have been included and the evidence is summarised in Table 6. Of those reviews, 11 were systematic (six 'high', three 'moderate' and two 'critically low' AMSTAR 2 score).

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 suggested facemask use is significantly protective, especially in HCSs, while others suggested limited or no effectiveness [76,86,90,101,104,123,132,133,145,158-160].

Overall, there is some evidence for a protective effect of facemasks and respirators against clinical and laboratory-confirmed respiratory infection among HCWs [78]. Evaluating the different types of facemasks, some studies have shown that compared to surgical masks, respirators may provide greater protection against clinical or bacterial respiratory infection and against self reported ILI, but the studies may have been underpowered to detect a superior protective effect of respirators against influenza [78,90,161]. Evidence of superiority was limited and other studies supported that surgical masks were not inferior to respirators [123,133]. Generally, the findings for the comparative effectiveness of surgical masks and respirators are often inconsistent within and across studies leading to some variability in current guidance documents [78,154,161-165]. No protective effect against SARS was reported for cotton, or paper masks [78].

It is unclear what constitutes a sufficient "threshold" for proactive facemask or respirator use to ensure its effectiveness; similar to hand hygiene, this may vary depending on several factors such as susceptibility of the host, level of exposure and risk of severe outcomes [76]. The frequency of use is an important factor that will influence the intervention effectiveness [76,155]. It is unclear what each study considers as regular, irregular, continuous facemask use in a quantitative manner, so this varied substantially in the included studies [76]; for example continuous facemask 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 [166]. Wearing a surgical mask or respirator from HCWs continuously throughout the work shift was shown to confer significant protection against self-reported clinical respiratory illness and ILI [78]. Wearing a facemask when ill and in close contact with other individuals has been shown to reduce airborne transmission [167].

A combined layered approach may increase the effectiveness of the measures [70,104,155]. 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 [76]. A targeted intervention strategy could be a combined approach, were frequent hand washing is combined with targeted facemask use, especially among high-risk populations (HCWs, school-aged children, the elderly) [104,168].

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, thus reducing their effectiveness, especially in the case of the more demanding respirators [161,169,170]. 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 [155,168].

Conclusively, there is evidence to support facemask 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 compared to facemasks when aerosol-generating procedures are performed [152,154,171-174], although superiority was not shown in all of the studies and universal use throughout the work shift was reported to be likely less acceptable due to greater discomfort [78,89,132,155].

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 [170]. 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 incurred due to facemask supply, disposal and training, with respirators having increased cost compared with surgical masks [175].

Likely acceptability: This measure will likely be highly acceptable among HCWs, 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 [176,177]. Perceived susceptibility to infection is likely to increase intervention uptake [74].

ECDC expert opinion: Surgical facemask use by HCW should be recommended in epidemics or pandemics to reduce transmission, in line with current policies mandating standard and droplet precautions when performing routine care for influenza patients. Respirators should be considered in high risk settings by HCWs especially when aerosol generating procedures are performed. 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 during ordinary seasonal influenza seasons and pandemics.

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: Twenty-one reviews have been included and the evidence is summarised in Table 6. Of those reviews, 11 were systematic (six 'high', three 'moderate' and two 'critically low' AMSTAR 2 score).

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 influenza remained unproven [159]. 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-base and compliance was considered low [146]. Data about the effectiveness of facemask use in such settings are limited, and results are contradictory, highlighting the need for future large-scale studies [145,146,159,178]. See previous 'facemask use in HCSs' chapter on evidence of effectiveness.

Operational considerations: Moderate costs will be incurred 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 selected mass gatherings used facemasks [159], while others suggest that compliance was low [146]. Please also see previous 'facemask use in HCSs' chapter on likely acceptability.

ECDC expert opinion: Use of surgical 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, although most evidence originates from HCSs. Facemask use by healthy individuals may be considered when caring for ill persons, especially 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). Wider use of facemasks may need to be considered in severe situations. Proper use and disposal of masks need to be ensured by training users prior to distribution of masks.

Facemask use outside the home by healthy people

This refers to healthy people in the community widely wearing masks outside the home to protect against acquisition of infection.

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: A recent systematic review and meta-analysis was conducted by WHO to quantify the efficacy of community based use of facemasks in the reduction of LCI [136]. In the pooled analysis, there was a non-significant relative risk reduction of 22% (RR = 0.78, 95% CI: 0.51–1.20, I2 = 30%, p = 0.25) in the face mask group and 8% in the face mask group regardless of the addition of practice of hand hygiene (RR = 0.92, 95% CI: 0.75–1.12, I2 = 30%, p = 0.40) [136]. Please see previous 'Facemask use' chapters for evidence of effectiveness.

Operational considerations: The costs would 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 high [175]. There would also need to be considerable planning to ensure adequate supplies. 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 [175]. 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 the facemask use will also affect its effectiveness; preliminary results related to influenza infections showed poor compliance with the measure [101,107,179]. Patients may wear facemasks to protect themselves from further infection, but often not to protect their surroundings [73,107]. 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 [73,74]. Perceived susceptibility and perceived benefits of mask-wearing appeared to be the most significant factors determining compliance [74]. Perceived barriers included experience or perception of personal discomfort and sense of embarrassment [74].

ECDC expert opinion: There is lack of evidence on effectiveness of wider use of facemasks in community settings, therefore such recommendations should only be considered in severe pandemic scenarios. With extensive implementation of the use of facemasks, the current production capacity of surgical facemasks would be rapidly exceeded, therefore stockpiling facemasks would be needed to ensure the implementation in a pandemic situation. There are implications for training and communication, because proper use and disposal of masks would need to be ensured. Combining facemask use with hand hygiene is likely to increase the effectiveness of the interventions. For high/exposure situations please refer to the 'Facemask use in other high-exposure situations' chapter.

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 facemask or respirator wearing during illness to protect others, and public health emphasis on facemask-wearing during illness may help to reduce influenza virus transmission. There are fewer data to support the use of facemasks or respirators to prevent transmission in households [88,136]. Please see previous 'facemask use' 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 incurred due to the supplies required per person [175]; 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 [57]. 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 masks are recommended exclusively for ill people, some social stigma may be attached to it.

ECDC expert opinion: Available evidence supports recommending facemask use for infected persons when in contact with other individuals. In HCSs the recommended practice for mask wearing should be followed. Depending on the severity of the pandemic, public health authorities should consider recommending facemask use by symptomatic people in the community. This may be the best use of resources when there are limited amounts of facemasks available.

1 **Table 6. Summary of recent reviews and meta-analyses on facemask use effectiveness**

Facemasks and respirators – evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Chao et al., 2017 [171]	Moderate	HCSs (1 study)	Droplet-borne infections	Lack of evidence for the superiority of N95 respirators compared to facemasks against droplet transmission.
Offeddu et al., 2017 [78]	High	HCSs (6 RCTs, 23 observational studies)	Respiratory illness (ILI, bacterial, SARS, other viral infections)	RCTs showed a protective effect of facemasks and respirators against acquisition of 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 [76]	High	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 against acquisition of influenza infection.
Smith et al., 2016 [90]	High	HCSs (3 RCTs, 1 cohort, 2 case-control, 23 surrogate exposure)	Lab-confirmed respiratory infection, ILI, workplace	No significant difference between N95 respirators and surgical masks in associated risk of (a) laboratory-confirmed respiratory infection (RCTs: odds ratio [OR] 0.89, 95% confidence interval [CI] 0.64-1.24; cohort study: OR 0.43, 95% CI 0.03-6.41; case-control studies: OR 0.91, 95% CI 0.25-3.36); (b) influenza-like illness (RCTs: OR 0.51, 95% CI 0.19-1.41); or (c) reported workplace absenteeism (RCT: OR 0.92, 95% CI 0.57-1.50). In the surrogate exposure

				studies, N95 respirators were associated with less filter penetration, less face-seal leakage and less total inward leakage under laboratory experimental conditions, compared with surgical masks, N95 respirators showed a protective advantage over masks in laboratory settings.
Barasheed et al., 2016 [159]	Moderate	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., 2013 [155,161]	Not systematic	HCSs	Respiratory infections	Authors conclude that respiratory and facial protection should be used to reduce transmission via the droplet and/or airborne routes or when airborne particles have been created during aerosol-generating procedures (AGPs). There is no strong evidence on superiority of respirators and the list of AGPs needs to be determined. For AGPs, respirators may be beneficial.
Wei et al., 2016 [167]	Not systematic	Various settings	Respiratory infections	Short-range airborne route is potentially very important and may be controlled by mask use and mechanical or natural ventilation.
MacIntyre et al., 2015 [154]	Not systematic	Community and HCSs	Influenza and other respiratory infections	Of the nine trials of facemasks identified in community settings, in all but one, facemasks were used for respiratory protection of well people. These studies found that facemasks and facemasks plus hand hygiene may prevent infection in community settings, subject to early use and compliance. Two trials in healthcare workers demonstrated greater effectiveness of respirators compared to facemasks. There is lack of evidence of effectiveness of cloth masks.
Smith et al., 2015 [89]	Moderate	Community – adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Evidence supporting facemask use in clinical settings, non-superiority of N95 respirators.

Wong et al., 2014 [86]	High	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 [145]	Not systematic	Community (mass gatherings)	Respiratory tract infections	Contradictory results on effectiveness of masks in Haji and low compliance.
Rainwater-Lovett et al., 2014 [180]	Critically low	Long term care facilities (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.
Haworth et al., 2013 [146]	Not systematic	Community (mass gatherings)	Respiratory tract infections	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 [178]	Not systematic	Mass gatherings	Influenza and other respiratory infections	Mask use may reduce exposure to (inhalation of) droplet nuclei.
Roberge et al., 2011 [177]	Not systematic	Community	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., 2012 [168]	Critically low	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. None of the studies established a conclusive relationship between mask/respirator use and protection against influenza infection. Some evidence suggests that mask use is best undertaken as part of a package of personal protection especially hand hygiene. The effectiveness of masks and respirators is likely linked to early, consistent and correct usage.

Jefferson et al., 2011 [133]	High	Community and hospital settings (56 RCTs, cluster RCTs, observational studies, case-control)	Respiratory viruses	Surgical masks or N95 respirators were effective prevention measures (OR 0.32, CI 0.25 to 0.40), wearing N95 masks (OR 0.09, CI 0.03 to 0.30). N95 respirators and surgical masks equally effective.
Aiello et al., 2010 [101]	Not systematic	Various settings	Influenza	The review concluded that both facemask use and combined approaches with hand hygiene were effective in preventing influenza virus infection.
Cowling et al., 2010 [160]	Critically low	Various settings (6 studies in HC)	Influenza	There is some evidence to support wearing of masks or respirators 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.
Carlson et al., 2010 [123]	Not systematic	HCSs	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., 2009 [132,134]	High	Various settings (4 RCTs, 14 cluster RCTs, 7 case-control, 16 prospective cohort, 5 retrospective cohort, 13 before-after)	Respiratory viruses	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) used 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: 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 [49,155]. 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 [56,57,89,123].

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: Seven reviews have been included and the evidence is summarised in Table 7. Of those reviews, three were systematic (two 'high and one 'critically low' AMSTAR 2 score).

Routine care of seasonal 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 may be needed in these occasions [155,181]. 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. There is lack of reviews focusing on the effectiveness of PPE against pandemic influenza infection.

Overall, data on physical interventions to prevent transmission of communicable diseases support the use of gowns, gloves, face shields and respiratory protection accompanied by hand hygiene in HCSs [123,182]. A meta-analysis suggested that physical measures are highly effective in preventing the spread of SARS: wearing masks, wearing gloves, wearing gowns and handwashing more than 10 times daily [132,134]. A combination of masks, gloves, gowns and handwashing, was also effective in interrupting the spread of influenza within households [132,134]. A literature review on the influenza outbreak control practices and the effectiveness of interventions in long-term care facilities, showed that PPEs may have modest protective effects [180]. Another review suggested that all means combined (handwashing, masks, gloves and gowns) achieved very high effectiveness [133].

Operational considerations: Additional costs due to the purchase of such equipment will be incured 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 [81]. 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 [81].

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

ECDC expert opinion: Available evidence supports recommending use of PPE is in health care settings, when performing aerosol-generating procedures or when risk of exposure to respiratory secretions is high. The selection and use of PPEs must be accompanied by appropriate education and training. PPE should always be used in combination with proper hand hygiene measures and proper equipment disinfection or disposal.

Table 7. 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	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Bunyan et al., 2013 [155,161]	Not systematic	HCSs	Respiratory infections	Authors conclude that respiratory and facial protection should be used to reduce transmission via the droplet and/or airborne routes or when airborne particles have been created during aerosol-generating procedures (AGPs). There is no strong evidence on superiority of respirators and the list of AGPs needs to be determined. For AGPs respirators may be beneficial.
Kilinc et al., 2015 [81]	Not systematic	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 [180]	Critically low	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.
Jefferson et al., 2011 [133]	High	Community and hospital settings (56 RCTs, cluster RCTs, observational studies, case-control)	Respiratory viruses	Barriers were shown to be effective in combination (handwashing, masks, gloves, gowns) (OR 0.09, CI 0.02 – 0.25) – result from two studies.
Jefferson et al., 2009 [132,134]	High	Various settings (4 RCTs, 14 cluster RCTs, 7 case-control, 16 prospective cohort, 5 retrospective cohort,	Respiratory viruses	Highly effective in preventing the spread of severe acute respiratory syndrome: wearing masks (OR 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,

		13 before-after)		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. Effective also in paediatric ward or combined with isolation.
Carlson et al., 2010 [123]	Not systematic	HCSs	Influenza	Data support the use of hand hygiene, gowns, gloves, face shields and respiratory protection.
Weber et al., 2010 [182]	Not systematic	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.

Environmental measures

Environmental countermeasures include routine cleaning of frequently used surfaces and objects and minimized sharing of routinely touched objects. 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 [121,183]. 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 [184]. 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 [184]. It may therefore assist in the refreshment of air from aerosolised influenza particles that cause infection through inhalation or contaminate surfaces and objects.

Evidence of effectiveness: Eighteen reviews have been included and the evidence is summarised in Table 8. Of those reviews, four were systematic (three were assessed and had 'moderate' AMSTAR 2 score). Overall, there is indirect evidence for the effectiveness of environmental measures that mostly originate from studies suggesting that they can mechanically reduce the viral load from surfaces/objects/air.

Studies have shown that disinfection of surfaces and objects reduces the risk of infection and the spread of influenza and other respiratory viruses [89,185-188]. 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 [189]. 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 [186]. 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 [185].

Although direct evidence of effectiveness against influenza infection is limited, the routine surface cleaning measures are considered to reduce the spread of viruses, like SARS and influenza and HC associated infections [183,190-193]. WHO has conducted a systematic literature review and identified three studies (two RCTs and one cross-sectional study) with evidence on object and surface cleaning effectiveness [136]. There was evidence that this could reduce detections of virus in the environment, but there was no evidence of effectiveness against LCIs [136]. Influenza viruses are sensitive to disinfection and can be removed from surfaces by routine cleaning using detergent-based cleaners (e.g. regular soap) or bleach. Other common disinfectants and heat have been also found effective at inactivating influenza viruses [194]. Phenolic compounds and glutaraldehyde were found to be effective against viruses [190]. Other means for inactivation of influenza viruses include methylene 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 (10 parts per million hydrogen peroxide) that is used in HCSs is found to have virucidal properties also for viruses dried on surfaces [193,195,196]. Vapour concentrations of 2 parts per million triethylene glycol can provide effective surface disinfection [197]. Formaldehyde and alcohol were also considered effective against pathogens and they are compatible with aircraft components [198]. On the other hand, surface-dried viruses were found to resist glucoprotamin-based disinfection [199]. In addition, it has been shown that the exposure of surfaces to disinfectants alone might be insufficient for virus inactivation and mechanical action should be applied to bring attached viruses into contact with virucidal compounds [199]. Self-disinfecting surfaces are under active investigation and could prove useful, especially in HCSs [200]. 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) [200]. Copper alloy surfaces have been considered effective in reducing the microbial load, although their effectiveness specifically against influenza viruses has not been studied [201-206].

To help prevent airborne infections, adequate ventilation in HC facilities in all patient-care areas is considered necessary [184,207,208]. It has been suggested from national guidance documents 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. There is mechanistic possibility for increased ventilation to reduce mainly aerosol transmission, and to a lesser extent droplet and indirect contact transmission and maintain the appropriate humidity levels in the air [136,209]. The ventilation rate, airflow pattern and flow direction impacts the effectiveness [207]. 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 [207]. Fresh air natural ventilation and sunlight has been shown to reduce the risk of infection [210,211]. However, evidence on the effectiveness of different ventilation measures are limited [144]. WHO recently conducted a systematic literature review to which only three simulation studies were identified [136]. It is concluded that there is mechanistic plausibility that increased ventilation may reduce influenza virus transmission, especially aerosol-mediated transmission [136].

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 [193,212]. 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 [200,213,214]. As influenza virus prefers low humidity levels, humidification is another measure that has been proposed [215]. WHO recently conducted a systematic literature review to which no evidence were identified that increasing or decreasing humidity is an effective intervention [136]. The use of novel disinfectants and no-touch decontamination technologies to improve disinfection of surfaces in healthcare is supported by some studies [214,216]. 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.

ECDC expert opinion: Available indirect and limited (for some measures) evidence supports recommending the use of environmental measures such as surface cleaning and disinfection, and sufficient ventilation, during epidemics and pandemics due to the transmission modes of influenza viruses and the potential of these measures to reduce transmission. Routine cleaning of frequently used surfaces and objects, minimal sharing of routinely touched objects and air ventilation are especially important in settings where people gather regularly.

There is lack of direct evidence on effectiveness against LCI and effectiveness on mitigating the pandemic. Evidence to support use of low-dose far UV-light and air humidification as a disinfection measure against influenza is not sufficient.

1 **Table 8. Summary of recent reviews and meta-analyses on effectiveness of environmental measures**

Environmental measures- Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Qian et al., 2018 [207]	Not systematic	HCSs	Respiratory viruses	Properly used ventilation systems can reduce the risk of airborne infection significantly.
Rajakaruna et al., 2017 [208]	Not systematic	HCSs	SARS, Ebola, MERS	Use of quarantine and ventilation functions supported.
Boyce et al., 2016 [214]	Not systematic	HCSs	Various pathogens	Newer disinfectants and no-touch decontamination technologies will improve disinfection of surfaces.
Cook et al., 2016 [203]	Not systematic	N/A	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 [198]	Not systematic	Aircraft	Various hogens	Formaldehyde, hydrogen peroxide, and alcohol allow the varying techniques of standard disinfection of surfaces.
Muller et al., 2016 [204]	Moderate	HCSs (11 studies on microbial contamination using copper alloy surfaces)	Various pathogens	Copper alloy surfaces have antimicrobial properties and are effective against health care associated infections (HCAI). Limited information on viruses.
Otter et al., 2016 [183]	Not systematic	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

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				surface contamination), droplet, and airborne routes.
Thomas et al., 2016 [196]	Not systematic	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.
Wei et al., 2016 [167]	Not systematic	Various settings	Respiratory infections	Short-range airborne route is potentially very important and may be controlled by mechanical or natural ventilation.
Lidal et al., 2015 [144]	N/A*	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 [89]	Moderate	Community – adults (2 RCTs, 5 cluster RCTs)	Influenza infections	Limited information on effectiveness of surface disinfection effectiveness.
McLean et al., 2014 [213]	Not systematic	-	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 [191]	Moderate	Day-care centres (8 guidelines)	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 [210]	Not systematic	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 [193]	Not systematic	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 [200]	Not systematic	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 [201]	Not systematic	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 [205]	Not systematic	Various settings	Microbes	Effectiveness of metallic copper surfaces.

*Not assessed because only short version was available in English

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, while others lack direct evidence of 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 [79,100,217-221]. 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 [70,222]. 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 [21,223]. 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 [71]. Common perceived barriers included beliefs about personal susceptibility, transmission of infection and concerns about self-diagnosis in emerging respiratory infections [71]. 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 [224].

ECDC expert opinion: Available evidence supports a layered approach of social distancing measures, depending on the severity level and the impact of the pandemic. Such measures may potentially have a high societal impact, so they would be mostly applicable in more severe pandemics. In the following chapters, the social distancing measures are considered separately.

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 or depending on the estimated infectious period of the pandemic virus).

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

Rationale: Typically, influenza virus can be transmitted 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. This may vary in the pandemic situation, according to the characteristics of the pandemic strain. Isolation of infected individuals should reduce the likelihood of transmission and spread of the virus.

Evidence of effectiveness: Four reviews have been included and the evidence is summarised in Table 9. Of those reviews, three were systematic (two 'high' and one 'critically low' AMSTAR 2 score).

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 [225]. This limits the efficacy of isolation, with maximum effectiveness if individuals are completely isolated almost immediately after contact with an infected person

[41]. Generally, the measure is considered effective, although the quality of evidence is low and partly originating from modelling studies. There is also an increased risk of intra-household transmission from index cases to contacts that may be reduced with the use of antiviral prophylaxis of household members (if available) [70,100,133]. 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 [226]. In the case of young children and immunocompromised patients, viral shedding and its duration will likely be increased.

WHO recently conducted a systematic literature review, to which four epidemiological studies and 11 simulation studies (and therefore evidence of low strength) were included. They suggested that isolation of sick individuals could reduce transmission in epidemics and pandemics [136,227-229]. There is also mechanistic plausibility for this measure to be effective in reducing transmission [136].

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 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 [71]. 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% [73].

ECDC expert opinion: Available evidence supports recommending voluntary isolation of infected individuals 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 needs to be carefully planned. 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 plague into these cities.

Voluntary quarantine of household contacts of a person with suspected influenza refers to remaining at home for a defined period (e.g. for the incubation period) 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: Four reviews have been included and the evidence is summarised presented in Table 9. Of those reviews, three were systematic (two 'high' and one 'critically low' AMSTAR 2 score).

Implementing transmission barriers, like quarantine, are considered effective at containing respiratory virus epidemics [70,132,133]. Most of the evidence originate from modelling studies that suggest that cumulative attack rates would be reduced by such measures although some argue that the reduction would be less than might be thought intuitively [227,228]. Household quarantine alone reduced overall AR by 10% and peak AR by 20%, whereas a 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% [228]. 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 [230]. WHO recently conducted a systematic literature review, to which six epidemiological and 10 simulation studies were included; overall, quarantine was effective in reducing burden of disease, transmissibility and in delaying the peak of the epidemic [136]. Some studies suggested a significant improvement in effectiveness of quarantine when combined with other measures, such as isolation, antiviral drug prophylactic use or school closure [136]. Severity is an important determining factor in the definition of a pandemic when considering to undertake such social distancing measures [231]. 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. The likelihood of a household contact who is concurrently quarantined with an isolated individual, becoming infected has been estimated to increase with each day of quarantine The likelihood of a household contact who is quarantined with an isolated patient becoming a second case has been estimated to increase with each day of quarantine [136,232].

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 [233]. 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 [233]. Experience from previous pandemics and the SARS epidemic is variable but often negative in communities with cultural similarities to Europe [105,234]. If such disruptive measures are implemented, national laws and regulations will need to be considered.

ECDC expert opinion: Available, limited, evidence, originating mainly from modelling studies that are considered evidence of weak strength, support recommending voluntary quarantine based on a situational risk assessment. Voluntary quarantine may delay the start of the local epidemic during early stages of pandemics, and as such it is an option that may be considered during pandemics of high severity, although the dis-benefits and issues of compliance would need to be carefully weighed against the benefits. Antiviral prophylaxis will further decrease the risk of infection among exposed persons, at least in household settings. Rapid identification of cases in the household will enhance the effectiveness of quarantine. If such a measure is implemented, support to households that are affected as a whole should be planned. Training/education on infection control in the home would be necessary.

Table 9. 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	AMSTAR 2	Setting (included	Infection	Conclusions

	score	studies)	type	
Rashid et al., 2015 [100]	Not systematic	Various settings	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.
Jefferson et al., 2011 [133]	High	Community and hospital settings (56 RCTs, cluster RCTs, observational studies, case-control)	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., 2009 [132,134]	High	Various settings (4 RCTs, 14 cluster RCTs, 7 case-control, 16 prospective cohort, 5 retrospective cohort, 13 before-after)	Respiratory viruses	Limited evidence showing social distancing is effective, especially if related to risk of exposure. Early identification of cases followed by isolation was effective.
Lee et al., 2009 [70]	Critically low*	Community (19 modelling studies)	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).

*According to AMSTAR 2 graded as critically low due to lack of description of risk of bias for their included studies, which may however not be appropriate for the included studies.

Interventions in educational and child care settings

School closure policies as an example of social distancing measures have been considered as a policy to mitigate influenza epidemics and pandemics spread [235]. 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 [235]. 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 [77].

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 [236].

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 [229].

Proactive school and day care closures

Proactive closures refer to the early and planned closure of schools and day care facilities 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 and children attending day care facilities 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: Six reviews on the effectiveness of school closures have been included and the evidence is summarised in Table 10. Of those reviews, four were systematic (all had 'critically low' AMSTAR 2 score, although the AMSTAR 2 tool may not be an appropriate tool to score three of these reviews that included only observational or modelling studies).

Reviews suggest that school closures can be a useful and effective control measure during an influenza pandemic, particularly for reducing peak demand on health services [9,100,136,220,221]. Some observational analyses have shown a decrease in virus transmission during seasonal influenza outbreaks or pandemics that coincided with school holidays [105,111,237,238]. The positive effects were however smaller than predicted by some modelling studies, perhaps because children also mix outside schools [179,236,239-242]. 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 [9,236,243]. Modelling studies generally support school closures and confinement in the home, as an effective measure for reducing overall attack rates within communities, especially when coupled with antiviral prophylaxis [70,242].

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, although they were not necessarily effective (or the effect could not be readily measured) for reducing overall community transmission [235].

A recent meta-analysis also investigated the impact of school closure and the optimal duration of closure [244]. 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 [244]. These findings suggest that policy makers could consider school closure policies as a response strategy to influenza pandemics, depending on the feasibility and the cost [84,244,245].

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 to activate and de-activate the measure, 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 [219]. Please also see 'Reactive school closure' chapter for evidence of effectiveness.

Operational considerations: There can be financial and practical disincentives [235] 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 [236]. School closures have the potential to cause adverse consequences, which may likely disproportionately affect students, families and the communities [246,247]. There would be disruption of education, as well as other services provided by the schools (e.g. school meals, doctor visits). Legal issues would need to be closely monitored [235]. The disruption caused by school closures would 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 [248]. Moderate costs will be incurred due to the planning and logistics of school closures. There is a need for studies of the cost-effectiveness of this measure [248]. Existing studies suggest that school closures may not be cost effective for mild pandemics, although they might be for more severe situations [249].

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 managed [84,221,250].

ECDC expert opinion: Available evidence supports recommending proactive closures of schools and day care facilities only during severe epidemics and pandemics, as they can be associated with significant societal and economic costs. The extent of proactive school closures should be decided taking into account the balance of the assessed severity level of the pandemic compared to the adverse effects of such closures on the community. The optimal timing and duration of the implementation of the measure would need to be carefully considered on a case-by-case basis. Whole-of-society plans to mitigate secondary effects should be considered. Policy makers should also consider intermediate options, such as partial school closures. 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 [236,251].

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: Six reviews on the effectiveness of school closures have been included and the evidence is summarised in Table 10. Of those reviews, four were systematic (all had 'critically low' AMSTAR 2 score, although the AMSTAR 2 tool may not be an appropriate tool for three of these reviews that included only observational or modelling studies).

The effectiveness of reactive school closure in reducing influenza transmission varied in the included studies, but was generally limited. 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%, 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% [70,228]. During the 2009 A(H1N1) pandemic, closures mostly occurred in schools that reported significant illness and were likely motivated by excessive absenteeism, rather than done proactively [252].

Few studies have analysed more specific policies; one model-based analysis categorised four types of school closures: reactive gradual closure, starting from class-by-class, then grades and finally the whole school [84]. 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 considered 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 [84]. Please see 'Proactive school closure' chapter.

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

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

ECDC expert opinion: Available evidence, which is generally of low quality and based on modelling studies, do not provide support for reactive school and day care closures on order to impact the evolution of a pandemic. Reactive school closures may however be necessary to prepare for, due to high absenteeism and operational issues. As for proactive school closures, the timing and duration of the closures 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. Whole-of-society plans to mitigate secondary effects should be considered.

1 **Table 10. Summary of recent reviews and meta-analyses on school closure effectiveness**

School closures- Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Bin Nafisah et al., 2018 [244]	Critically low	Educational settings (31 studies)	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 [224]	Not systematic	Educational settings	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 [100]	Not systematic	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 [220]	Critically low*	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 [219]	Critically low*	Educational settings (79 epidemiological	Influenza	Effective to reduce influenza transmission, but due to

		studies)		heterogeneity in the available data optimum strategy remains unclear (e.g. ideal length and timing of closure).
Lee et al., 2009 [70]	Critically low*	Educational settings (19 modelling studies)	Influenza	Effective if done early, decisively, and for prolonged periods.

* According to AMSTAR 2 graded as critically low due to lack of description of risk of bias for their included studies, which may however not be appropriate for the included studies.

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 of 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 [70].

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: Six reviews have been included and the evidence is summarised in Table 11. Of those reviews, five were systematic (two 'high', two 'moderate' and one 'critically low' AMSTAR 2 score, although the AMSTAR 2 tool may not be an appropriate tool to score one of these reviews that included only modelling studies).

Influenza attack rates in working-age adults (aged 18-64 years) have been reported to be as high as 15.5% over an influenza season [24]. Measures at work, such as home working, are considered modestly effective and could reduce the overall and peak number of influenza cases, as well as delaying the peak occurrence [100,253]. Combination with other interventions can improve the effectiveness [136].

Overall the evidence on effectiveness of workplace closures is limited and of low strength, mostly originating from simulation studies [136]. 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 [72,228,254,255]; 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 [70]. Workplace closures in combination with home working were found to be modestly effective and were acceptable, but likely to be economically disruptive [100]. Overall, large-scale workplace closures could delay the epidemic peak for more than 1 week, and small-scale closures may have a modest impact on attack rate or peak number [136]. 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 [105,111]. 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 [253]. 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 [253]. It also delayed and reduced the peak influenza attack rate [253]. 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 [253].

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 [256]. 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 and effective.

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.

ECDC expert opinion: Available evidence supports recommending measures at workplaces (e.g. teleworking, social distancing), which can be modestly effective and feasible during all phases of a pandemic. The selection of measures will depend on the company and the type of work and may have significant economic and social consequences. Other personal protective and environmental measures should be applied in combination with workplace measures. Limited evidence from modelling studies support recommending workplace closures in pandemics of higher severity. Business continuity plans should include pandemic scenarios.

Table 11. Summary of recent reviews and meta-analyses on effectiveness of measures at workplaces and public places

Workplace/Public place measures- Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Ahmed et al., 2018 [253]	Moderate	Workplaces (12 modelling studies, 3 epidemiological)	Pandemic Influenza	Epidemiological and modelling studies indicated that workplace social distancing reduced the overall number of influenza cases. It also reduced and delayed the influenza peak. 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 [125]	Moderate	Workplace settings (3 cluster RCTs, 2 prospective interventional, 2 pre-post design)	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 [100]	Not systematic	Various setting	Pandemic influenza	Work closure and home working are also modestly effective and are acceptable, but likely to be economically disruptive.
Jefferson et al., 2011 [133]	High	Community and hospital settings (56 RCTs, cluster RCTs, observational studies, case-control)	Respiratory viruses	Insufficient evidence to support social distancing (spatial separation of at least one metre between those infected and those non-infected).
Jefferson et al., 2009 [132,134]	High	Various settings (4 RCTs, 14 cluster RCTs, 7 case-control, 16 prospective cohort,	Respiratory viruses	Limited evidence for social distancing being effective, especially if related to risk of exposure.

		5 retrospective cohort, 13 before-after)		
Lee et al., 2009 [70]	Critically low*	Community (19 modelling studies)	Influenza	Workplace closures in combination with other measures may be effective, although will have marked implications.

* According to AMSTAR 2 graded as critically low due to lack of description of risk of bias for their included studies, which may however not be appropriate for the included studies.

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 [257-262]. Combined use of other NPCs will aim to reduce the person to person viral transmission.

Evidence of effectiveness: Six reviews on the effectiveness of measures in mass gatherings have been included and the evidence is summarised in Table 12. Of those reviews, two were systematic (2 'moderate' AMSTAR 2 score).

Large meetings, conferences, religious pilgrimages, sports events and other national and international events play an important role in spreading infectious diseases [257,261-267]. In the case of gastrointestinal and respiratory illnesses, the explosive spread following small or large gatherings is commonly reported [145,264,265]. The most common outbreaks at these mass gatherings involve respiratory infections and vaccine preventable diseases, mainly influenza and measles [83,145,159].

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 [136,145]. Models suggest that cancellation of non-essential public gatherings might help to decrease rates of transmission and overall morbidity, but the effectiveness of the intervention has not been quantified [41,257]. 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 [268]. A modelling study has 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 [269]. 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 case-by-case approach for any upcoming events in their countries [235].

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 [145]. 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 [159], while others suggested that adherence was low [145,146]. Facemask use seems to be beneficial against certain respiratory infections at mass gatherings, although evidence is lacking regarding the effectiveness against influenza [145,146,159,178].

Operational considerations: There will 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 based on the perceived pandemic severity. The use of other NPCs during mass gatherings will also be likely acceptable [270].

ECDC expert opinion: Available limited evidence, mainly from modelling studies, supports recommending cancellations of mass gatherings only before the peak of severe pandemics.

Available limited evidence, mainly indirect in describing the extent of transmission that takes place during mass gatherings, supports recommendations for other measures (e.g. facemask use, web-casting, education campaigns, environmental measures) during moderate or more severe pandemics, depending on the type of the event and a risk assessment. The risk assessment should consider the severity assessment of the pandemic, the local pandemic situation, the timing, duration, type of venue (indoor/outdoor) and size of the event and the area from and to which the attendees are commuting (affected or non-affected). Instead of cancellation, the postponement or re-scheduling of the event can be considered. Other personal protective and environmental measures should be considered in combination.

Table 12. Summary of recent reviews and meta-analyses on mass gathering measure effectiveness

Mass gatherings- Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Hoang et al., 2018 [264]	Not systematic	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 [159]	Moderate	Mass gatherings (12 cross sectional, 10 cohort, 2 case studies, 1 RCT)	Respiratory infections	Pooled estimate showed significant protectiveness of facemasks 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 [145]	Not systematic	Mass gatherings	Respiratory tract infections	Contradictory results for effectiveness of hand washing, cough etiquette and facemasks. Low compliance with travel advice to postpone participation.
Al Tawfiq et al., 2013 [178]	Not systematic	Mass gatherings	Respiratory tract infections	The practice of social distancing, hand hygiene, and contact avoidance was associated with reduced risk of respiratory illness.
Haworth et al., 2013 [146]	Not systematic	Mass gatherings	Respiratory tract infections	Observational studies failed to demonstrate any clear benefit of using facemasks or hand washing among Hajj pilgrims.

Ishola et al., 2011 [268]	Moderate	Mass gatherings (9 observational, 7 outbreak reports, 3 historical outbreak analyses, 4 event surveillance reports, 1 quasi-experimental study)	Influenza	Some evidence suggests that restricting mass gatherings together with other social distancing measures may help to reduce transmission. However, the evidence is not strong enough to advocate legislation or proscription. 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].

Nine reviews on the effectiveness of travel-related measures have been included and the evidence is summarised in Table 13. Of those reviews, five were systematic (two 'high' and one 'moderate' and two 'critically low' AMSTAR 2 score, although the AMSTAR 2 tool may not be an appropriate tool to score one of these reviews that included only modelling studies).

International and domestic travel advice

Travel advice (or travel recommendations) can refer to official government advice, which has legal and economic implications on 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: There is lack of evidence of effectiveness of travel advice on reducing influenza transmission.

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 and modelling studies suggest in order to have a small delaying effect, adherence to international advice should be 100% [271]. While border control is considered impractical and ineffective (see next chapters), travel advice, even at border entry points is considered to be likely more effective 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 [46]. There is, however no evidence to quantify the effectiveness of travel advice during an influenza pandemic.

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.

ECDC expert opinion: Although there is lack of evidence to quantify the effectiveness of travel advice to mitigate a pandemic, issuing relative travel advice, particularly regarding personal protective measures, consistent with IHR and national law, is recommended during the early stages of 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: The reviews on travel-related measures that have been included in this document are presented in Table 13.

Experience from the SARS outbreak and influenza 2009 pandemic showed that both entry and exit screening were ineffective in preventing spread [136,272,275]. 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 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 studies [271].

Reviews suggested that there is insufficient evidence that support screening at entry/exit points [46,132-134]. Studies from the 2009 pandemic found that the positive predictive value of detecting a laboratory-confirmed pandemic influenza using NCITs ranged from 0.9% to 76.0%, and was likely to be too low to effectively detect and contain pandemic infection [276]. Molecular diagnostics or point of care antigen detection tests could be considered, but will be expensive, resource intensive if used in a large population and there is no evidence of effectiveness to mitigate a pandemic [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].The general consensus appears to be that even rigorous and extensive border control measures will likely delay the spread of pandemic influenza by only a few days [9,280]. It is 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 would 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 would 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, if undertaken, 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.

ECDC expert opinion: The available 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 of current systems 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: The reviews on travel-related measures that have been included in this document are presented in Table 13.

Overall, the evidence for the effectiveness of internal travel restrictions mainly originate from simulation studies and are therefore of lower strength [136]. This measure may 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 [99,100]. Internal mobility restriction could be effective only if prohibitively high (50% of travel) restrictions are applied [100]. 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 [41,257]. A systematic review has concluded that internal travel restrictions could delay the spread of influenza epidemics by one week [80,281]. In this review, 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 [80]. 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 [72,80], although combined approaches (antiviral treatment and prophylaxis, household quarantine, school and workplace closure, combined with effective border control) have been shown to be increase effectiveness [228]. 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 [55,282].

Operational considerations: There would 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 would be considerable though internal travel is likely to decline anyway. Other direct costs on travel-dependent industry and trade would 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].

ECDC expert opinion: Available evidence does not support recommending domestic travel restrictions, except for very specific, isolated, settings. Broad domestic travel restrictions are unlikely to have a major impact on transmission in modern, mainly urban, populations. They have significant economical, legal and ethical implications and should only be considered in early phases of pandemics with extraordinary high consequences.

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: The reviews on travel-related measures that have been included in this document are presented in Table 13.

Systematic reviews mainly based on modelling studies (and therefore provide evidence of lower strength) have 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 depending on the extent of its implementation [70,80,136]. There will be limited effectiveness from border closures, unless almost complete and rapidly implemented in the early pandemic phases [46]. Travel restrictions reduced the incidence of new cases by less than 3%, while the positive impact was even more reduced when restrictions were implemented more than six weeks after the notification of epidemics or when the level of transmissibility was already high [80].

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 [80]. The experience is that, unless there is almost complete stop of travel to a country, the attempts of border closure will be unsuccessful in preventing entry [271]. 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 undesirable due to massive secondary effects [37].

Operational considerations: There would be massive secondary effects within Europe due to the high extent of essential day-to-day travel across borders. For most settings in Europe, the direct and indirect costs of trying to close borders would be very high. Border closures should be carefully considered even in small island nations, because they may affect the supply of essential items to the population.

Likely acceptability: The general public and decision-makers may perceive the need to close borders during a pandemic.

ECDC expert opinion: Evidence mainly originating from modelling studies shows that border closures may delay the introduction of influenza into a country only in specific contexts, such as on small, isolated, island nations, if they are almost complete and rapidly implemented in the early pandemic phases. Available evidence therefore does not support recommending border closures in Europe. Border closures will create large secondary effects and significant societal and economic disruption. Due to public health risks, they are regulated internationally under the IHR. Within the EU, freedom of movement may be limited for public health reasons within the limits of the EU Treaties and in accordance with Directive 2004/38/EC (art. 29).

1 **Table 13. Summary of recent reviews and meta-analyses on travel-related measure effectiveness**

Travel-related measures – Evidence of effectiveness				
Study	**AMSTAR 2 score**	**Setting (included studies)**	**Infection type**	**Conclusions**
Huizer et al., 2015 [46]	Not systematic	Community	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 [100]	Not systematic	Various settings	Pandemic influenza	Internal mobility restriction is effective only if prohibitively high (50% of travel) restrictions are applied.
Selvey et al., 2015 [272]	Not systematic	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 [80]	Moderate	Community (19 modelling, 1 time-series analysis, 2 literature reviews and 1 systematic review)	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 and 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., 2011 [133]	High	Community and hospital settings (56 RCTs, cluster RCTs, observational studies, case-control)	Influenza	Insufficient evidence to support screening at entry/exit points.
Cowling et al., 2010 [280]	Not systematic	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., 2009 [132,134]	High	Various settings (4 RCTs, 14 cluster RCTs, 7 case-control, 16 prospective cohort, 5 retrospective cohort, 13 before-after)	Respiratory viruses	Insufficient evidence to support screening at entry/exit points.
Bitar et al., 2009 [276]	Critically low	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.
Lee et al., 2009 [70]	Critically low*	Community (19 modelling studies)	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.

* According to AMSTAR 2 graded as critically low due to lack of description of risk of bias for their included studies, which may however not be appropriate for the included studies.

4. 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 instil 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 [redacted] 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; an option would be to establish collaborations and sleeping contracts, with pre-approved protocols, in advance of a future pandemic that can be activated when needed. 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 and feasibility studies [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 [78].

Influenza transmission

Enhancing knowledge in the area of influenza transmission and shedding is crucial for 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 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 [78]. There is lack of evidence on effectiveness of cough 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].

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Annex. I

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 ("pharmaceutical"[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 "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 ("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 ("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]

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	(("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]

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	(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] OR "isolation"[All Fields]) AND ("pandemics"[MeSH Terms] OR "pandemics"[All Fields] OR "pandemic"[All Fields]) AND Review[ptyp]
School closure	(("schools"[MeSH Terms] 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] [MOR ("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 ("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 restriction[All Fields] AND effectiveness[All Fields]) AND Review[ptyp]
	(("border"[All Fields]) AND closure[All Fields] AND effectiveness[All Fields]) AND Review[ptyp]