GLOBAL INFLUENZA PROGRAMME

BACKGROUND DOCUMENT
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PUBLIC HEALTH
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AGENDA FOR
INFLUENZA

advance science to address unmet public health needs

2017 UPDATE

LIMITING SPREAD

Limiting the spread of pandemic, zoonotic, and seasonal epidemic influenza

World Health Organization

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Limiting the spread of pandemic, zoonotic, and seasonal epidemic influenza

WHO Public Health Research Agenda for Influenza 2017 Update

Contents

BACKGROUND DOCUMENT

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Abbrevations

ILI	Influenza-like Illness
IPP	Invasive Pneumococcal Pneumonia
LTCF	Long-term Care Facility
PCR	Polymerase Chain Reaction
SARS	Severe Acute Respiratory Syndrome
WHO	World Health Organization

STREAM 2

2.0 Introduction

Influenza causes a substantial disease burden worldwide. An estimated 5–20% of the world's population is affected each year by seasonal epidemic influenza. Pandemics arise through antigenic shifts that result in a new virus that is not related to previous human seasonal influenza viruses. The population lacks immunity to the new pandemic virus, which therefore causes widespread infection. Influenza pandemics and epidemics can have substantial effects on health (e.g. clinical illness, hospitalization and death) and socioeconomics (e.g. absenteeism from work and, in the case of pandemics, decreased travel and trade).

Globalization has led to increased travel and trade both within and between countries; in turn, this has resulted in the rapid spread of disease. This situation was typified by the rapid spread of severe acute respiratory syndrome (SARS) across three continents within weeks in 2003 (Skowronski et al., 2005) and by pandemic (H1N1) 2009 influenza.

Preparedness, early detection and outbreak response are critical elements in limiting the spread of seasonal and pandemic influenza at the local, national and global levels. However, controlling the spread of influenza has been challenging. There is a lack of definitive scientific evidence on important aspects of disease transmission and on the effectiveness of different strategies to limit transmission. Expansion of the current evidence base is critical for formulating evidence-based preparedness and response measures that are effective while also being minimally disruptive to individuals and communities.

This document updates the substantial body of research that has been undertaken since the 2009 WHO Research Agenda (including the scientific review of 2011) to identify research gaps and unmet public health needs, and inform future areas of research. To assist in identifying key research questions related to the control of influenza, this document highlights available information as well as gaps in our knowledge in three main areas:

- factors affecting human-to-human transmission of influenza;
- the dynamics of virus spread at the global and local levels; and
- the effectiveness of public health measures to limit the spread of influenza.

Substream 2.1
Factors affecting person-to-person transmission

To formulate and implement effective influenza control measures (e.g. personal hygiene measures, social distancing, and infection prevention and control), it is critical to understand the factors affecting transmission of influenza among humans. Despite new research, there is insufficient evidence in key areas; for example, how influenza spreads and transmission patterns in different settings. In this section we discuss current knowledge about the transmission of influenza among humans and identify important knowledge gaps.

Research recommendation 2.1.1

The relative importance of droplet, contact and airborne transmission in seasonal and pandemic influenza for effective intervention planning

Summary of key accomplishments 2.1.1

Mode of spread of influenza

Previous research suggested that respiratory droplets are the main mode of transmission of influenza (Bridges, Kuehnert & Hall, 2003). However, since the last review in 2010–2011 (World Health Organization, 2013), evidence for the biological plausibility of aerosol transmission (see Box 2.1) of influenza has increased, with studies showing infectious virus in aerosols produced by infected individuals, and showing that aerosols are more likely to transmit over a short range than a long range (Bischoff et al., 2013; Cowling et al., 2013; Lindsley et al., 2016; Milton et al., 2013). The clinical impact of aerosol transmission was previously thought to be low (Brankston et al., 2007), but recent data suggest a more substantial impact. For example, a modelling study on secondary infections demonstrated that aerosol transmission constitutes about half of all transmission events in households (Cowling et al., 2013).

Transocular entry of live attenuated influenza vaccine was detected in volunteers in a recent study, and it has been suggested that ocular protection may have to be considered in addition to classic respiratory protection (Bischoff et al., 2011). Transocular protection should be considered based on risk (e.g. it may be required when performing aerosolizing procedures or dealing with novel influenza).

Influenza was previously thought to be spread via direct contact of the respiratory mucosa with contaminated fomites such as hands or towels (Bean et al., 1982; Morens & Rash, 1995). Contact transmission and virus contamination on household surfaces and the fingertips of infected children have been demonstrated in household transmission studies (Simmerman et al., 2010). However, more recent studies have suggested that contact transmission may be less important a route than previously assumed, with influenza viruses not detected on high-touch surfaces in public and hospital settings (Killingley et al., 2016; von Braun, Thomas & Sax, 2015).

Box 2.1 – Definitions of aerosol transmission

Aerosol transmission is a form of transmission resulting from the inhalation of a suspension of tiny infectious particles or droplets in the air, where particles up to 100 µm in size are considered inhalable (inspirable). Aerosols are generated through bodily processes (e.g. cough, sneeze, talking, exhaling) and medical procedures (Jones & Brosseau, 2015).

Airborne transmission is a form of transmission resulting from the inhalation of either infectious droplet nuclei (small-particle residue [generally <5 µm in diameter] of evaporated droplets containing microorganisms that remain suspended in the air for long periods of time) or dust particles containing the infectious agent (Garner, 1996).

Furthermore, studies investigating indirect transmission via finger contamination showed that the virus does not survive long on fingers and contaminated skin (Mukherjee et al., 2012; Thomas et al., 2014). The significance of this route of transmission relative to other routes remains unclear.

Distance of close contact

Close-range transmission of influenza has been assumed to be primarily due to droplet or aerosol transmission. There have been no new studies since the last review. Previous studies found that droplets travel only a short distance through the air, and close contact with an infected person has been often cited as a risk for exposure and subsequent infection. Public health policies for tracing close contacts or infection control guidance often use a distance of up to 2 metres or 6 feet.

Viral properties

Previous studies found that the likelihood of individual infection and transmission is affected by viral properties such as the fitness for replication in the respiratory tract and the relative preference for localization of replication in the upper respiratory tract versus the lower respiratory tract (Nicholls et al., 2007; Nicholls et al., 2008). Upper respiratory tract infections (the usual site of infection for seasonal and pandemic influenza) may be more likely than lower respiratory tract infections to result in viruses being expelled and circulated through coughing or sneezing. In avian influenza viruses, there is new research on the viral properties that affect replication and transmissibility (de Vries et al., 2014; Yamaji et al., 2015), such as the role of several amino acid mutations in aiding avian virus adaptation to mammalian hosts.

Unmet public health needs and knowledge gaps 2.1.1

The unmet public health needs for Recommendation 2.1.1 are to:

- determine the relative importance of various modes of influenza transmission for effective intervention planning; and
- understand the factors constituting an aerosol-generating procedure for infection control guidance.

Knowledge gaps include:

- the survival of the virus in aerosols and the infectious dose needed for onward transmission;
- the lack of evidence-based infection control guidance (e.g. the appropriate times to use respirators); and
- the importance of superspreading events – how they can be identified, their levels of disparity in viral shedding and aerosol generation, and their interaction with social networks.

Understanding the mechanisms of superspreading events is important for guiding interventions on reducing such events, and this is also an important aspect in model building (*see Stream 5: Promoting the development and application of modern public health tools*).

Research recommendation 2.1.2

Evaluation of transmission dynamics of influenza and the factors that influence infectivity in different settings and activities

Summary of key accomplishments 2.1.2

Transmission in different settings

The risk of influenza transmission can vary by setting. However, it can be difficult to determine the exact mode of transmission in many outbreak investigations. Factors that facilitate transmission may include increased mixing and contact among individuals, poor hygiene, and individual characteristics such as susceptibility to infection and immunity from previous exposure. Since the last review there has been substantial work advancing the understanding of influenza transmission in different settings.

Household transmission

In previous observational studies, seasonal influenza transmission within households has ranged from 13% to 32% (Foy, Cooney & Allan, 1976; Hall, Cooney & Fox, 1973; Longini et al., 1982; Philip et al., 1961). Recently, numerous household transmission studies during the 2009 influenza A(H1N1) pandemic reported variable secondary infection risk for the novel virus of 3–38%, with the heterogeneity being largely due to differences in case ascertainment methods and study designs (Lau et al., 2012). A standardized approach for case ascertainment in household transmission studies was recommended (Lau et al., 2012). Most infections in household contacts are acquired within the household (Poon et al., 2011), and household transmission may involve mothers and children more than fathers (Thai et al., 2014). The patterns of viral shedding, clinical illness and transmissibility were broadly similar between influenza A(H1N1)pdm09 and seasonal influenza A viruses in the household setting (Cowling et al., 2010).

Determinants of the attack rate in households include age (children have higher attack rates than adults), the number of susceptible occupants in the household (Longini et al., 1982), and household size (Cauchemez et al., 2009b). Some recent studies found that children are more susceptible than adults, but when infected may be as infectious (Cauchemez et al., 2011; Cauchemez et al., 2009a; Lau et al., 2015). The likelihood of child-to-adult transmission decreases with the increase of household size (Cauchemez et al., 2011). The estimated generation interval, often assumed to be similar in different settings, was found to be shorter in households (2.1 days) and camps (2.3 days) than in workplaces (2.7 days) and schools (3.4 days) (te Beest et al., 2013). Using viral shedding to approximate influenza infectivity did not accurately explain the timing of household transmissions. It will be necessary to identify more accurate correlates of infectivity (Tsang et al., 2015). It is essential to continue to study the impact of interventions on reducing transmission risk in household settings, to build on previous studies of household-level interventions.

Schools

Transmission in schools is fuelled by higher attack rates among children. Many previous studies reported a higher attack rate and basic reproductive number (R0) of influenza in the school environment than in community settings (Chen & Liao, 2008; Zhao, Joseph & Phin, 2007). In a recent study in Thailand, classroom overcrowding and increased mixing of students due to inter-class activities contributed to influenza A(H1N1)pdm09 transmission, with a R0 of 3.58 (Jongcherdchootrakul et al., 2014). New studies also found that intra-class and intra-grade contact is more common in elementary and middle schools, but contact networks in high schools are more well connected, with substantial inter-grade contacts observed (Cauchemez et al., 2011; Guclu et al., 2016). Another new study found that the implementation of non-pharmaceutical interventions (e.g. making hand sanitizers available) and the early implementation of communication and education initiatives may reduce reported pandemic-rated influenza-like illnesses (ILIs) by 8–11% in some schools (Miller et al., 2013).

Closed environments

Closed environments such as boarding homes and military facilities have some of the highest rates of influenza transmission. Previous studies found that boarding schools and military ships and facilities could have an overall attack rate of 42–71% in an outbreak (Belbin & Smithson, 1979; Earhart et al., 2001; Liu et al., 2009). More recent studies reported that military personnel in a shipboard may experience higher attack rates of influenza infections due to crowded living conditions, poor ventilation systems, shared sanitation, and prolonged and close contact between individuals (Kak, 2007; Vera et al., 2014). In addition, a superspreading event was observed in a train carriage, a confined space with insufficient air renewal, with high attack rates of 91% in children and 60% in adults (Pestre et al., 2012).

On a separate note, rather than the institution type per se, one recent study found that the attack rate is determined by the nature of mixing, occupation and population size. Military personnel and children suffer a greater attack ratio than other occupational types (e.g. staff and prisoners), and as the community size increases, the attack ratio declines sharply (Finnie et al., 2014).

Health-care facilities

Attack rates of 30–50% have been reported previously for seasonal influenza among health-care workers and hospitalized patients (Balkovic et al., 1980; Horcajada et al., 2003). Nursing homes also experience attack rates of about 40% (Patriarca et al., 1987). High attack and death rates continue to be reported in vaccinated long-term care facility (LTCF) residents, but recent studies found that early reporting of outbreaks in this setting is associated with rapid control, and lower attack and mortality rates (Mahmud et al., 2013).

A recent study in Australia found that hospital-acquired influenza infections are uncommon but are usually associated with severe complications (Macesic et al., 2013). Hospitalized patients with influenza are also likely to be more infectious than community cases, because they may have been admitted due to severe influenza, and severity correlates with viral load peak and duration (Leekha et al., 2007). Immunocompromised people have a longer duration of viral shedding and constitute a much greater proportion of the hospital population than the general population (Lee et al., 2009a). Conversely, nosocomial transmission (i.e. infections acquired during the hospital stay) constitutes a lower proportion of transmitted influenza in some studies than influenza acquired via community or other institutions (Macesic et al., 2013; Taylor et al., 2014; Valley-Omar et al., 2015). This is observed in diagnosed Australian patients with confirmed influenza, where nosocomial acquisition of influenza is much less common than community acquisition (4.3% versus 95.7%) (Macesic et al., 2013). Another study found 17.3% of inpatients with laboratory-confirmed influenza, compared with 60.5% and 39.5% of cases acquired in LTCFs and acute care facilities, respectively (Taylor et al., 2014).

Compared with nosocomial transmission, a bigger contribution is multiple independent introductions of influenza A viruses into the hospital; this finding was shown using molecular epidemiology rather than traditional epidemiology (Valley-Omar et al., 2015). More data using novel techniques such as molecular epidemiology and next-generation sequencing would be useful to elucidate such transmission pathways in hospitals. The spread of influenza in health-care facilities is probably influenced by the movement of health-care staff and patients, compliance with appropriate infection control precautions and susceptibility among hospitalized patients. This suggestion was substantiated by a study that found a correlation between improvements in hand hygiene compliance and decreased transmission of influenza in the hospital (Weedon et al., 2013). A previous study recommended vaccination of health-care workers (*see Stream 3: Minimizing the impact of pandemic, zoonotic and seasonal epidemic influenza*) to assist in reducing the spread and impact of influenza in the health-care setting (Salgado et al., 2002). However, no benefit was identified in a recent Cochrane review of health-care workers' vaccination in LTCFs (Thomas, Jefferson & Lasserson, 2016).

Transportation

A previous study of transmission of influenza during air travel found that 72% of passengers developed respiratory symptoms within 3 days of exposure to an ill passenger on an airplane (Moser et al., 1979). Only two instances of influenza transmission in an aircraft were found by two previous comprehensive reviews of the risk of influenza transmission (Leder & Newman, 2005; Mangili & Gendreau, 2005). More reports of transmission on airplanes have been published recently, and a systematic review found five instances of in-flight influenza transmission, and five other studies highlighting the role of air transportation in accelerating the spread of influenza to new areas (Baker et al., 2010; Browne et al., 2016). Influenza outbreaks aboard cruise ships affect 2–7% of passengers, but there is no evidence of sea transport accelerating influenza spread to new areas. Influenza transmission has been observed aboard ground transport vehicles, but the role of ground transportation systems in respiratory virus propagation and transmission to new geographic areas in pandemic situations is unclear owing to high heterogeneity between studies and the inability to exclude other sources of infection (Browne et al., 2016).

Age-dependent spread and risk of infection

Previous studies found that influenza usually transmits much more intensely among preschool children, possibly due to poor respiratory hygiene (Neuzil, Hohlbein & Zhu, 2002; World Health Organization, 2009). There have been some documented occurrences of mother-to-neonate transmission in recent years, but the risk appears to be low (Cantey et al., 2013; Milupi et al., 2012). It is now better understood that virus shedding correlates with symptom severity and duration, and that age-specific differences in shedding reflect underlying immunity (previous exposure) rather than age per se (Fielding et al., 2014; Ip et al., 2016; Noh et al., 2014; Thai et al., 2014; Tsang et al., 2015).

Effect of comorbid conditions on spread and risk of infection

There have been no new studies since the last review. Previous studies showed that influenza may spread more readily among those with pre-existing medical conditions. Viral clearance is slower among individuals with comorbid conditions and those on corticosteroid therapy (Lee et al., 2009a). Individuals who are immunocompromised also have a higher frequency of influenza infections (Kunisaki & Janoff, 2009). Pandemic (H1N1) 2009 influenza has been shown to result in more complications and increased hospitalizations and mortality among pregnant women than previous influenza epidemics (Jamieson et al., 2009). Those with chronic lung diseases are also at higher risk for severe illness (World Health Organization, 2009) (*see Stream 3: Minimizing the impact of pandemic, zoonotic and seasonal epidemic influenza*).

Unmet public health needs and knowledge gaps 2.1.2

In general, there are less data available about transmission in other settings than in household settings. There are knowledge gaps in the impact that interventions will have in these other settings on reducing transmission risk, despite several studies of household-level interventions. The unmet public health needs are studies focusing on the impact and feasibility of interventions – for example, the vaccination of health-care workers, and the use of antiviral medications in institutions such as nursing homes (Centers for Disease Control and Prevention, 2002; Monto et al., 2004) (see Stream 4: Optimizing the treatment of patients) – in reducing transmission risk in various settings. Future research in this area should focus on better understanding which interventions would be effective in reducing transmission in each of these settings, rather than simply studying or describing transmission per se. Next-generation sequencing of influenza viruses is also a useful tool for determining the extent and pathways of transmission, and for evaluating the efficacy of intervention measures.

Research recommendation 2.1.3

Transmission of influenza during different stages of infection in humans

Summary of key accomplishments 2.1.3

Infectivity after illness onset

Previous studies showed that influenza is most infectious during the first 3 days of illness (Bell & World Health Organization Writing Group, 2006; Nicholson, Wood & Zambon, 2003), and virus has been isolated from 24–48 hours before onset of clinical symptoms (Davis et al., 1961; Frank et al., 1981; Khakpour, Saidi & Naficy, 1969) to about 5–7 days after onset of symptoms in adults (Frank et al., 1981; Hayden et al., 1998; Philip et al., 1961; Witkop et al., 2010), to up to 2 weeks in children, and longer in immunocompromised individuals (Nicholson et al., 2003). Shedding usually ceases once illness has resolved (Frank et al., 1981; Monto, Koopman & Longini, 1985). Recent studies found that, in influenza A infections, the dynamics of viral shedding correlate with the symptom severity (Fielding et al., 2014; Noh et al., 2014). A difference in viral shedding dynamics between influenza A and B infections is also apparent. Shedding for influenza A infections peaked on the first 1–2 days of clinical illness, and decreased gradually to undetectable levels by days 6–7. Shedding in influenza B infections, on the other hand, peaked up to 2 days before the onset of symptoms, and persisted for 6–7 days, with evidence of a bimodal pattern (Ip et al., 2016). Measurement of viral shedding by polymerase chain reaction (PCR) correlated well with measurement by viral culture (a better measure of viable and potentially infectious virus) (Fielding et al., 2014). However, the mean and median durations of viral detection were 1.5–2 days shorter for the latter (Ip et al., 2016), suggesting that the viral shedding detectable by PCR may be longer than the infectious period (Tsang et al., 2015). The measurement of duration of viral shedding is highly variable among studies, and a standardized approach to this measurement was recommended by Fielding et al. (2014). Viral shedding is often considered to correlate with the infectivity of influenza, but Tsang et al. (2015) found that viral load was not proportional to infectivity in a model. This implied that other factors such as behaviour and nature of symptoms (e.g. wet cough) may affect infectivity (Thai et al., 2014), or that measurement of viral shedding by PCR may overestimate the duration of infectivity (Tsang et al., 2015).

Asymptomatic and subclinical infection

Previous studies have isolated influenza viruses from respiratory samples in persons with subclinical or asymptomatic infection and in those with mild symptoms. More evidence on pre-symptomatic transmission for pandemic H1N1 has become available since the last review (Freitas et al., 2013; Gu et al., 2011). However, it is unclear how infectious individuals with pre-symptomatic, mildly symptomatic, asymptomatic and subclinical infections are, and how the amount of virus shed correlates with infectiousness over time. Pre-symptomatic shedding can occur in up to two thirds of cases (Ip et al., 2016; Loeb et al., 2012; Suess et al., 2012), while asymptomatic infections can comprise 10–40% of all infections (Esbenshade et al., 2013; Fielding et al., 2014; Ip et al., 2016; Loeb et al., 2012; Suess et al., 2012; Thai et al., 2014; Yan et al., 2012), with afebrile influenza A(H1N1) pdm09 cases estimated to be 33–47% in household studies (Lau et al., 2012). Though a modelling study suggests transmission from subclinical or pre-symptomatic cases may be important at a population level (Fielding, Kelly & Glass, 2015), the contribution of pre-symptomatic and asymptomatic shedding to transmission remains unclear.

Unmet public health needs and knowledge 2.1.3

There are no unmet public health needs or knowledge gaps in this recommendation that are relevant to Stream 2. However, a better understanding of how assumptions about the contribution of pre-symptomatic or subclinical shedding on transmission affects estimates of the effectiveness of various public health interventions would be an important topic for modelling studies on pandemic influenza viruses (*see Stream 5: Promoting the development and application of modern public health tools*).

Research recommendation 2.1.4

The role of factors such as age, pre-existing immunity, antiviral treatment and prophylaxis, and vaccination in modulating influenza transmission

Summary of key accomplishments 2.1.4

Recently, several studies investigated the effect of age on viral shedding, and the results are conflicting. A systematic review did not demonstrate a longer duration of viral shedding of influenza A (H1N1)pdm09 in children than in adults (Fielding et al., 2014). However, results from another study showed a longer duration of viral shedding for infected children than for adults (Tsang et al., 2015). The different findings are probably related to age-dependent differences in cross-protective immunity to specific subtypes, where prior exposure to antigenically related viruses may influence the duration of viral shedding. Thus, findings from studies of A(H1N1)pdm09 conducted during its emergence may not hold for non-novel subtypes. The role of superspreading events in influenza transmission is not well established, but data are accumulating that such events may be important (Lau et al., 2013; Pestre et al., 2012). One study estimated that the top 20% of infectious individuals were responsible for about 78–96% of the total infectiousness in each age group (Lau et al., 2013). This area warrants further study. New data suggest that antiviral treatment of cases reduces household transmission (Fry et al., 2015; Lansbury & Nguyen-Van-Tam, 2017), and that antiviral treatment in the first 48 hours reduces the duration of viral shedding (Fielding et al., 2014; Fry et al., 2014), although other studies found no such evidence (Cheung et al., 2015; Ng et al., 2010). It has been suggested that delayed antiviral treatment is correlated with prolonged shedding (Leung et al., 2012; Ryoo et al., 2013; Wang et al., 2012), but the causes for this are unknown.

Unmet public health needs and knowledge gaps 2.1.4

An unmet public health need is the need to determine the effect of antiviral treatment and prophylaxis, and vaccination on the transmission of influenza. Most of the current studies are based on mathematical modelling (Lee, Lye & Wilder-Smith, 2009b), and more observational studies are needed. The role of antipyretics in influencing transmission risk is controversial but potentially important and worthy of further study (Earn, Andrews & Bolker, 2014; Jefferies et al., 2016)

Research recommendation 2.1.5

Stability of human and zoonotic influenza viruses on varying environmental surfaces and conditions and its relevance in the transmission of influenza virus

Summary of key accomplishments 2.1.5

Previous studies have proven that influenza viruses can persist for up to 12 hours on porous surfaces such as cloth and paper at 28 °C and at humidity levels of 35–40% (Bean et al., 1982). Viruses were found to be transferred for 24 hours after initial contamination of non-porous surfaces, and transfer could occur for 15 minutes after contamination of tissues. Influenza virus concentrations on hands decreased by 100–1000 fold within 5 minutes of transfer, and virus could only be recovered during the first 5 minutes. In another study, influenza A viruses were also found on over 50% of fomites tested in homes and day care centres during the influenza season (Boone & Gerba, 2005). Higher temperatures and humidity levels have also previously been shown to reduce viral survival, and it is hypothesized that transmission of influenza in temperate regions is primarily by aerosol spread, whereas transmission in the tropics is by contact (Bean et al., 1982; Lowen et al., 2007; McDevitt et al., 2010; Steel, Palese & Lowen, 2011; Sundell et al., 2016). New studies found that influenza virus deposited into the environment could survive for short periods of time (rarely more than 9 hours) on most surfaces (Greatorex et al., 2011). Non-porous materials pose the greatest risk, with influenza viruses surviving for 24–48 hours on plastic (Bean et al., 1982) and up to 7 days on steel, and metals demonstrated to have low levels of anti-viral activity (Greatorex et al., 2011; Perry et al., 2016). Hence, although it is possible for influenza to be transmitted via fomites, this route of transmission is unlikely if surface contamination occurred some time ago, unless frequent re-inoculation occurs. There have been several recent studies on virus survival in the touched environment (Greatorex et al., 2011; McDevitt et al., 2010; Mukherjee et al., 2012; Oxford et al., 2014; Perry et al., 2016; Steel et al., 2011; von Braun et al., 2015); further work using similar investigational methods is unlikely to advance knowledge.

Unmet public health needs and knowledge gaps 2.1.5

Overall, the topic on the stability of human influenza viruses on various surfaces and under varying conditions is reasonably well understood. There are no unmet public health needs or knowledge gaps for this recommendation.

Substream 2.1 key brainstorming questions:

- What is the relative importance of measures targeting various modes of influenza transmission interventions?
- What is the infectious dose needed to transmit infection via an aerosol, and what constitutes an aerosol-generating procedure in clinical settings? How long is virus survival in aerosols (by virus type and subtype)?
- What is the importance of superspreading events and how can such events be identified? How do these events differ in terms of viral shedding and aerosol generation, and the involved social networks?

Substream 2.2
Dynamics of virus spread at global and local levels

Influenza is a global disease that does not respect borders, and that spreads quickly through travel and trade. Experience with pandemic (H1N1) 2009 influenza in many countries has demonstrated the importance of school children in amplifying transmission of the pandemic virus, both within schools and the wider community. Although research studies have demonstrated the effectiveness of public health measures against influenza, most of these measures were undertaken in limited local settings. In addition, different local characteristics – such as the geography, socio-cultural-economic framework, demographics and population susceptibility – affect the spread of influenza locally and across borders. It is important to understand the dynamics of virus spread at global and local levels to optimize the use and effectiveness of public health measures.

Research Recommendation 2.2.1

Seasonality of influenza virus infection in different regions and implications for global virus spread

Summary of key accomplishments 2.2.1

Influenza epidemics exhibit clear seasonal patterns, although the mechanism for this is not well understood. Previous studies have shown that seasonal influenza epidemics occur during colder winter months, with a single peak in temperate countries (Nicholson, Webster & Hay, 1998). However, in the tropics, which lack defined seasons, influenza can have a high baseline level of activity with multiple peaks (Azziz Baumgartner et al., 2012; Chadha et al., 2015; Chew et al., 1998; Saha et al., 2014; Saha et al., 2016). New studies have found that semi-annual influenza activities, with peaks occurring in winter and summer, have been observed in several temperate locations and many tropical locations in South-East Asia, but varying in intensity from year to year (Ang et al., 2016; Bloom-Feshbach et al., 2013; Widdowson & Monto, 2013).

The different seasonality patterns were hypothesized to relate to the timing of the global circulation of influenza viruses in previous studies. Influenza viruses continually circulate in the tropics, especially in East and South-East Asia, resulting in overlapping epidemics and seeding of epidemics in temperate regions in both the northern and southern hemispheres (Russell et al., 2008). More recent studies found that the seasonality of influenza activities may also change with latitude and climate. In Asia, countries located above 30°N have influenza A epidemics during winter seasons, those below 30°N and above 10°N have seasonality during monsoon seasons, whereas those near the equator have year-round circulation (Chadha et al., 2015; Saha et al., 2014; Saha et al., 2016; Yu et al., 2013). The seasonality of influenza B epidemics coincides with the seasonality of influenza A in areas above 30°N, but there is a year-round circulation of influenza B activities in areas below 30°N (Saha et al., 2016). In Africa, where seasonal influenza characterization is limited, the main season of influenza activities occurs between October and January in northern Africa, between April and August in southern Africa, between July and October in east Africa, and throughout the year in tropical Africa (Badar et al., 2013; Hirve et al., 2016). Environmental factors have also been associated with the seasonality of influenza (Chadha et al., 2015). Cold temperature, low specific humidity and minimal solar radiation facilitate influenza transmission in temperate regions, whereas high humidity in the rainy season is associated with influenza activities in some tropical or subtropical regions (Soebiyanto et al., 2015; Tamerius et al., 2013). The annual variation in climatic factors was found to be more important than their absolute values in terms of their effect on the seasonality of influenza (Kamigaki et al., 2016).

Unmet public health needs and knowledge gaps 2.2.1

There are knowledge gaps about how differences in transmission patterns affect the timing and effectiveness of vaccination campaigns. Studying the seasonality and differences in virus transmission in different regions therefore remains relevant, but the focus for this recommendation should be directed towards developing good surveillance systems in resource-limited settings, which remains an unmet public health need.

Research recommendation 2.2.2

Assessing spread of influenza under different epidemiological settings.

Gaining a better understanding of how influenza spreads in different settings can assist in planning appropriate response measures. In the years following the emergence of influenza A(H1N1) pdm09, several studies were published on transmission in different settings; however, less information was available for A(H3N2) and B viruses.

Summary of key accomplishments 2.2.2

Pre-existing immunity in the population

The relationships between prior influenza virus exposure, pre-existing immunity and rates of infection and illness are well described. A new study found a correlation between the haemagglutinin subtype of the first infecting seasonal influenza strain and subsequent protection against severe infection or death against both H5N1 and H7N9 (Gostic et al., 2016). This has important implications for predicting the impact of newly emerged influenza viruses.

Rural versus urban regions

New studies found that R0, population size, and birth and death rates are the key factors that strongly influence the migration of influenza viruses (Wen, Bedford & Cobey, 2016). In one study of pandemic influenza in Queensland, Australia, more populous regions displayed a lower transmission rate and had more synchronized epidemic patterns (Huang et al., 2016). There is more heterogeneity in transmission rates in rural areas and among populations with a small size (e.g. indigenous communities); this increased heterogeneity may be due to the high prevalence of comorbidities and poor living conditions (Huang et al., 2016; La Ruche et al., 2009). The emergence of a new pandemic influenza is likely to be detected in an urban setting; however, the source may be in a rural setting with significant animal and human interaction.

Social determinants affecting influenza transmission

New studies found that people at lower socioeconomic levels have a greater risk of influenza infections, which might be due to low vaccination rates, crowded living conditions and a high prevalence of underlying conditions (Hadler et al., 2016). Other social determinants that may affect influenza transmission and illness include lack of access to vaccination, neighbourhood disadvantage, absence of sick-leave policies in the workplace, and limited support for families during school closings (Cordoba & Aiello, 2016).

Transmission among migrants, refugees or displaced persons

The potential role of mass movements in the spread of influenza and its impact on travellers has not been well characterized. This group of people may have an increased risk of influenza infection. Further studies are needed to determine the factors (e.g. social structures and social determinants) affecting influenza infections in this group, as well as possible interventions to prevent influenza infections.

The impact of mass gatherings

Previous studies have shown that influenza occurs among pilgrims in significant numbers during the Hajj pilgrimage every year, due to overcrowding and prolonged close contacts (Gatrad et al., 2006). A few recent articles were found, notably those regarding the Hajj; however, the impact of mass gatherings (e.g. Olympic Games and World Cup) on the spread of influenza has not been well described (Al-Tawfiq et al., 2016).

Unmet public health needs and knowledge gaps 2.2.2

There are knowledge gaps about the factors – including social structures and behaviours (population density, living conditions and interactions) – that affect the spread of influenza, particularly for low-income populations or individuals, and refugees or migrants. The impact of local practices on delaying viral spread within and between countries is another knowledge gap.

Research recommendation 2.2.3

Interaction between influenza strains and other respiratory pathogens, and their effect on transmission and spread

Summary of key accomplishments 2.2.3

Since the 2009 A(H1N1) pandemic there has been an increase in knowledge about the interactions between different influenza strains, and interactions between influenza and other circulating respiratory pathogens; such knowledge is crucial to understand the impact of influenza relative to other respiratory diseases. Information on global seasonal patterns of influenza and other respiratory viruses would also be useful for evaluating postulated mechanisms driving seasonality.

Co-circulation and co-detection of influenza and other respiratory viruses have been observed globally (Bloom-Feshbach et al., 2013; Skevaki et al., 2015; van den Bergh et al., 2012), but data about Africa and Central America are lacking. Previous studies show that coinfection of influenza with Streptococcus pneumoniae is associated with severe outcomes (Palacios et al., 2009), and that there is a significant association of influenza activity with increased incidence and severity of invasive pneumococcal pneumonia (IPP), varying by age, comorbidity groups and pneumococcal serotypes (Walter et al., 2010; Weinberger et al., 2013; 2014). Studies of all-cause pneumonia also suggest that influenza accounts for a relatively small percentage of total cases (Jain et al., 2015; Simonsen et al., 2011).

Few studies have explored the facilitation or interference of influenza with other respiratory pathogens on the spread of these diseases. This phenomenon of facilitation or interference was described in studies showing shifts or changes in timing and prevalence of other influenza A and respiratory viruses in the population caused by the introduction of an epidemic or pandemic influenza strain (Gröndahl et al., 2014; Mak et al., 2012; van Asten et al., 2016). In animal studies, viral interference occurs and appears to be independent of antigenic similarities between human influenza viruses; instead, it appears to depend on an apparent hierarchy of influenza viruses inducing different levels of temporary immunity (Laurie et al., 2015). Influenza prevention or vaccination has been shown to increase the risk of other non-influenza viral infections through a lack of temporary non-specific immunity (Cowling et al., 2012), but more studies are required to validate this finding.

Unmet public health needs and knowledge gaps 2.2.3

The unmet public health needs are to investigate the factors that make novel (seasonal or newly emerged) viruses successful, including issues on co-circulation of viral strains, replacement of other viral strains (Furuse & Oshitani, 2016) and viral fitness. This is especially important for influenza viruses with pandemic potential. Another knowledge gap is the impact of influenza infection or prevention on the risk of subsequent other respiratory infections.

Research recommendation 2.2.4

Utility and timing of different response strategies during early spread of human cases of an animal or pandemic influenza virus.

The timing and effectiveness of response strategies have not been comprehensively studied because of the complexities of performing randomized trials during an epidemic. However, mathematical modelling studies can help to evaluate different strategies under varying assumptions.

Summary of key accomplishments 2.2.4

Containment of influenza at its source

There have been no new studies about containment of influenza at its source. However, two previous key modelling studies done in rural areas of South-East Asia (Ferguson et al., 2005; Longini et al., 2005) suggested that a combination of interventions – pharmacological measures (antiviral prophylaxis and pre-pandemic vaccination) and public health measures (school and workplace closures, and area quarantine) – under favourable conditions (e.g. early detection and low R0) had the potential to successfully contain the initial emergence of a pandemic virus. Although it is unlikely that a pandemic could be contained, containment strategies may be useful in specific circumstances; for example, to prevent spread in closed environments (Lee et al., 2010b), or to contain emerging avian or zoonotic influenza viruses if there is low transmissibility.

Border control measures

Previously, entry screening and quarantining of travellers crossing international borders, traveller education and exit screening during the early phases of a pandemic have not prevented the spread of a pandemic. New studies have shown that border control measures may delay the spread, but the impact is reduced if these measures are implemented more than 6 weeks after the notification of an epidemic (Mateus et al., 2014). A recent study in China found that border entry screening delayed spread for no more than 4 days (Yu et al., 2012), and is unlikely to be useful when implemented alone. Moreover, there is a substantial overlap in the symptom profiles between various respiratory viruses; hence, the positive predictive value for detecting febrile passengers is very low when the prevalence of fever among travellers is low (Bitar, Goubar & Desenclos, 2009; Jennings et al., 2015; Pitman et al., 2005; Priest et al., 2015). In addition, travellers infected with influenza may not be febrile if they are in the incubation phase, have subclinical infection or are using antipyretics. In addition, travel restrictions may result in a substantial economic burden, and the effectiveness of travel restrictions on the containment of influenza pandemics is limited (World Health Organization, 2009). International travel restrictions and international border restrictions can only delay the transmission of influenza infections (travel restrictions by about 1 week to 2 months, and border restrictions by a few days to 4 months) but cannot prevent it, and the effect is minimal in large and densely populated urban areas that have massive travel networks (Mateus et al., 2014). Thus, travel restrictions and border controls are unlikely to be useful and are generally not recommended by WHO (Bell & World Health Organization Writing Group, 2006; Mateus et al., 2014).

Unmet public health needs and knowledge gaps 2.2.4

There are no unmet public health needs or knowledge gaps of importance for Recommendation 2.2.4.

Substream 2.2 key brainstorming questions:

- What are the implications of seasonality and differences in transmission (temperate versus tropical countries) on the timing of vaccination?
- How is the spread of virus affected by social structures and behaviours (e.g. population density, living conditions and interactions)?
- What is the impact of local practices on delaying the spread of virus between and within countries?
- What makes novel (seasonal or newly emerged) viruses successful, including replacement of other viral strains?
- Does influenza infection or prevention influence the risk of subsequent respiratory infections?
- What is the impact and what are the transmission dynamics among lower income individuals?

Substream 2.3 Public health measures to limit transmission

Public health measures have been the mainstay for the prevention of infectious diseases for centuries, and they remain important and relevant today. Pharmaceutical interventions such as antiviral drugs and vaccines are additional prevention and control measures that have come into prominence in recent decades; however, other than in well-resourced settings, they may not be available in sufficient or timely quantities. Thus, in many countries, public health measures may be the only measures available for the control of influenza.

Individual and community-level measures have been adopted to reduce the spread of influenza within households and institutions, in the general population and across borders. These practices have been widely adopted, and many studies have been implemented to evaluate the effectiveness of individual intervention measures since the 2009 A(H1N1) pandemic. However, it is difficult to discern the relative importance and effectiveness of individual measures because they are often used in combination. Mathematical modelling can aid policy-makers and decision-makers in planning for the implementation of these measures under varying conditions. However, mathematical models are only as good as the epidemiological and clinical data available as the input for models.

Research recommendation 2.3.1

Effectiveness and feasibility of individual-level measures

Summary of key accomplishments 2.3.1

Personal hygiene

Personal hygiene measures have long been recommended; they include measures such as covering the mouth and nose when coughing or sneezing, avoiding touching of the mouth or eyes with unwashed hands, washing of hands with soap and water, and other similar hygiene and etiquette measures. Previous studies found that frequent handwashing was effective in reducing viral transmission by 6–44% in various settings (Rabie & Curtis, 2006), especially during the SARS outbreak (Fung & Cairncross, 2006; Jefferson et al., 2009). A previous study in Pakistan also found that providing soap and education about handwashing reduced the incidence of pneumonia by 50% among children aged under 5 years (Luby et al., 2005).

New studies found that the effectiveness of hand hygiene depends on setting, context and compliance. Evidence of the effect of hand hygiene interventions on infection incidence in educational settings is mostly equivocal, but the interventions may decrease respiratory tract infection among children (Willmott et al., 2016), whereas their effectiveness in nursing home settings is still inconclusive (Hocine & Temime, 2015). Moreover, no significant reduction in secondary transmission of influenza was found in household settings (Warren-Gash, Fragaszy & Hayward, 2013). A study of an internet-delivered handwashing intervention reported a significant decrease in the transmission of respiratory tract infections (Little et al., 2015).

Previous studies have shown that virucidal tissues are effective in limiting transmission of rhinoviruses and that commercial alcohol hand disinfectants are effective in inactivating influenza viruses (Jennings & Dick, 1987; Schürmann & Eggers, 1983).

Masks

Many countries have stockpiled masks and recommended their use in community and health-care settings. A previous study in households in Hong Kong Special Administrative Region showed that surgical masks and hand hygiene decreased transmission if started within 36 hours of the onset of illness in the index patient, although compliance was a problem (Cowling et al., 2009). New evidence also supported mask use being best undertaken as part of a package or "bundle" of personal protection including hand hygiene, particularly within the community or household setting. In clinical settings, mask use (either surgical or nonfit-tested FFP2 masks) could significantly reduce the risk of ILI among health-care workers, but no significant difference between FFP2 masks and surgical masks was found in protecting health-care workers from influenza infections and in reported workplace absenteeism (Loeb et al., 2009; MacIntyre et al., 2009; Smith et al., 2016). Protection inside-outward is less effective than protection outside-inward, so caregivers are better protected by wearing a mask themselves than by asking patients to wear one (van der Sande, 2016). The updated evidence strengthens the argument that early initiation and regular wearing of masks or respirators may improve their effectiveness in health-care and household settings. The effectiveness of masks or respirators is probably linked to consistent, correct usage and compliance, which remains a major challenge. Given the potential loss of effectiveness with incorrect usage, masks or respirators should be used under particular, specified circumstances, and in combination with other personal protective practices (Aiello et al., 2012).

Cloth masks were reported to be commonly used in low-resource settings for pandemic preparedness; however, their effectiveness in preventing respiratory infections among health-care workers remains unclear (Chughtai, Seale & MacIntyre, 2013).

Social and behavioural aspects are just as important as the technical effectiveness of these measures, as shown by the household studies of MacIntyre and Cowling (Cowling et al., 2009; MacIntyre et al., 2009). A previous hospital-based simulation exercise in the United Kingdom reinforced the need for ongoing training and education for health-care workers (Phin et al., 2009). However, there is still a lack of knowledge about the potential factors that foster the correct and consistent use of these individual-level measures.

Unmet public health needs and knowledge gaps 2.3.1

An unmet public health need is the need to investigate the relative effectiveness of surgical masks and fit-tested respirators, in addition to hand and respiratory hygiene, in preventing the spread of influenza, particularly in clinical settings.

Research recommendation 2.3.2

Effectiveness and feasibility of community-level measures.

Many different community-level public health measures have been used during influenza epidemics and pandemics. They include contact tracing, school and workplace closures, reduction of mass gatherings, temperature screening and travel restrictions, some of which are discussed in greater detail in this section.

Summary of key accomplishments 2.3.2

Contact tracing and quarantine

Contact tracing and quarantine of close contacts have been used in an effort to contain and delay the spread of influenza within countries. However, there is still no clear evidence for the effectiveness of these measures.

School closures and other social distancing measures in community settings

A few of the key decisions that policy-makers often consider during epidemics and pandemics are social distancing measures, and the closure of schools and possibly workplaces, to reduce the spread of influenza. Previous studies showed that total closure of schools and workplaces could reduce the overall population attack rate by 95%; however, the socioeconomic consequences would be devastating and could outstrip the impact of a pandemic (Carrat et al., 2006; Sadique, Adams & Edmunds, 2008). A French modelling study showed that early and prolonged school closures and limiting contact among children outside school could reduce the overall attack rate by 17% and the peak attack rate by 45% (Cauchemez et al., 2008). However, there is still insufficient evidence to recommend any particular school closure policy (e.g. proactive or reactive). The timing and duration of closures needed to produce an effect in delaying the spread and overall impact of influenza is also unclear. Recent studies showed that enhanced surveillance with case isolation, social distancing and segregation, and adoption of personal protective equipment could reduce infection rates from 44% to 11–17% in closed environments (Lee et al., 2010a). For a pandemic virus with R0 <2, early closure of schools could reduce the overall population attack rate by up to

40%, depending on model assumptions; however, this would decrease to a reduction of less than 10% in the attack rate for pandemic viruses with higher R0 values (Jackson et al., 2014; Vynnycky & Edmunds, 2008). The contact rate was 17% lower during school holidays compared with school terms, which suggests that school closures may reduce influenza transmission during outbreaks (Jackson, Vynnycky & Mangtani, 2016). In practice, the actual timing and length of school closures remain difficult to determine, and school closures are not effective if they are implemented after ILI infections have become widespread (Davis et al., 2015; Jackson et al., 2013; Russell et al., 2016; Wu et al., 2013). Policies should be responsive to the features of a new pandemic virus. For example, if transmission occurs mainly in schools (as occurred during the 2009 pandemic), there is stronger justification for school closures than in the situation where much of the transmission occurs in adults (Jackson et al., 2014). In the early stages of a pandemic, a precautionary approach may be considered, particularly if the virus is believed to be highly pathogenic. School closures should be accompanied by advice that children should avoid meeting in large groups.

Reducing mass gatherings

Reducing mass gatherings and avoiding crowded places have also been recommended during epidemics and pandemics. There is little new evidence to help address questions around mass gatherings and influenza transmission, especially in the context of an influenza pandemic. Mass gatherings are very varied, and the type, size, duration and setting (i.e. indoor or outdoor) of such events may play a role in the risk of influenza transmission (Ishola & Phin, 2011). There is also some evidence that influenza may be transmitted at certain kinds of mass gatherings. Such gatherings facilitate the transmission of influenza if there are more than five people per square metre and if participants stay close together for prolonged periods (e.g. during the Hajj and music festivals) (Ishola & Phin, 2011). However, major sporting events such as the World Cup and Olympic Games may not have a substantial effect on the spread of influenza infections because of the open-air setting and good between-seat spacing (Gundlapalli et al., 2006; Ishola & Phin, 2011; Lim et al., 2010; Schenkel et al., 2006). Large international conferences held indoors may have high attack rates of influenza infections among participants (Ishola & Phin, 2011; Saenz, Assaad & Cockburn, 1969).

Unmet public health needs and knowledge gaps 2.3.2

There are knowledge gaps concerning the benefits of school closures in reducing spread versus the socioeconomic cost; such information is needed to assist policy-making (Cauchemez et al., 2009b; Davis et al., 2015; Public Health, 2014). An unmet public health need is the need for studies on the effectiveness, timing and optimal implementation of school closures, other social distancing measures, and environmental control methods in actual settings. There have been numerous modelling studies on the effectiveness of community-level public health measures in controlling the spread of influenza transmission, but observational studies are lacking.

Research Recommendation 2.3.3

Factors to consider in the selection and timing of public health measures

Summary of key accomplishments 2.3.3

Public health professionals and policy-makers face challenges in selecting the most appropriate public health measures for a given influenza epidemic or pandemic. Many factors must be considered to ensure that the response is appropriate for the situation and does not result in a greater impact than the disease itself. In addition, the timing of these measures is important to maximize their effectiveness while minimizing any collateral damage.

Previous mathematical modelling studies have shown a synergistic effect on reducing the impact of influenza if pharmaceutical and public health measures are used in combination rather than singly (Duerr et al., 2007; Ferguson et al., 2006; Germann et al., 2006; Halloran et al., 2008; Lam, Dawson & Fowler, 2015). A recent systematic review by Lam et al. (2015) also suggested that adopting a comprehensive primary care approach involving multiple strategies will be effective in preventing household transmission of influenza. Such strategies include public regulations, instruction to drug retailers, community engagement, hand hygiene and mask usage.

The rate and extent of the spread and severity of disease will determine the urgency and scope of the response. A severe epidemic with high morbidity and mortality that spreads quickly across the world may warrant more extreme measures than a "mild" pandemic.

The timing of the response measure is important to maximize its effectiveness. Previous studies showed that use of antiviral pre-exposure prophylaxis in health-care workers was effective in maintaining essential services only if it was timed to include the peak of the pandemic; poorly timed prophylaxis had no or a negative impact (Lee & Chen, 2007). Moreover, new studies found that school closures may only have a significant impact if this intervention is implemented before ILI infections become widespread (Davis et al., 2015; Russell et al., 2016).

The demography, sociocultural determinants and geopolitical framework are also important determinants. These factors must be studied in the local context to facilitate compliance with the selected measures. New studies found that hand and respiratory hygiene are well-accepted concepts, whereas personal distancing and wearing of masks in some contexts may cause concern (Teasdale et al., 2014). Personal and cultural beliefs, and misconceptions about transmission and preventive measures are the key barriers to adopting non-pharmaceutical interventions, and there is variation in public perceptions on public health interventions between different countries (Bults et al., 2015; Teasdale et al., 2014). Acceptance and compliance by the affected population is as important as the technical effectiveness of the measure.

Finally, it is important to make the best use of scarce resources, given the wide range of possible scenarios and solutions available, and there is still no new research on resource planning and optimization.

Unmet public health needs and knowledge gaps 2.3.3

The unmet public health needs are to conduct health services research (e.g. resource optimization studies and economic evaluations) in local settings to determine the relative cost–effectiveness and resource-effectiveness of the available measures. Policy decisions can then take into account the results of these types of studies along with the range of factors described in previous sections.

Research recommendation 2.3.4

The usage of surveillance data in assessing the needs and effectiveness of public health interventions in different situations.

Summary of key accomplishments 2.3.4

Systems for surveillance coupled with focused investigations can help to assess the needs and effectiveness of public health interventions in different situations, and guide the most appropriate response. Research is needed to determine the effectiveness of different surveillance strategies and recommend the best approaches for different local settings.

Many countries have established surveillance networks for detecting influenza infections or ILI, and there has been a large increase in the number of publications on influenza and ILI surveillance since the 2009 A(H1N1) pandemic. Recent studies have found that ILI surveillance using electronic health records shows high sensitivity and specificity, and is similar in quality to manual sentinel surveillance and virologic data (Keck et al., 2014; Sugawara et al., 2012; Yih et al., 2014). The development of biologically complex models that track the evolution of influenza viruses in animals can also inform optimal interventions, to assist in pandemic preparedness planning (Coburn, Wagner & Blower, 2009).

Social media

Recent studies showed that social media data on ILI demonstrated high correlation with national health data (correlation coefficient 0.55–0.95), and could provide earlier detection of outbreaks than the standard outbreak surveillance systems in certain situations (Charles-Smith et al., 2015). Social media data together with traditional data sources could provide accurate real-time predictions up to 3 weeks ahead using autoregressive models (Santillana et al., 2015).

Syndromic surveillance

Various types of syndromic surveillance data have been evaluated recently. Emergency department based syndromic surveillance, web queries and medical hotline statistics for influenza or ILI were able to provide a faster estimation of influenza attack rate, and data of a similar quality to the traditional surveillance methods (Hiller et al., 2013; Ma et al., 2015). However, the reliability of using school absenteeism data in predicting influenza outbreaks is still unclear. A United Kingdom study compared school absenteeism data with the existing syndromic surveillance system during the H1N1 pandemic (Kara et al., 2012). It found that weekly school absenteeism surveillance would not have detected pandemic influenza earlier, but it peaked concomitantly with the existing syndromic surveillance system.

Surveillance for avian and swine influenza

Avian influenza surveillance in wild birds may be useful for monitoring the evolution, maintenance and spread of avian influenza viruses. Hence, countries should collaborate and standardize the sampling, testing and reporting methods for better information sharing (Machalaba et al., 2015). The surveillance of gene flow, particularly in East Asia and South-East Asia, may bring benefit for monitoring swine influenza outbreaks (Trevennec et al., 2011).

Unmet public health needs and knowledge gaps 2.3.4

There are still knowledge gaps in the actual impact of the surveillance methods described in this section on actions to limit the transmission of influenza infections.

Substream 2.3 key brainstorming questions:

- What is the relative effectiveness of surgical masks and fit-tested respirators, in addition to hand and respiratory hygiene, in preventing the spread of influenza in clinical settings?
- What is the actual impact of school closures and other social distancing measures in community settings and holidays in different settings?
- Which interventions are effective in reducing influenza transmission, and are there any standardized approaches?
- What is the impact of surveillance methods on limiting the transmission of influenza infections?

SUMMARY

There has been substantial research on influenza since the 2009 A(H1N1) pandemic, yet there are still many knowledge gaps and unmet needs. The 2009 influenza pandemic has been the most closely studied of all pandemics. It offers an opportunity to gain new insights into the transmission of influenza, the dynamics of spread in different settings, and the effectiveness of various prevention and control measures. This information in turn can be used to refine and improve influenza preparedness and response at global and country levels.

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