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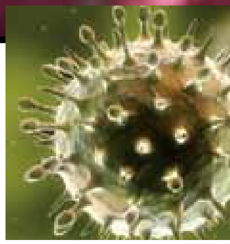

Social Distancing as a Pandemic Influenza Prevention Measure

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Social distancing measures minimize influenza transmission by reducing contact between susceptible and infectious individuals, and include school closures, travel restrictions, and restrictions on mass gatherings. Here we review the recent literature to evaluate the effectiveness of this approach as a pandemic prevention measure.

Key Points

- **School Closures:** Mathematical simulations provide evidence that school closures can reduce influenza transmission in an ideal setting. What is less clear is if these effects are still evident when key assumptions are only partially met. Empirical evidence from the last pandemic suggests that school closures reduce community transmission; however, few studies systematically compare community transmission in areas with and without this intervention. Furthermore, school closures are likely not effective during severe pandemics (high R_0) and not economically or socially acceptable during mild pandemics (low R_0). As a result, widespread proactive school closures are likely not an effective prevention measure during an influenza pandemic.
- **Travel Restrictions and Border Control:** Stringent travel restrictions and border control may briefly delay imminent pandemics; however, these approaches are neither economically nor socially feasible except in unique settings (e.g. small island).
- **Mass Gathering Restrictions:** There is no recent evidence outlining the effectiveness of mass gathering prohibition. While such approaches should logically reduce influenza transmission, they are not socially acceptable in most situations, especially for religious gatherings. Resources should instead be dedicated to case identification and patient treatment and isolation.

Social Distancing

Social distancing (SD) measures reduce influenza transmission by limiting the contact frequency between infected and susceptible individuals (1). SD measures include school or workplace closures, the restriction or prohibition of mass gatherings, travel restrictions, measures to reduce community contacts, and/or border control. These non-pharmaceutical approaches, also known as public health measures, are currently part of the World Health Organization (WHO), U.S. Centers for Disease Control and Prevention (CDC) and other pandemic response plans (2). Widespread use of these measures likely helped reduce mortality rates during the 1918-1919 influenza epidemic (3, 4, 5) and to quell the recent 2009 pH1N1 outbreak in Mexico (6). Furthermore, SD measures are the only intervention with guaranteed availability during the early stages of a novel influenza pandemic before vaccine development (7, 8).

Despite the importance given to SD measures in influenza pandemic plans, there is limited evidence on the effectiveness of such interventions (9); the majority of evidence that does exist focuses on seasonal influenza, modeling of past pandemics (1918, 1958, 1967),

Key unanswered questions

- Are proactive school closures more effective than reactive closures?
- How long must schools remain closed, and when is it is safe to re-open schools?
- Is there a threshold number of school closures required to reduce community transmission?
- How important are hygiene practices in the school setting?

or more recently, the H5N1 avian influenza. The 2009 pH1N1 pandemic represents an opportunity to re-evaluate the effectiveness of SD approaches used as part of the pandemic response plans.

School Closures

Background/Rationale

Prevention measures are most effective when they are directed at those at greatest risk of infection (8). Children and young adults experienced more severe illness during the pH1N1 pandemic (10), and up to 20% of transmission occurred in the school setting (11). School start dates were correlated with the timing of pH1N1 outbreaks (12), and school-centred outbreaks were reported in France (13), England (14, 15), New York (16, 17), Canada (18) and China (19). It is estimated that each infected school child had spread the virus to 2.4 other children (95% CI: 1.8-3.2). School closures are therefore one potential method of reducing influenza transmission early in an epidemic before the creation of a vaccine and/or distribution of antivirals (7, 8).

Evidence: Observational Studies

School closures in Hong Kong for children under 13 years of age reduced the reproductive number (R_0)[1] from 1.7 to 1.5, which decreased further to 1.1 after all schools were closed for the summer (20). This drop in R_0 likely resulted from an estimated 70% reduction in intra-age-group transmission caused by school closures. However, no comparison data from locations without school closures is presented and secular trends may be responsible for the observed patterns. Furthermore, school closures in previous Hong Kong winters did not appear to affect community transmission of seasonal influenza (21).

Prefect-wide school closures implemented in Osaka, Japan in response to approximately 100 ill students in May 2009 decreased the number of newly reported cases from 30 on May 17 to 0 by May 25 (22). Only 13 schools reported a single new case during this period. School closures are also thought to have helped contain Japan's first pH1N1 outbreak (23). Modeling of these data shows that school closures were effective when combined with post-exposure prophylaxis and home isolation, but only slowed transmission when used in isolation, doing little to reduce the total number of infected individuals (23).

A published abstract of work from the Dallas-Fort Worth area comparing acute respiratory infection (ARI) rates in communities with and without an 8-day school closure reveals compelling preliminary results. The odds of having an ARI during the period of closure were 50% lower than before the closure in the intervention community (OR=0.50, p<0.01), while the odds increased by 64% in the non-intervention community over the same time period (OR=1.64, p<0.01) (24).

Non-influenza-driven school closures also provide information on the effectiveness of SD measures. Pandemic H1N1 infection rates in children in France decreased by 20%-29% during holiday periods (no observable impact on adults), and holidays are estimated to cause a 16%-18% reduction in seasonal influenza in all individuals (25). Extrapolating to prolonged school closures during a pandemic suggests a potential 13%-17% decrease in cumulative cases in the community, with peak attack rates decreasing by 39%-45% (47%-52% in children). However, contact patterns during holidays differ from those occurring during pandemics and such extrapolations should be evaluated with care (25).

Hospital visit data from Israel show that the ratio of influenza-like diagnoses to non-respiratory diagnoses decreased most rapidly two weeks after an elementary school strike in Macabbi, during which time 80% of children aged 6-12 years remained home (26). This decrease was significant for both school-age children and adults without children. Furthermore, influenza rates rebounded after the strike ended, indicating that school closures reduce community transmission (26, 27). It should be noted that children comprise 34% of Maccabi's population and study findings may not hold in locations with proportionately fewer children (26).

In contrast, no difference in pre/post absentee rates, a proxy measure for

[1]The number of secondary cases caused by a single index case in a susceptible population.

influenza activity, was observed between schools with and without a winter break during the peak of an influenza outbreak in King County, Washington (28). These findings were still valid in a sub-analysis of elementary schools only. However, the school closure reported here likely occurred too late in the influenza season to alter the viral transmission patterns (28).

Evidence: Mathematical Simulations

Simulations created prior to the pH1N1 pandemic indicate that school closures can reduce attack rates, but that the effectiveness of such closures decreases with later implementation and with increasing R_0 (29); recent studies support these findings. Simulations of a pH1N1 outbreak in a small Ontario city show that 7-day rolling school/daycare closures reduce attack rates from 21.7% to 4.5% in the absence of vaccination, and that such closures are more effective if implemented early in the course of the epidemic (30). Here the combination of early school closures and vaccinations successfully halted transmission, but school closures are not required if the population has pre-existing immunity or if vaccines are distributed early in the pandemic (30).

Agent-based simulations[2] using data from Pennsylvania show that school closures longer than 8 weeks may delay the epidemic peak by up to 1 week, providing additional time to distribute antivirals and vaccinations (31). However, school closures of less than 8 weeks have limited effectiveness and closures of under 2 weeks may increase outbreak severity. Interestingly, this model predicts no meaningful difference between closing schools individually when sick children present themselves, and system-wide closures (31). Furthermore, the timing of the intervention had minimal impact on its effectiveness, contrasting with previous work (29, 30).

Simulations of the Australian community of Albany (population 30,000) show that school closures of 2 weeks could decrease influenza attack rates by 19%, while 4-week closures combined with antiviral treatment reduce influenza attack rates from 32.5% to 9% (32). However, school closures are most effective for mild epidemics (R_0=1.5), with effectiveness increasing as school closure duration lengthens (33). Attack rates can be reduced by up to 15% for a variety of R_0s by combining school closures and antivirals. These models agree with previous findings (31) in suggesting that closing individual schools is more practical than system-wide closures, with the former being less dependent on the timing of their initiation and more responsive to where and when cases are occurring.

Additional simulations of Albany support the effectiveness of the concurrent use of multiple SD measures. The application of school closures, isolation of symptomatic individuals in their households, workplace non-attendance, and reduction of contact in the wider community reduces attack rates from 33% to 10% if introduced in the first 6 weeks of a simulated epidemic with an R_0 of 1.5 (7). Such prevention approaches must be applied sooner at an R_0 of 2.5, with 2, 3 and 4-week starts resulting in final attack rates of 7%, 21%, and 45% respectively. At an R_0>3.5, all prevention measures are ineffective. Others show that a combination of adult and child SD, antiviral treatment and prophylaxis can reduce the total number of cases in the population from 35% to 10% for a low severity epidemic (R_0<1.6 and a case fatality rate of <0.5%), compared to a decrease from 35% to 22% if only SD and school closures are implemented (1).

Strict movement restrictions prohibiting students, professors and staff from leaving their institutions (*fengxiao*) is an alternative measure used in China (34). Simulation findings indicate that these movement restrictions delay the epidemic peak if implemented early, but are less effective than local measures focused on quarantine and hygiene. Furthermore, *fengxiao* may lead to more severe outbreaks in a university setting if not applied properly (34).

The importance of early implementation to school closure effectiveness, coupled with the economic costs of the intervention, mean that practical triggers are needed to guide school administrators and public health personnel. Retrospective analysis of school closure data from Japan indicate that a threshold of 5% single-day influenza-related absenteeism, double-days >4%, or triple-days >3% are optimal for alerting school administrators to consider school closure (35). However, use of such triggers may result in schools being closed too late in the pandemic to affect viral spread (27). Careful consideration must also be given to the timing of reopening schools, as a secondary peak in influenza cases may occur if schools are re-opened before herd immunity has been reached or before immunization of students and the general population has occurred (27).

The variation in the estimated effect of school closures on attack rates is likely due to differences in model assumptions regarding the timing of intervention implementation, the degree of contact or mixing outside of the school setting, and the duration of the school closure (7, 36). However, in general, model findings indicate the following:

- Short duration school closures (<2 weeks) are unlikely to be effective in reducing community transmission;

[2]A simulation approach used to model dynamic systems in which “agents” are programmed to follow specific rules. These simulations have minimal assumptions and allow the system to evolve over time.

Table 1

Summary of empirical work on social distancing interventions and their impacts on influenza transmission.*

Measure	Author	Intervention	Design	Location	Finding
School Closures	Wu, J. 2010 (21)	2 week school closure for children < 13, increased to entire summer.	Age-structured susceptible-infectious-recovered transmission model	Hong Kong	Drop in R_0 from 1.7-1.5 with 2 week closure. R_0 decreased to 1.1 after full summer closure.
	Ryosuke et al., 2009 (22)	Closure of 270 high schools/ 526 junior high schools in Osaka Prefect from May 18- May 24. Antivirals prescribed to students with infection.	Evaluation of simple case counts	Osaka Prefect, Japan	13 schools reported only 1 case during school closure, compared to >100 cases in a single school prior to school closure. No further outbreaks.
	Copeland et al., 2010 (24)	8 day school closure	Comparison of acute respiratory infection in schools with and without closure	Dallas-Fort Worth	Odds of having ARI during closure were 50% lower in intervention community than before closure, while increasing by 64% in non-intervention community
	Cauchemez et al., 2008 (25)	School holidays	Combined analysis of surveillance data and the timing of holidays.	France	pH1N1 rates decreased by 20-29% during holidays (no decrease in adults).
	Heymann et al., 2009 (26)	School Strike, 80% children aged 6-12 kept home.	Regression on ratio of influenza like illness to non-respiratory illness for school children, children household members, and all children aged >12.	Israel	Ratio ILI to non-ILI decrease most rapidly 2 weeks after strike. Influenza rates rebounded after strike.
	Rodriguez et al., 2009 (28)	Winter Break during peak influenza season	Comparison of pre-post absenteeism rates	King Country, Washington State	No difference in absenteeism rates. Results held for sub-analysis of elementary schools only.
Air Travel Restrictions	Hsu and Shih, 2010 (54)	Travel restrictions to top 50 airports. Restrictions of up to 99% of flights.	Dynamic transmission models	Global	Delay influenza pandemic by 1-3 weeks. Restrictions of 99% delay pandemic 1-2 months.
Entry Screening	Cowling et al., 2009 (57)	Entry Screening of individual travelers	Examination of entry screening policy in relation to first reported case	Multiple countries	Entry screening may delay local transmission 7-12 days.
Border Control	Nishiura et al., 2009 (62)	Quarantine of incoming travellers for >8.6 days.	Modeling of epidemiological characteristics of influenza	Global	Quarantine 99% effective in preventing infection.

* Simulation studies are not found in the table because the complexity of such simulations does not allow for easy summarization.

- The effectiveness of school closures in reducing transmission decreases the later they are implemented;
- School closures in isolation are ineffective at R0>2.5;
- The concurrent use of multiple SD measures, or pharmaceutical and non-pharmaceutical measures, has a greater impact than the use of any in isolation [see (37) for a review];
- Individual school closures are more practical than system-wide closures; and
- School closures do not halt transmission, but likely provide additional time for the distribution of antivirals and vaccination.

School Closures and Contact Patterns

School closures are effective only if student contact is reduced, and many models assume limited mixing of children outside of the school setting (27). However, survey-based estimates of contact patterns during school closures suggest there is continued student interaction (38, 39, 40, 41). In Australia, 74% of students participated in activities outside of the home during school closures, with an average of 3.7 out-of-home activities per student/week, including sporting events, outdoor recreation, shopping and parties (38). In Pennsylvania, students remained at home for 77% of their days during a one-week elementary school closure, but 69% of students visited at least one other location (39). In Boston, students interacted with the community and with other students during a week-long school break, with contacts being more frequent in older students (40). In 39 U.S. states, 56% of parents responded that their children participated in at least 1 activity involving persons outside the home during a three-day school closure (41).

Economic and Social Consequences of School Closures

The decision to close schools depends not only on the effectiveness of the intervention, but must be balanced by the social and economic costs. School closures are estimated to result in absenteeism of 16% of the entire UK workforce (42) and from 6%-19% (43) to 21% (27) of health care personnel. Surveys in New South Wales indicate that up to 37% of public health personnel may miss work due to school closures (44). Such absenteeism is especially problematic during pandemics when hospitals may be running at capacity (27).

Absenteeism makes school closures a more costly option than pharmaceutical measures despite the latter's higher initial costs (1). An influenza pandemic could decrease the gross domestic product (GDP) of select countries by 0.5%-2%, but these costs could double or triple with the addition of school closures (45); associated costs would double again if closures were extended from 4 weeks at the peak to the entire wave (13 weeks) (46). A single week of school closures in the U.S. could cost between 10 and 47 billion dollars (0.1%-0.3% of GDP) (1), while a 26-week school closure could cost 6% of GDP, 14-21 times the cost of using only targeted antiviral prophylaxis or vaccines (47). The estimated total cost of a combined intervention using adult and child SD, school closure, and antiviral treatment for a community of 10,000 individuals is estimated to be as high as 12.4 million dollars, with 74% of that cost resulting from absenteeism (1). In such a setting the addition of school closures to pharmaceutical interventions becomes cost-effective only for severe outbreaks (R_0>2.0, case fatality 1%) (1).

Closing schools also has social consequences that disproportionately affect the disadvantaged. School closures interrupted school lunch programs that fed 29 million U.S. children in 2004 (9). Prolonged school closures also affect educational continuity, which most negatively impacts children who are struggling academically (9). People in lower wage occupations, many of whom may be single parents, are typically unable to work from home or to miss work (48). Underprivileged children are therefore forced to care for themselves if a parent is unable to remain home. Self-care situations are associated with high-risk behaviors such as drug use and alcohol consumption (9) and may have long-term societal implications.

Travel, Border Control, and Entry Screening

Movement of infected individuals within and between countries, especially by air travel, facilitates influenza transmission by: 1) placing passengers in close contact for extended periods of time, and 2) increasing the connectedness of populations. Recent molecular evidence identified a single viral strain in six passengers traveling from the U.S. to Europe, which indicates in-flight transmission had likely occurred (49). One-quarter of 116 case patients in Singapore with travel-associated infection traveled after the onset of illness, and 15% became ill while traveling (50). Risk of in-flight transmission appears dependent on proximity (51, 49), which explains why transmission is higher in Economy than in First Class (52). However, no clustering was observed in 9 of 123 positive passengers travelling to China (53).

Worldwide transmission of influenza is greatly accelerated once the virus spreads to the top 50 global airports, and strategies that apply control measures to these airports may help contain the virus (54). International air travel restrictions could delay influenza pandemics by 1-3 weeks, while restricting 99% of air travel could provide an additional 1-2 months for vaccine administration (55).

However, such drastic restrictions are not economically feasible and are predicted to delay viral spread but not impact overall morbidity (24, 56).

Identification and quarantine of sick individuals at points of entry may delay the introduction of influenza to select countries. Screening consists of temperature checks, health declaration surveys, observing arriving passengers for symptoms, and/or thermal scans (57). Novel screening methods that quickly identify ill travellers by measuring and analyzing an individual's heart rate, breathing rate, and facial temperature have also been recently reported (58). A review of first-recorded pH1N1 dates in relation to entry screening policies show that entry screening may delay local transmission by 7-12 days (57). However, simulations from Japan suggested that border detection and quarantine had only limited effectiveness, with the initial case being detected after >100 cases had already entered the country (59).

In general, border control has limited effectiveness in large countries with porous borders. Given the current scale of air transport, effective border control would require unrealistic detection rates in order to delay or limit transmission (60, 61). However, border control may be effective in small island settings with a limited number of travellers where quarantine of incoming travellers for >8.6 days could have 99% effectiveness in preventing the release of infectious individuals into the community (62). However, few island nations could rely on such measures in isolation (63).

The importance of air travel in spreading influenza does, however, mean that analysis of air traffic data can help predict potential infectious disease hotspots (64). Real-time web-based disease surveillance systems combining information on worldwide patterns of commercial air traffic with RSS feeds that monitor news stories for references to infectious diseases from previously identified high-volume cities of origin may enhance global awareness of infectious disease threats (65).

Mass Gatherings

Mass gatherings are events that attract sufficient numbers of participants to "strain the planning and response resources of the community, city or nation hosting the event" (66). Examples include sporting events, concerts, World Youth Days, and the Hajj. Mass gatherings bring together participants and influenza strains from a variety of locations; six viral strains were detected at World Youth Days in 2008 in Australia alone (67). Prohibition of public gatherings has been linked to reduced mortality and delays in reaching peak mortality during the 1918 influenza pandemic (4, 68). However, national governments generally do not recommend prohibiting mass gatherings during mild influenza epidemics because of potential social disruption.

Mass gatherings in developing countries, or involving populations from poorer nations, pose a particular problem due to the limited resources available for surveillance and treatment.

The principles used to reduce seasonal influenza transmission generally hold for mass gatherings, yet additional cooperation and coordination between public health agencies is required to optimize the implementation of prevention efforts (69). Planning considerations should focus on detection and monitoring (screening, surveillance, laboratory testing, epidemiological analysis), reducing the spread of infection (infection control), managing and treating ill persons, and disseminating relevant public health messages (69, 70). Consideration must also be given to contingency planning, surge capacity, staffing, space for quarantine/isolation, and equipment for detection and prevention (71). In many mass gatherings, the density of individuals makes SD approaches impossible; hence facemasks, cough etiquette and hand washing should be actively promoted and readily available (72).

Pandemic H1N1 was detected during the Asian Youth Games in Singapore (71), a music festival and an international sporting event in Serbia (73), and a music festival in Belgium (74). Frequent temperature checks were used to identify cases in Singapore, while the Serbian and Belgian strategy focused on self-identification facilitated through the use of posters containing information on signs and symptoms, communication with the general public, sensitizing medical personnel, and deployment of 24/7 mobile epidemiological teams in the Serbian case. Individual isolation of identified cases was used in Singapore (71) but not in Serbia and Belgium, which instead recommended self-isolation (73, 74). All identified cases were provided with antiviral treatment in the above situations.

Mass gatherings in developing countries, or involving populations from poorer nations, pose a particular problem due to the limited resources available for surveillance and treatment. The Hajj, the annual Muslim pilgrimage to Mecca, represents one of the largest mass gatherings worldwide. In 2008, 2.5 million pilgrims from 140 countries converged in Mecca, 11.3% of whom came from low-income countries with limited ability to provide influenza vaccines (75). The incidence of vaccine-preventable influenza-like illness in 2,070 Pakistani pilgrims at the 1999 Hajj was 22/100 (76), while the influenza attack rates in 115 participants of the 2003 Hajj was 38% upon returning to London (77). Memish et al. (70) provide a review of recommendations aimed at improving public health preparedness during the Hajj, one of the primary recommendations being that those pilgrims with risk factors should stay home. However, survey results indicate that European pilgrims are unlikely to follow these recommendations (78). The scale of such an event and the potential for high attack rates, coupled with the limited feasibility of SD measures in such settings, point towards the need for international vaccination support (72).

Research Priorities

The current lack of strong empirical evidence results from both the rarity of influenza pandemics and the difficulty of implementing robust epidemiological study designs at the community level. While simulation studies are helpful, research priorities should focus on well-designed epidemiological studies (with inclusion of control groups ideally) in a community setting. Practical information on how to effectively implement SD measures, specifically school closures, is required to guide public health, governmental agencies, and school personnel during a pandemic and other infectious disease outbreak.

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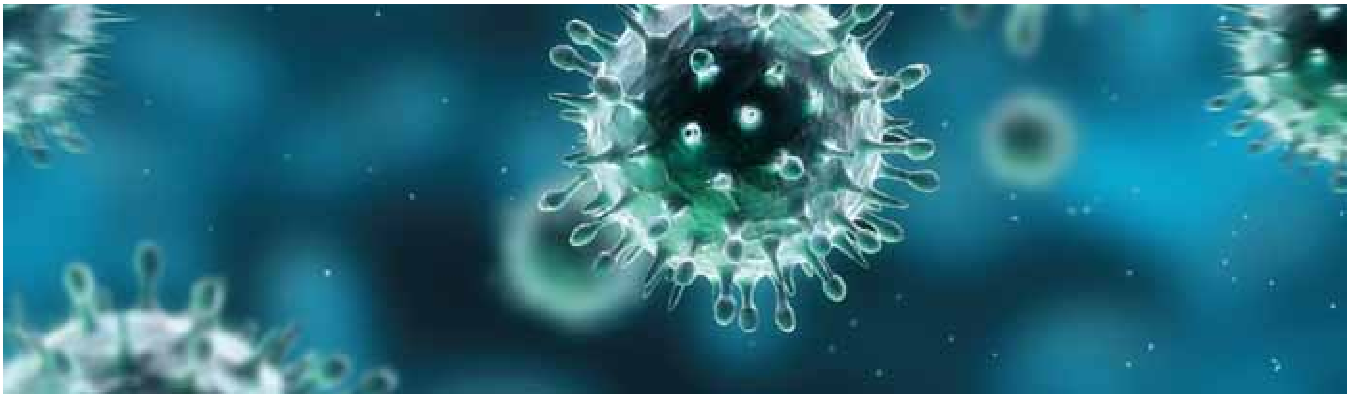

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