Respiratory and Hand Hygiene in an Influenza Pandemic

Scientific Evidence Base Review

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Respiratory and Hand Hygiene

Scientific Evidence Base Review

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This review was commissioned by the Department of Health in October 2010. The document was subsequently reviewed and endorsed by the Scientific Pandemic Influenza Advisory Committee (SPI).

The review was limited to respiratory hygiene and hand hygiene ("personal hygiene") and did not look at evidence for the role of environmental cleaning of solid surfaces and any potential contribution to a reduction in the transmission of influenza. The review examined scientific literature published up until the end of 2010. This document thus represents a contemporary summary of the evidence base for the impact of respiratory and hand hygiene on pandemics as of 2010. It is anticipated that further studies from the 2009 H1N1 pandemic will be published over the course of 2011 and 2012. The review will therefore be updated periodically to reflect any additions to the scientific literature that might alter any of its conclusions.

Contents

Executive summary

Hand and respiratory hygiene interventions for influenza control in the general population are non-pharmaceutical interventions that may be useful for slowing down transmission, especially in the early phase of a pandemic when vaccines are not yet available. A review was carried out the scientific evidence on biological plausibility, risk of adverse effects, acceptability, compliance and scalability, as well as evidence from trials testing the effect of hygiene interventions on influenza. Subsequently, the level of evidence that would be needed to justify hygiene interventions in the general population, households and schools was compared with the actually available evidence from field trials.

It was found that hand and respiratory hygiene interventions are biologically plausible interventions for influenza control, but that the expected effect size is likely to be small to moderate only. The risk of adverse effects is very low, and there is a potential for additional benefits such as a reduction in gastro-intestinal infections which could make hygiene interventions more cost-effective.

Acceptability of hand and respiratory interventions is likely to be high, but this does not guarantee compliance with better hand and respiratory hygiene. There is some evidence to suggest that hand hygiene has actually improved during the 2009 H1N1 pandemic, but compliance is likely to be low in schools as known foci of influenza transmission.

Hand and respiratory interventions are generally scalable interventions, but the scalability of enhanced hygiene measures in schools needs to be confirmed. These findings suggest that little evidence is required to justify widespread promotion of hand and respiratory hygiene for influenza control via mass media and distribution of leaflets.

Hygiene interventions targeting households of cases require more evidence than mass media campaign because the logistical efforts are likely to be higher. There is some evidence suggesting that interventions targeting households of cases delivered by health services could be effective in reducing household transmission of influenza. Household interventions therefore may be a useful addition to mass media campaigns.

There is little evidence in support of enhanced hygiene interventions in schools. Given low expected compliance with hand and respiratory interventions especially during break times, and considerable logistical constraints, one would hesitate to implement intensive hygiene intervention in schools unless there is good evidence that it actually works. Good evidence, however, is not available. Trials previously conducted in schools or similar settings are of poor quality and did not specifically measure the effect on influenza.

In conclusion, mass media campaigns and leaflet distribution can be justified given current knowledge. Interventions targeting households of cases have the potential to contribute to influenza control. School hygiene interventions that go beyond simple hygiene education and basic hygiene measures which are already practiced in many schools are difficult to justify given the available evidence. The overall paucity of evidence with regard to hand hygiene and especially respiratory hygiene suggests a need for further research.

1. Introduction

Hand and respiratory hygiene have been recommended by virtually all international, European and national health agencies as a simple measure for preventing influenza transmission since the emergence of the novel H1N1 Influenza A virus in spring 2009. Recommendations made by WHO and ECDC are broadly similar to UK national guidelines from the NHS and the Department of Health.[1-4] These propose 'regular handwashing' usually with a washing agent, most often soap. The use of 'rinse-free' methods with hand sanitizers is recommended in situations where water and soap are not available. Sanitizers should contain active ingredients such as alcohol to inactivate pathogens including respiratory viruses.

Respiratory hygiene, or 'cough etiquette' is also recommended, for example, 'covering mouth and nose when coughing or sneezing, using tissues and disposing of them appropriately'[5] or 'sneezing into a tissue and quickly putting it in a bin'.[6] Such recommendations are often linked with advice to wash hands immediately after coughing, sneezing or disposing of tissues. Hand and respiratory hygiene are usually treated as directly related behaviours. Both can be regarded as "personal hygiene", in contrast to domestic hygiene measures such as surface disinfection. Although this is not thought to be a major route of transmission for influenza, there is evidence that the risk can be reduced by environmental cleaning of solid surfaces.[71]

Most of the recommendations issued by international, European and national health agencies concerning hand and respiratory hygiene were developed before the 2009 H1N1 influenza pandemic.[5] These were then reissued when that pandemic emerged. However, these guidelines were widely acknowledged to have been based on plausibility rather than on controlled studies.[7;8] There were a number of reasons why hand and respiratory hygiene for influenza control were nevertheless added to the range of other control options such as pharmaceutical interventions (vaccination, antivirals) or social distancing methods such as school closure.

First, during an influenza pandemic the impact of vaccination can be compromised by the rapid spread of a pandemic strain and the time needed to develop, produce and distribute a vaccine (issues that indeed played a role in the current pandemic). Antiviral drugs may help to slow the spread of influenza in households,[9] and have been used, for example, in asymptomatic and

symptomatic schoolchildren to contain school outbreaks in the early phase of the pandemic,[10] but the impact on slowing the epidemic remains difficult to assess. Improved hand and respiratory hygiene may have a useful early contribution to make in slowing the progress of an epidemic.

Second, it was recognized prior to the pandemic that closing schools would affect working parents who might need to stay at home to take care of their children,[1] thus aggravating the economic impact of influenza and putting at risk the maintenance of essential services including health services.[2] School closures may therefore not be feasible for prolonged periods of time, during which successive waves of pandemic influenza may occur. If schools are kept open hygiene measures can plausibly make schools safer places for children and staff.

Vaccination, the prophylactic use of antiviral drugs, closing schools and other social distancing measures are invasive measures that have logistic and economic constraints and can impact considerably on people's lives. The decision to implement them is not easy to take, not least because they can lead to political controversy and fierce public opposition. In contrast, public health interventions to improve hand hygiene, respiratory hygiene or 'cough etiquette' are seen as less controversial because they target behaviours that are already socially acceptable. They are also useful in filling any publically perceived 'intervention gap' before the arrival of vaccines and in the face of difficulties with other measures.

However, achieving population compliance with hand and respiratory hygiene to a level that can have an impact on the progression of a pandemic is not as simple as it may sometimes seem. Distribution of messages via television or radio certainly is not very invasive or logistically demanding. Sending leaflets to every household in the country may be somewhat more costly but can still be regarded as a simple unobtrusive measure. Little hard data is available, however, about the level of behavioural response to such mass measures. Other interventions to improve hand and respiratory hygiene in the general population present more difficult choices. For example, should rinse-free alcohol hand sanitizers be available at public places and offices, as they often are in hospitals? Should every person diagnosed with Influenza be given a 'hygiene package' containing items to facilitate hand and respiratory hygiene? Should bins be distributed in the public sphere to allow 'disposing of tissues appropriately'? And should school children undergo a strict hygiene regime, for example by lining up 6 or 7 times a day in order to practice handwashing in the classroom?

In short, achieving major changes in behaviour in large populations is not just a simple matter of providing information, but requires careful planning and substantial investment.

The question faced by governments in the case of a pandemic is what is the right level of investment to allocate to each candidate intervention. Such decision-making requires evidence as to the effectiveness of interventions in changing behaviour, and in changing the course of a pandemic. The crucial point is that the ‘heavier’ an intervention is, the more evidence required to justify its implementation. This review examined the currently available evidence and, as a consequence, discusses the issues around what level of hand and respiratory hygiene intervention can be justified.

2. Methods

For the review a tool for public health decision making was used that was developed by David Ross from the London School of Hygiene and Tropical Medicine.[11] This tool has been applied successfully to a range of public health interventions.[11;12] It is based on the principle that an intervention that is potentially very effective (in terms of biological plausibility), is scalable and acceptable, of low risk, and associated with benefits other than reducing the target disease requires relatively little evidence with regard to its actual effectiveness. In contrast, an intervention that is characterised by a small potential health effect (based on just on biological plausibility, for example), of doubtful or unproven acceptability and scalability, with potential for adverse outcomes and with a lack of benefits other than reducing the target disease requires a high level of evidence before large scale implementation should be promoted.[11] Thus, we will first determine how much evidence we need to justify rolling out a specific intervention, then assess the currently available epidemiological evidence and decide whether both are in agreement.

Specifically, the tool has three steps:

(1) Define the strength of evidence needed to justify widespread implementation of hand and respiratory hygiene interventions, based on the potential size and biological plausibility of a health effect, and the intervention's scalability, acceptability, risk of adverse outcomes and potential secondary benefits.

(2) Summarize the strength of the available epidemiological evidence on the effectiveness of hand and respiratory hygiene interventions to reduce influenza, by critically reviewing published studies and systematic reviews.

(3) Synthesis: Compare the strength of the available evidence against the level of evidence that would be needed to recommend widespread implementation.

Respiratory and hand hygiene are treated as separate interventions where necessary, i.e. the recommendations made may differ between these measures. Due to the availability of several updated reviews on various aspects of hand and respiratory hygiene as interventions to reduce influenza and other respiratory infections we did not need to conduct a formal systematic review. However, to update these with recent publications we searched Medline using the following terms: [Influenza AND hygiene]; ["Respiratory hygiene"];[Influenza AND tissue];[Influenza AND sneezing];[Influenza AND coughing];[Influenza AND handkerchief]. The vast majority of articles, however, were identified from previous reviews. We decided not to conduct a meta-analysis (formal pooling of effect estimates) of the studies, since they were clearly too few and too heterogeneous for such purposes.

Hand and respiratory hygiene for influenza control can be promoted by a great variety of means in different settings and be aimed at different target populations. In this review we will consider evidence relating to hand and respiratory hygiene delivered; (1) to the general population via mass media, (2) to households of cases, as was tested in a recent trial in Hong Kong,[13] (3) in schools.

The review was not restricted solely to studies on influenza. Rather, where appropriate, studies on other respiratory viruses such as Rhinovirus, Respiratory Syncytial Virus (RSV) or SARS, were included. This approach may be criticized because the biology, pathogenicity, modes of transmission and survival in the environment of these viruses may be different to that of the influenza virus. However, it would be incorrect to say that studies involving respiratory viruses other than influenza, or studies that do not specify the respiratory pathogen at all, cannot, as a principle, be used to assess issues concerning the effectiveness of hand and respiratory hygiene. For example, if experimental studies on volunteers show that rhinovirus can be transmitted by contaminated surfaces via hands, then it becomes more, not less, likely that this may also be true for influenza, even if influenza viruses target different areas in the respiratory tract.

3. Results & Discussion

Define the level of evidence required for widespread implementation of hand and respiratory hygiene interventions

Biological plausibility

How plausible is it that hand hygiene can in principle can reduce influenza transmission? The answer to this question depends on: (1) the ability of influenza viruses to survive on surfaces and hands; (2) the ability of influenza viruses to be transferred from hands to the respiratory tract; (3) the potential of hand hygiene to remove influenza virus from hands, thus interrupting transmission. Answering (1) and (3) poses few difficulties. Influenza virus can survive on surfaces for several hours, and on hands for short periods of time, which should, in principle, allow for viable virus to be transferred to the face (for further details refer to the reviews by Weber[14] and Brankston[15]). Hand hygiene, whether with soap and water or rinse-free sanitizers, reduces virus load on hands substantially.[16] However, (2), the transfer of viable influenza virus from hands / fingers to the respiratory tract is controversial, because no experimental or epidemiological field studies have addressed this question. The major methodological problem lies in singling out transmission via hands and direct contact from droplet spread, which is nearly impossible in the field, and difficult in the laboratory. Laboratory experiments under controlled conditions have been carried out for RSV and Rhinovirus but not influenza. Experiments at the MRC common cold unit[17] and other institutions have shown that RSV and Rhinovirus infection can be produced in volunteers who rub their fingers in their eyes after artificial contamination or after indirect contact with sick individuals (for details see review by Goldman[18]). In the absence of studies on influenza, and in the absence of studies that have shown that transmission does *not* occur from hands to nose and eye for other respiratory viruses, this transmission pathway could apply to many respiratory viruses.

The biological plausibility of respiratory hygiene (“covering mouth and nose when coughing or sneezing, using tissues and disposing of them appropriately”) to reduce influenza transmission is difficult to assess. Using tissues may lead to more large droplets being caught so that they do not reach the airspace around the emitter (large droplets are thought to travel for about one meter[5]). A less porous surface such as the flat hand may deflect and spread large droplets to a

greater degree. Tissues may reduce hand contamination with virus. Disposing of tissues safely may reduce the contamination of hands and fomites, and may reduce contact transmission. It seems less likely that respiratory hygiene can prevent airborne transmission. This review found no systematic or even anecdotal evidence to support or disprove any of these assumptions.

Conclusion

Hand hygiene is a biologically plausible way of reducing the transmission of influenza virus, since this has been clearly demonstrated for other respiratory viruses. Reducing transmission by respiratory hygiene may not be implausible, but the lack of experimental data leaves this issue unclear.

Potential effect size

The review assessed the reduction of influenza spread attributable to hand and respiratory hygiene interventions if no data from field trials were available. The potential effect size primarily depends primarily on (1) the proportion of infections a targeted transmission pathway contributes to the overall epidemic; and (2) the proportion of infections due to a targeted transmission pathway that the intervention can prevent, assuming reasonable compliance.

It can be hypothesised that hand hygiene targets contact transmission and respiratory hygiene large droplet transmission and perhaps also contact transmission. This leads to a controversial issue in influenza epidemiology - the relative importance of the three hypothesized transmission pathways: airborne, large droplet spread within approximately 1m, and direct contact via hands.[15] In this field, strong opinions are prevalent. Based on the same data, experts either come to the conclusion that airborne transmission is common, or that it is a rare event indeed.[14;15;20] Two recent outbreak investigations on pandemic H1N1 (perhaps the most relevant in this context) suggest a major role for droplet spread at close range, but do not exclude contact transmission.[21;22] Since the role of hands in the transmission of influenza has actually never been demonstrated, one may hesitate to attribute a great proportion to this pathway. Thus, respiratory hygiene as an interventions with an unknown biological plausibility targets a potentially very common transmission pathway (droplet spread), while handwashing, the biological plausibility of which is supported by some experimental evidence, probably targets a minor pathway.

Influenza spread by large droplets and by contact between people in close proximity are difficult to separate in epidemiological studies. Close proximity thus appears to be the major risk factor for influenza spread, and this is where hand hygiene and respiratory hygiene can play a major role, if they are effective. The effectiveness of hand and respiratory hygiene probably depends on the setting. They may be effective in households with a known case, because facilities for hand and respiratory hygiene are readily available, and household members have some control over situations involving close contact. The potential effect size of hand and respiratory hygiene in schools is much more questionable, even if schools and school children showed good compliance with the interventions. Contact rates between children, for example, during break time, may simply be too high. Hand and respiratory hygiene cannot be practiced continuously even in compliant schools, which means that a large proportion of contacts between school children may remain unaffected by hygiene measures.

By contrast, if many or all schools are able to reduce transmission, for example through hand and respiratory hygiene, then this could affect influenza transmission in the population as a whole.[23] An intervention specifically targeting households of cases will only have a small impact on the whole population, since many cases will not receive the intervention because they will not seek treatment.

Independent of the setting, the potential effect size of personal hygiene messages in the context of an ongoing influenza epidemic may be enhanced by indirect effects. General awareness of a flu epidemic, coupled with graphic TV spots or images, raises fear of bodily emanations and close contact and may hence lead people to practice some degree of social distancing, e.g. leaving a room before coughing or sneezing, or avoiding large crowds or people with obvious symptoms.[24]

Conclusion

The potential effect size of interventions to improve hand and respiratory hygiene in the general population is difficult to quantify but probably only small to moderate. They could be more effective in preventing transmission within households and in the public sphere than in schools, perhaps aided by indirect effects hygiene promotion may cause, such as social distancing.

Risk of adverse effects

One of the major advantages of hand and respiratory hygiene lies in its very low potential for adverse effects. These are behavious that are practiced by most people some of the time; interventions usually aim at making people practice more of what they usually do. Washing hands with soap and using tissues for coughing and sneezing have low to zero adverse affects. More attention needs to be paid to the use of hand sanitizers or other products for hand and respiratory hygiene, such as “antibacterial soap” or “antiviral tissues”. Rinse-free hand sanitizers are recommended by some national health agencies as an alternative in situations where hand washing with water and soap is not possible. Rinse free hand sanitizers are usually based on alcohol or contain other antiviral substances such as benzalkonium chloride. It has been claimed that conventional alcohol-containing hand sanitizers are not suitable for children,[25 26] although we found no evidence for this in a formative research study in East London.[27] It is not even clear whether alcohol sanitizers are more damaging to the skin than soap and water.[28] Alcohol based hand sanitizers are inflammable products but have long been in use in health care settings. There is little evidence for fires from alcohol-based hand rubs.[29] Accidental ingestion of alcohol based hand rubs by children is not uncommon,[30] and can in exceptional cases lead to serious intoxication.[31] Intoxication in alcohol addicts can also occur. Poisoning with alcohol sanitizers is rare overall, but one needs to consider the effect of rolling out the use of alcohol sanitizers on a national scale including schools. Serious events, even if very unlikely, are almost certain to happen occasionally if alcohol rubs are used everywhere.

There are a broad range of commercially-available “antiviral” products, for example, in the form of soap or in tissues for respiratory hygiene. This review was unable to determine whether there is any risk associated with the use of such products.[32]

One type of Obsessive Compulsive Disorder (OCD) is associated with looming fears of contamination[69]. The disorder is relatively common and occurs on a continuum of severity in the general population.[70] It is plausible that interventions to promote hand and respiratory hygiene in the face of a pandemic could heighten fears/disgust of contamination and hence lead to more debilitating compulsive behaviour in those suffering clinical and subclinical manifestations of OCD.

Conclusion

The risk associated with conventional hand and respiratory hygiene as recommended by national and international health agencies is very low. The use of alcohol hand sanitizers poses a very small risk that, however, is not trivial. The risk associated with new antiviral products for hand and respiratory hygiene is unknown.

Potential for beneficial effects unrelated to influenza control

In contrast to vaccination and antivirals, the benefits of hand and respiratory hygiene are not specific to influenza. Improved hand hygiene may reduce the risk of gastro-intestinal infections[33;34] and other respiratory infections.[35;36] The quality of most trials conducted in the general population testing the effects of hand hygiene on infections is poor, but a substantial effect remains a realistic possibility. This adds to the potential cost-effectiveness of hand and respiratory hygiene.

Substantial exposure to messages and interventions targeting personal hygiene may contribute to habit formation and change in social norms.[37-39] In the long term, thanks to hygiene interventions primarily initiated to control influenza, personal hygiene could improve on a broad basis. Social pressure to practice hygiene could increase. Patients in hospitals may become more aware of staff not practicing hand hygiene.

Such considerations currently are speculative but it is worth noting that two repeated cross sectional surveys at the same sites across England found lower colonization rates of faecal bacteria on hands after the H1N1 pandemic started compared to before (details below).[39;40] This could indicate an effect of hygiene interventions on the transmission of gastro-intestinal pathogens.

A further benefit may be psychological. An important feature of the anxiety associated with influenza may well be the feeling of helplessness, since the virus can easily be perceived to spread everywhere and by whatever means. Promoting simple measures such as hand and respiratory hygiene that can be practiced by everyone at all times could reassure the population and give some sense of control.[41]

Conclusion

Hand and respiratory hygiene are potentially associated with substantial benefits in terms of general infection control.

Acceptability and compliance

For the purposes of this review, ‘acceptability’ means whether the target population perceives an intervention as being justified by the threat of influenza, associated with an acceptable risk and associated with an acceptable level of intrusion into daily life. In this context, ‘compliance’ means whether an intervention, even if regarded as acceptable by the target population, is actually practiced. A high level of acceptability of hygiene interventions does not guarantee a high level of compliance. However, it can be assumed that an intervention perceived as unacceptable will also be associated with a low level of compliance.

The acceptability of most hygiene interventions can be regarded as not posing major difficulties, as was confirmed in a qualitative research study from southern England.[42] In the recent H1N1 pandemic, vaccination, antiviral prophylaxis and school closures have caused considerable public controversy, but we are unaware of any major outrage over hand and respiratory hygiene recommendations in the UK or elsewhere.

Formative research on hand hygiene has shown that in most countries personal hygiene is regarded as an important part of daily life and of social norms.[38;43] Because social norms are drivers of hygiene behavior (as we have shown for the UK[39]), most people would find enhancing it in pandemic times acceptable. However, for some, such measures may be seen as excessive, or even to contribute to allergy (despite the fact that this is unlikely).[44 43] Hand hygiene may be regarded as more acceptable and feasible than strict respiratory hygiene measures.[42]

Acceptability may be an issue in school interventions, although a study from the US found no evidence for this.[45] We have shown in a formative research study in East London that enhanced hygiene interventions can meet with resistance from teachers, who wish to avoid disruption of the school routine.[27] We found that acceptability of hygiene interventions in schools can be improved if the measures are implemented only temporarily, for example for 4

to 6 weeks in the initial phase of a pandemic. Enhanced hand hygiene was only perceived as feasible and acceptable when we tried rinse-free alcohol rubs. Getting a whole class to wash hands with soap and water frequently ended in chaos.[27] Acceptability of alcohol rubs was also high in a US school study .[46] Frequent use of alcohol rubs, however, may not always be acceptable for parents. In our research we encountered no opposition from parents. The use of alcohol products was also deemed acceptable by Muslim parents. However universal approval cannot be extrapolated from individual studies.

Poor compliance is perhaps the central issue with most hand and respiratory hygiene interventions. More data are available for hand hygiene than for respiratory hygiene. Many studies in hospital settings or the general population in different parts of the world have shown that compliance with handwashing is often poor, and that self-reported hygiene practices hugely exaggerate actual behavior,[47] which is why studies using self-report[48] need to be treated with extreme caution. For example a study Hong Kong using telephone surveys claimed that 46.65% washed hands more than 10 times/day, 88.75% wore face masks when having influenza-like illness, and 21.5% of respondents wore face masks regularly in public areas.[49] However, though self-report is a poor way to measure real behavior, it does provide a useful indicator of beliefs and social norms, especially if measured at different times during an epidemic. Another study from Hong Kong showed that reported practices and risk perception changed little during the H1N1 pandemic.[50] Surveys in the UK identified a strong link between how much people are worried about influenza and reported uptake of protective behaviours[51].

Compliance with handwashing can be observed directly. A study during the SARS epidemic at North American Airports employing observations in rest rooms suggested a large increase in hand washing in cities affected by this public health threat.[52] There is some evidence on the effect of the H1N1 pandemic from unobtrusive measures of hand hygiene from a study conducted in a motorway service station. The first experiment was conducted from August to September 2008. Handwashing with soap was monitored electronically by counting infrared signals from the entrance of restrooms and the use of soap dispensers.[39] When no handwashing messages were displayed, around 32% of men and 65% of women washed hands with soap. In the same period in 2009 (when the devices without hygiene messages were reinstalled) the proportion of men using soap dispensers had increased to 53%. There are no reliable data for women.

The Figure below shows the trend in soap use for handwashing over time in men during our 2009 study. There is some confounding because handwashing during holiday times usually increases, because the population traveling at these times is different. Nevertheless, it is possible that the much higher soap use and handwashing rates in 2009 and the overall increase from June to August reflects a real behavior change coinciding with the H1N1 pandemic.

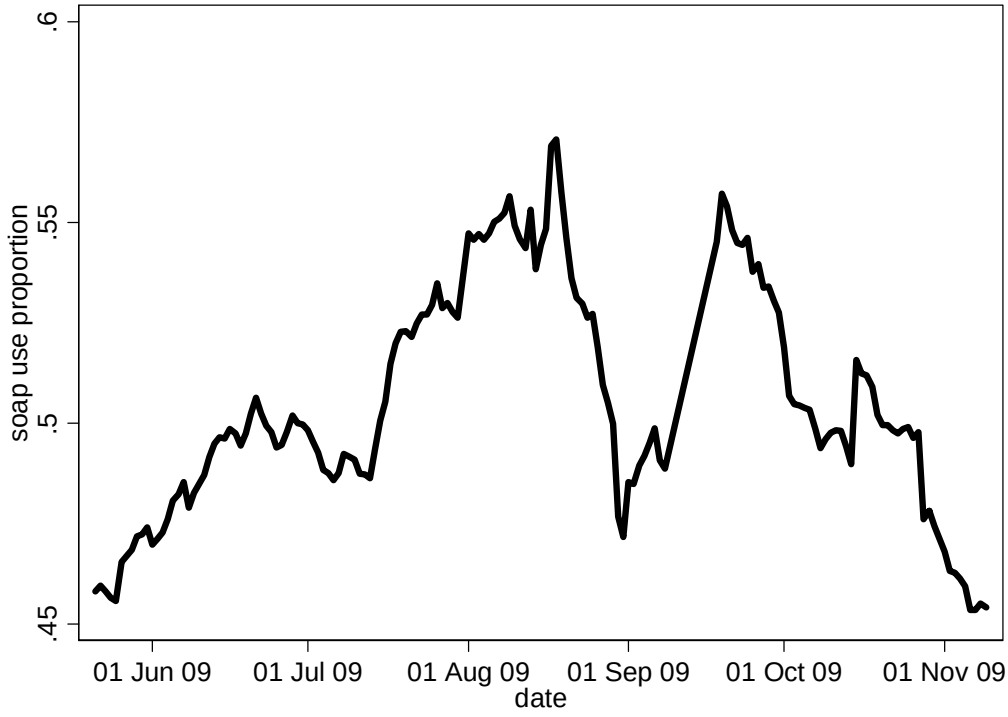

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Figure 1. Soap use in men at a large service station in England during the H1N1 pandemic.(Judah G, Schmidt WP, Curtis V, unpublished data)

Some evidence for improved hand hygiene can also be derived from our above mentioned repeated cross sectional surveys on contamination of hands with feacal bacteria in male commuters in London, Birmingham, Liverpool and Newcastle conducted in 2008 and 2009 (women were included only in 2008). The surveys were done during July and August of both years using the same sampling procedures and microbiological methods. Contamination rates were markedly lower in 2009 (Figure 2). It is not easy to make causal inferences from these data, however they are consistent with a pandemic related increase in hand hygiene. It could be shown experimentally that handwashing reduced feacal contamination as assessed by this microbiological tool,[53] and that risk behaviours such as reported hygiene and number of handshakes on the day of the sample were clearly associated with contamination.[40] Still, secular trends independent of a potential H1N1 pandemic-driven behavior change cannot be excluded.

On the whole, evidence from the motorway station experiment and the microbiological surveys suggest that compliance with handwashing can be improved during a major public health threat such as an influenza pandemic. Conducting similar studies on respiratory hygiene would be of great interest, but they are currently unavailable.

Compliance with hygiene interventions in schools is a difficult issue. One may expect low compliance with respiratory hygiene and hand washing in unsupervised young children especially during break times. On the other hand, schools are environments where teachers have some control over pupils' risk behavior and where hygiene measures (in contrast to most other environments) can, to some extent, be enforced.[27] School studies have shown that compliance with the use of alcohol rubs can be achieved and maintained over several weeks.[27;46;55;56] In practice, teachers can line pupils up before or after every session and use bottles of alcohol-based sanitizers to deliver a portion of gel to every student. This procedure takes much less time than one might expect. In our behaviour trials in classes with up to 30 children, this could be done in 3 minutes without rush.

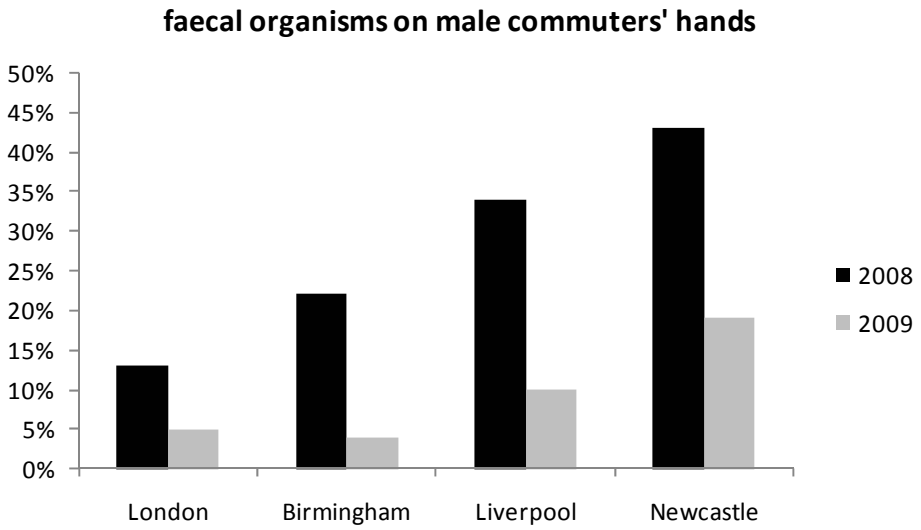

Figure 2. cross sectional surveys of faecal contamination in English cities.[40;54]

Teachers find respiratory hygiene much more difficult to enforce than hand hygiene. Respiratory hygiene in the school environment cannot be scheduled since coughing and sneezing are natural reflexes over which there is little control. Teachers said that they would be unwilling to interrupt sessions to make a child use a tissue and wash hands afterwards. Field staff in the East London school study found it very difficult to observe coughing, sneezing and related hygiene behaviors in a class during a session because there was so much of it. One study from Pittsburg (USA) reports to have achieved an increase of respiratory hygiene ("cover your coughs and sneezes") in school children using a multilayered non-pharmaceutical intervention approach. However, compliance was assessed by teachers' questionnaires, a weak method for measuring hygiene behavior. Also, the improvements were small in absolute terms.[55;56]

Teachers often routinely educate children in good manners that include hand and respiratory hygiene.[27] They hope to contribute to the good upbringing of children and also wish to protect themselves from disease transmission.[27] These motivations can, to some extent, be utilized to

improve compliance with personal hygiene measures in pupils. Two studies from the US suggest that simple teacher-led interventions can achieve some improvement in hand hygiene,[57;58] although the methods of ascertainment of compliance were not reliable. Whether the level of compliance with hand and respiratory hygiene achievable in a school environment will be sufficient to make a difference, given the expected high contact rates between young children is not clear, but may be questionable.

Conclusion

Hand and respiratory hygiene interventions are generally highly acceptable. At least moderate levels of compliance with hand hygiene are achievable in the general population and, under supervision of teachers, even in schools. Compliance with respiratory hygiene is unclear.

Scalability

In this context, ‘scalability’ of an intervention means how much money and staffing an intervention requires to be effective, and whether these means are available. The reivew did not identify specific information on the costs of different interventions for implementing agencies. This section therefore can only be an outline of some general considerations.
Mass media and distribution of leaflets to all households in the country achieve widespread, near-universal coverage at reasonable cost. No special equipment or products are needed. The commercial sector in the UK can readily supply hygiene products such as soap, alcohol sanitizers or tissues. Thus, using mass media and leaflets to promote hand and respiratory hygiene should be scalable.

Interventions targeting the households of cases could be delivered by doctors, nurses, hospitals[13] and pharmacies. During a major event such as an influenza pandemic these services will be stretched in their capacity. Distributing additional detailed information on hygiene practices in the home via mass media, booklets or leaflets, and perhaps also providing products to facilitate hygiene such as hand sanitizers[13] does not need to be time-consuming. Overall, interventions specifically targeting cases are less scalable than mass media campaigns because they require the cooperation of a large number of staff involved in health care delivery.

No data was found on the feasibility of national level implementation of hygiene interventions in schools, hence the following considerations are speculative. School interventions depend to a large degree on the cooperation of teachers and head teachers.[27] By and large, basic measures of hand and respiratory hygiene can be implemented at schools at no great cost. Hand hygiene in schools is greatly facilitated by the use of alcohol hand sanitizers, as we have seen above. Providing all schools with adequate supplies may be a challenge, and will also increase costs. In recent years, however, the availability of alcohol-based sanitizers via the commerical sector has increased considerably, especially following the 2009 H1N1 pandemic. Safe storage of alcohol based products needs to be assured, although these may be less toxic than some cleaning products routinely used in schools, such as bleach. Overall, in the event of a major threat, such as an influenza pandemic associated with a high mortality, we believe that even more intense school hygiene interventions are scalable, but this may require tested and pre-established logistics.

Conclusion

Mass media and leaflet campaigns are easily scalable and can reach a large part of the population at low cost per person targeted. Household and school hygiene interventions require more sophisticated logistics which, in the event of an influenza pandemic associated with high mortality, are unlikely to be insurmountable.

The evidence required for implementing hand and respiratory hygiene

A synthesis of the criteria determining the level of evidence required for implementing an intervention is shown in Table 1. Importantly, the different criteria are not independent from each other. For example, an intervention with many benefits is likely to be more acceptable and scalable, and is also less likely to be a waste of resources if the true effect on disease is smaller than assumed or non-existent.

Table 1. The level of evidence required for hand hygiene

	Mass media and leaflets targeting the general population	**Interventions targeting households of cases**	**School interventions**
Biological plausibility	Plausible	Plausible	Unclear
Potential effect size	Small to moderate	Small to moderate, small at population level	Small to moderate
Risk of adverse effects	Very small	Very small	Very small
Potential for other benefits	High	High	High
Acceptability	High	High	High
Compliance	Moderate	Moderate	Low
Scalability	High	Feasible	Feasible
Level of evidence required	Low	Moderate	Good

Table 2. The level of evidence required for respiratory hygiene

	Mass media and leaflets targeting the general population	Interventions targeting households of cases	School interventions
Biological plausibility	Unclear	Unclear	Unclear
Potential effect size	Moderate	Moderate, small at population level	Unclear
Risk of adverse effects	Very small	Very small	Very small
Potential for other benefits	Moderate	Moderate	Moderate
Acceptability	High	High	High
Compliance	Unclear	Unclear	Low
Scalability	High	Feasible	Feasible
Level of evidence required	Low	Moderate	Good

The overview in Tables 1 and 2 suggests that we require a similar level of evidence for implementing hand and respiratory hygiene interventions. There is less evidence of biological plausibility and compliance for respiratory hygiene than for hand hygiene, but the transmission pathway targeted by the former is probably more important than direct contact spread – the domain of hand hygiene. On the whole, mass media campaigns require little epidemiological evidence of their true effect on influenza transmission because of the ease of implementation, low risk of adverse effects, potential for other benefits and high acceptability. Household interventions require somewhat more evidence because of the lower potential effect size at population level and more challenging scalability. School interventions which aim to reduce influenza require good evidence of effectiveness because: (1) compliance may need to be exceptionally high to make hygiene interventions effective, given high contact rates among young children; (2) challenges of scalability. We would therefore hesitate to roll out intensive school interventions involving scheduled use of alcohol-based hand sanitizers without evidence that this actually reduces transmission.

In the next section we explore how much evidence from epidemiological studies is actually available for hand and respiratory hygiene interventions to reduce influenza transmission.

Assess the available evidence from epidemiological studies and trials conducted to estimate the effect of respiratory and hand hygiene to reduce influenza transmission.

In this analysis, studies from respiratory infections other than influenza included, as were studies with school or workplace absence as the main outcome, based on the assumption that most episodes of absence may be due to respiratory infections.[59]

Table 3 shows an overview of published systematic reviews. Four were found. Jefferson et al. did not exclude respiratory hygiene interventions *a priori* but could not find any related studies. No studies were identified estimating the effect of respiratory hygiene on respiratory infections.

Table 3. Reviews on hand hygiene to reduce respiratory infections

Author	Intervention	Study types	Setting	Outcome	Estimated disease reduction	Conclusion
Rabie[36]	Hand washing with water (+/- soap)	RCT and observational	Not restricted	Respiratory infections	16%	Poor study quality, high potential for bias
Jefferson[60]	Handwashing, hand sanitizers	RCT and observational	Not restricted	Respiratory infections	No pooled estimate provided	Hand hygiene highly effective
Meadows[61]	Hand sanitizers	RCT and quasi RCT	Schools	Absenteeism	No pooled estimate provided	Poor study quality, high potential for bias
Aiello[62]	Handwashing, hand sanitizers	RCT	Not restricted	Respiratory infections	21%	Hand hygiene effective

There is considerable overlap among the reviews. Aiello[62] and Jefferson[60] include many studies that previously were also included separately by Rabie[36] and Meadows.[61] The conclusions are greatly influenced by how severe the authors perceive the risk of bias. Rabie and Meadows conclude that the risk of bias is severe enough to threaten the validity of all studies included. This view is confirmed by recent methodological work in the field of epidemiology. Randomised controlled trials are often regarded as the "gold standard" to evaluate the effect of health interventions. Randomised controlled trials work well if the treatment and the outcome assessment can be blinded both from the study participant and the observer. However, hand hygiene cannot easily be blinded. Unblinded randomised controlled trials can still provide largely unbiased estimates if the outcome is an objective measure such as death. Randomised controlled trials using a more subjective outcome measure, such as self-reported respiratory symptoms, do not usually provide unbiased estimates.[63] Study participants in the intervention arm have a strong incentive to under-report disease for fear of being seen as non-compliant. This is especially be the case in trials where the intervention is related to issues of morality and social norms which is typical (or even definitive) of hygiene interventions. Another source of bias could come from over-enthusiastic field workers who, out of commitment, or for the sake of job security want to demonstrate the effectiveness of an intervention (observer bias).

An illustrative example is provided by a review on water purification interventions at household level.[12] There, unblinded trials reported on average a 50% reduction of gastro-intestinal infections. In three trials the water purification method was blinded to participants by using a placebo disinfectant. These trials found a pooled disease reduction of 0%. Thus, even a 50% observed reduction in unblinded trials with a subjective (self-reported) outcome may be compatible with a true effect of zero. Systematic reviews of unblinded studies with a subjective disease outcome simply average the bias effect. Most available studies on the effect of hand hygiene on respiratory infections have used self-reported symptoms as outcome.

The challenges in conducting hand hygiene studies for influenza control can be illustrated by two recently published trials, both funded by CDC, Atlanta, USA, in a large initiative designed to fill the gaps in the knowledge of influenza control.[64]

The first trial was in Hong Kong.[13] Households of confirmed influenza cases were randomized to hand hygiene, facemasks + hand hygiene, or control. Hand hygiene was promoted by health

education and provision of liquid soap and alcohol sanitizers. The trial was remarkable because (1) health services delivered a household intervention that could potentially be replicated at large scale, (2) laboratory confirmed influenza in household contacts was specified as the main outcome, (3) the outcome assessment minimized bias since samples were taken independent of symptoms. The only major issue was the small number of cases (60 overall) which led to low study power and wide confidence intervals. Hand hygiene reduced the secondary attack rate by around 46%, but this was not statistically significant (p= 0.22). In a subgroup analysis in households where the intervention was implemented with 36 hours of the index case showing symptoms, the reduction was 68% and statistically significant (p= 0.04). Despite low study power, this trial remains the best one available on non-pharmaceutical interventions for influenza control.

The second trial funded by CDC in this initiative was conducted in university student halls in the US[65]. The trial compared facemasks, facemasks + hand hygiene with a control group. The authors randomized only 7 halls overall (the minimum required is 5 clusters per intervention arm[66]; an insufficient number of clusters is a common feature of school and university trials.[61]) As a confounding factor, the 7 halls were merged into 3 groups “to ensure equal size” prior to randomization, i.e. there were really only three randomization units. The outcome was self-report. The intervention was reported to be effective in the second half of the study period. Significant reductions were reported in ILI during weeks 4–6 in the mask and hand hygiene group, compared with the control group, ranging from 35% (confidence interval [CI], 9%–53%) to 51% (CI, 13%–73%), after adjusting for vaccination and other covariates. It remains possible that participants complied increasingly less with the intervention over the 6 week trial period, and as a consequence, avoided reporting illness for fear of being seen as not compliant. In such a case, the reduction of reported respiratory symptoms in the intervention arm later in the study, would be consistent with the increase in the effect size as the trial progressed (Table 4).

Conclusion

There is weak but suggestive evidence that hand hygiene interventions in households of cases can reduce influenza transmission. There is very weak evidence for an effect in schools and no evidence for respiratory hygiene interventions in any setting.

Table 4. Effect of a hygiene and facemasks intervention in 7 US university halls[65]

Week	Face mask only vs control		Face mask and hand hygiene vs control	
	RR (95% CI)	P^a	RR (95% CI)	P^a
1	0.89 (0.61–1.30)	.54	0.98 (0.67–1.44)	.92
2	0.81 (0.61–1.08)	.16	0.86 (0.65–1.15)	.31
3	0.75 (0.58–0.96)	.02	0.76 (0.59–0.98)	.03
4	0.68 (0.51–0.92)	.01	0.67 (0.49–0.91)	.01
5	0.63 (0.42–0.93)	.02	0.59 (0.38–0.89)	.01
6	0.57 (0.34–0.97)	.04	0.51 (0.30–0.90)	.02

Synthesis of the evidence

A synthesis of the evidence and the resulting recommendations are shown in Tables 5 and 6 separately for hand and respiratory hygiene. In the following sections we discuss hand and respiratory hygiene interventions jointly because our assessment (Table 5 and 6) suggests that conclusions for both interventions are similar.

Table 5. Synthesis of the evidence for hand hygiene interventions for influenza control

	Mass media and leaflets targeting the general population	**Interventions targeting households of cases**	**School interventions**
Level of evidence required	Low	Moderate	Good
Level of evidence available	Very weak	Weak but suggestive	Very weak
Conclusion	Recommended	Recommended with caution	Intense interventions not recommended

Table 6. Synthesis of the evidence for respiratory hygiene interventions for influenza control

	Mass media and leaflets targeting the general population	Interventions targeting households of cases	School interventions
Level of evidence required	Low	Moderate	Good
Level of evidence available	Very weak	Very weak	Very weak
Conclusion	Recommended	Recommended with caution	Intense interventions not recommended

Mass media and leaflets targeting the general population

The synthesis of the available data shows that there is little epidemiological evidence in support of hygiene interventions for influenza control delivered by mass media or leaflets. However, even if the true effect on influenza were small, for example a 5% to 10% disease reduction, the intervention would in all likelihood still be cost-effective, especially if this translates into a 5% to 10% reduction in hospital admissions and intensive care attributable to influenza at national scale. Other benefits of the interventions only add to the cost-effectiveness.[67]

It seems unlikely that research studies in the foreseeable future will come up with results that will alter such conclusions. The effect of mass media campaigns on disease is difficult to study, especially if the effect is small. Once can conclude that promoting hand and respiratory hygiene by mass media and leaflet campaigns could reasonably be considered as part of any national control strategy for pandemic or seasonal influenza.

Interventions targeting households of cases

Interventions targeting households of cases have perhaps the greatest potential for a disease reduction in the target population; however, the impact will be limited to a small fraction of the general population. Thus, a small effect in the general population by mass media campaigns may prevent more cases than interventions targeting households of cases. The RCT in Hong Kong[13] suggests that health services may be able to deliver enhanced health education to families of cases. The delivery of such interventions could be combined with other interventions such as facemasks or antiviral prophylaxis which reduces the logistics for a single intervention, but still could be a burden to overstretched health services. Improving the evidence base by conducting further RCTs is both necessary and (as the Hong Kong trial shows) clearly possible.

School interventions

Intensive hand and respiratory hygiene interventions in schools in the form of scheduled hand hygiene and maintaining strict compliance with respiratory hygiene currently do not appear to have a realistic prospect of making an impact on influenza transmission. The logistical burden for schools and the interruption of teaching, but in particular the high contact rates coupled with an expected low compliance with hand and respiratory hygiene in children during break times, when most transmission is likely to occur, are serious concerns.

Improving personal hygiene in school children is recognized by many teachers and school nurses as an important educational and public health goal.[27] To a certain degree it is feasible to incorporate enhanced hand and respiratory hygiene into the school routine in the event of a major health threat like an influenza pandemic. This could be encouraged, for example, by developing and testing realistic guidelines that are easy and cheap to implement.

The evidence base for hand and respiratory hygiene may be improved on a broad basis by conducting transmission experiments under controlled conditions in the laboratory or well-defined naturalistic settings. Such experiments have provided valuable data on the importance of different transmission routes for rhinovirus and RSV.[17;18] The uncertainty with regard to the role of different transmission pathways of influenza viruses is a major limitation of decision

making on non-pharmaceutical interventions for influenza control.

Little is still known about the effectiveness and cost-effectiveness of interventions to change hand and respiratory hygiene in the general population. Whilst hand hygiene did apparently improve during the recent pandemic it is not clear how far this was due to specific efforts at hygiene promotion, and how much due to general awareness and a ‘pandemic mentality’. No information is available on changes in respiratory hygiene. Much more work is needed to develop effective interventions, and this should be based on careful formative research in different settings. It is noteworthy, for example, how much useful information for this review was generated by one small study assessing the feasibility of hand hygiene interventions in schools[27].

There has been a general tendency to assume that simply providing information is sufficient to lead to changes in behavior. This is unlikely to be true; more sophisticated approaches to behavior change take into account environmental factors, products, emotions and motives, such as affiliation and disgust as well as habit.[38;39]

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