



From: "Entrekin, Tyler" <Tyler.Entrekin@kingcounty.gov> on behalf of "Disclosure, Public" <Public.Disclosure@kingcounty.gov>
Date: Friday, June 26, 2020 at 5:05 PM
To: "Disclosure, Public" <Public.Disclosure@kingcounty.gov>
Subject: Your PRA request - Covid-19

EXTERNAL SENDER

Below is a link to installment 4 of your public records request regarding Covid-19. We anticipate having another installment or an update on your request by July 24, 2020.

https://kc1-my.sharepoint.com/:f:/g/personal/tyler_entrekin_kingcounty_gov/EhHzWG-EyIIIpNlye9HX_5cBzVmRE9ct6fIFysCV53yW2g

Regards,
Tyler Entrekin, Manager
Health Information, Release and Records Management
Public Health – Seattle & King County
Ph: 206-263-8249
F: 206-205-3945

From: [Elsenboss, Carina](#)
To: [Hayes, Patty](#); [Worsham, Dennis](#)
Subject: Authorities PPT
Date: Sunday, March 1, 2020 9:18:21 PM
Attachments: [COVID_Authorities Briefing_030120.pptx](#)

Hello – I revised the PPT for the authorities discussion tomorrow. The KC numbers need to get updated but will do that tomorrow. Slides 10 (LHO I&Q) and 12 (governor limiting movement) have some new info from the AG and highlighted in red. Kathy mentioned she was working on a new slide deck on NPI for another governor briefing today or tomorrow.

Dennis – could you ask for this?

Stephanie – will have a couple of tweaks before the briefing tomorrow.

Thanks,
Carina

Carina Elsenboss, MS

Preparedness Director
Public Health – Seattle & King County
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Coronavirus Disease 2019 (COVID-19) Response

Powers and authorities discussion with state, local
and elected officials

Outline

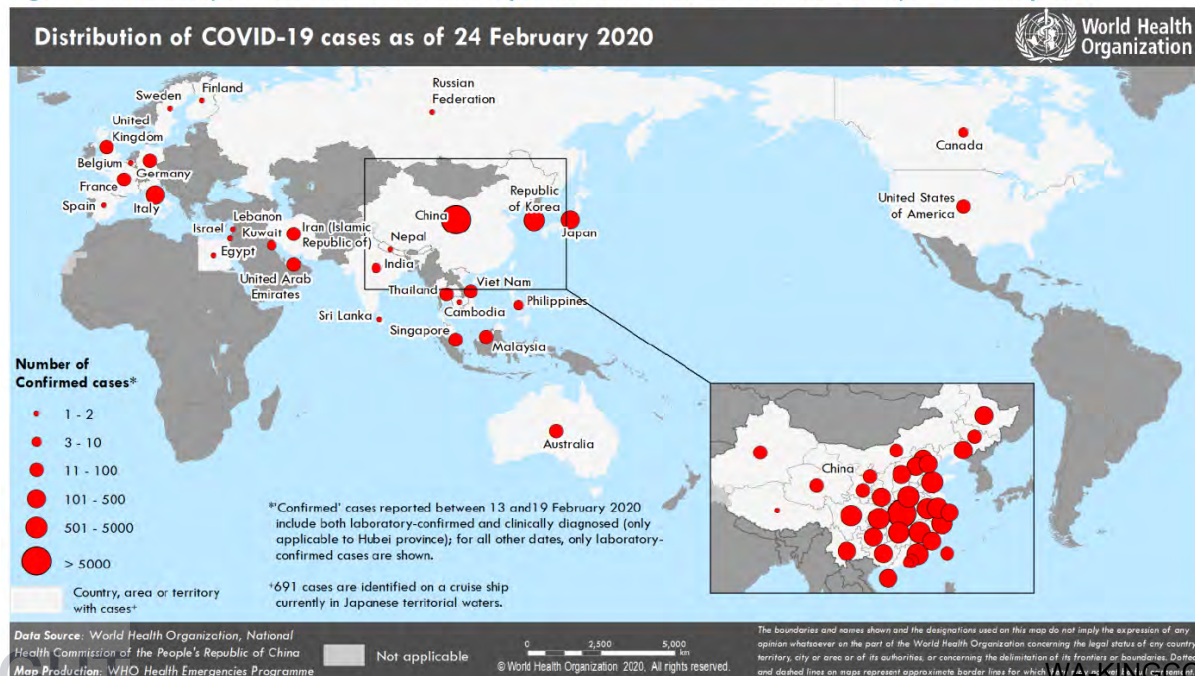
- International & national situation update
- Update on severity of COVID-19
- Community mitigation strategies
- Powers and authorities

International Situation

**numbers current as of 3/1/20*

- Total confirmed cases: 87,137
- Total confirmed deaths: nearly 2,977
 - China: 79,968
 - Outside of China: 7,169
 - 58 countries

Figure 1. Countries, territories or areas with reported confirmed cases of COVID-19, 24 February 2020



International Situation

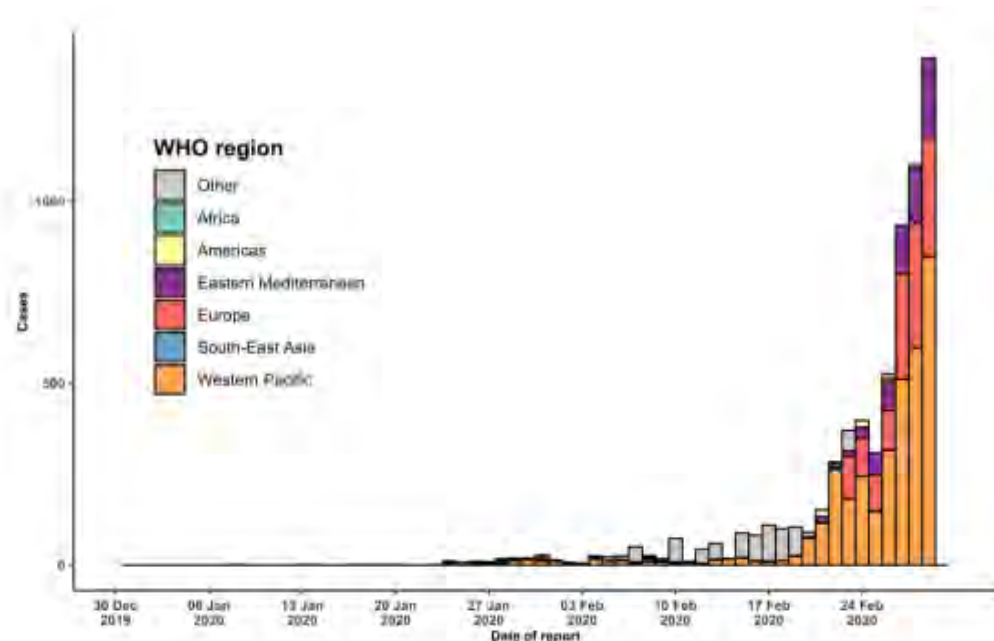
**numbers current as of 3/1/20*

- Widespread sustained (ongoing) transmission

and restrictions on entry to the US

- China * travel restrictions
- Iran *travel restriction
- South Korea
- Italy
- Sustained (ongoing) community transmission
 - Japan
- Limited community transmission
 - Hong Kong

Epidemic Curve of COVID-19 cases (n=2069) identified outside of China, by date of report and WHO region with complete days of reporting through 29 February, 2020



Source: <https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html>

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>

WA-KINGCO-20-0492-D-000005

Local Situation

**numbers current as of 3/1/20*

- **USA**
 - 22 confirmed cases
 - 47 confirmed cases – infected overseas
 - Diamond Princess Cruise Ship
 - Others evacuated out of China
- **Washington State**
 - 1 confirmed case
- **King County**
 - 268 persons assessed
 - 17 persons tested (all neg)
 - 488 persons have been placed on watch

Risk Assessment

- “Tremendous” public health threat to the United States
- Low health risk for COVID-19 to the general public in the United States and Washington at this time
- Strategy now is to slow the spread of the virus (i.e., contain the virus) so that we have time to:
 - Prepare the healthcare system and the general public
 - Better characterize the infection to guide public health recommendations and development of medical countermeasures including diagnostics, therapeutics, and vaccines
- Community spread very likely in Washington

Goals of Community Mitigation for Pandemic Influenza (Non-pharmaceutical Interventions [NPIs])

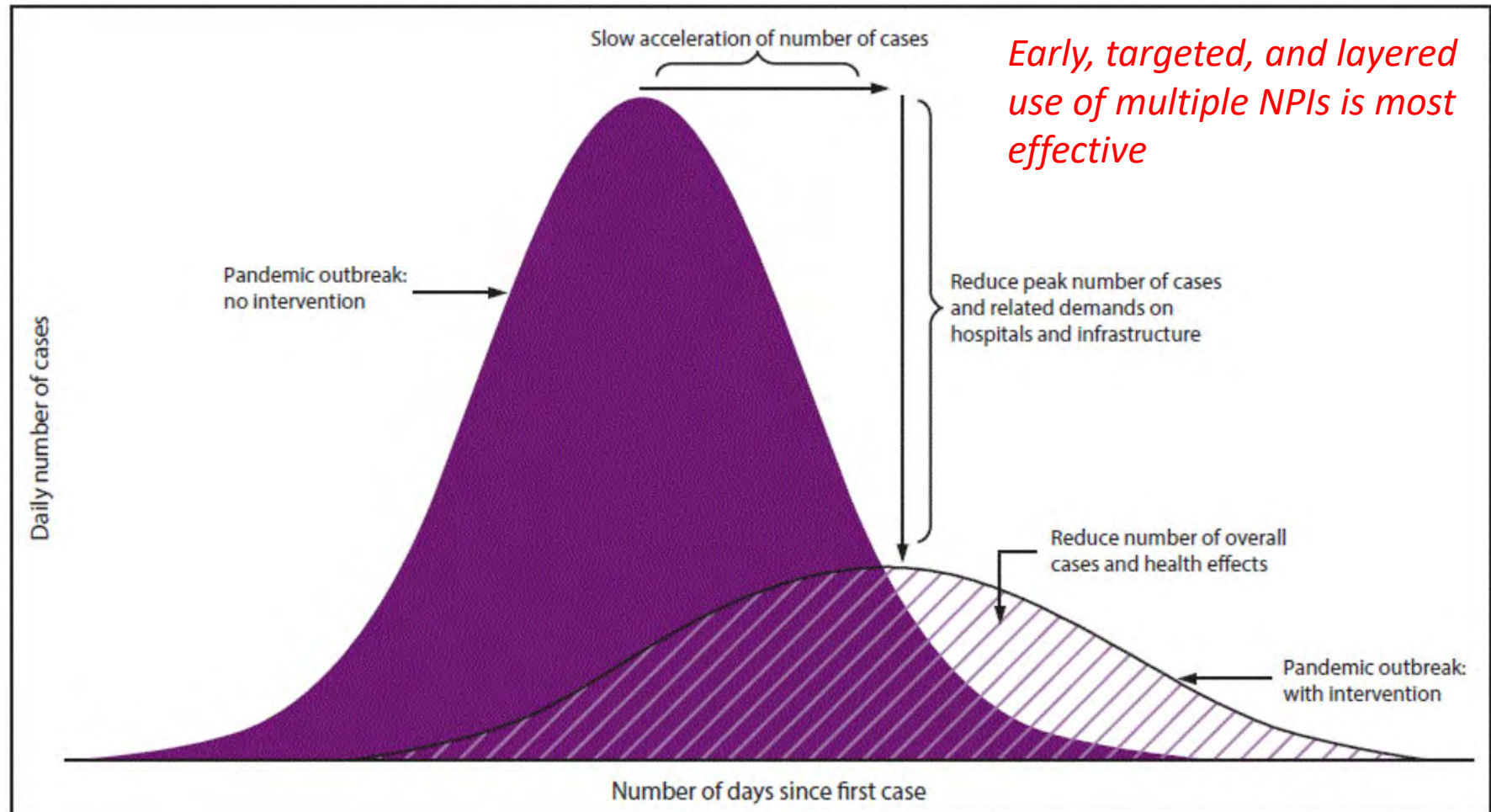


TABLE 1. Non-pharmaceutical Interventions Matrix

Assessment*		Intervention	Expected Result	Example Implementation	Begin NPI use	NPI Type
Transmissibility	Clinical Severity					
1	1-4	1. Increase handwashing and use of alcohol-based sanitizer	Reduce probability of direct and indirect transmission of the disease by disinfecting hands	Conduct public messaging and media campaigns to encourage and educate the public and to promote enhanced hygiene and social distancing measures. Targeted messaging to major employers may be beneficial in encouraging the enhance behaviors in the workplace.	Y N	Personal
1	1-4	2. Respiratory Hygiene/Cough Etiquette	Reduce probability of droplet transmission of the disease by reducing the range of respiratory droplets and aerosols		Y N	
1	1-4	3. Keep distance from others (>6 feet)	Reduce probability of direct and droplet transmission by reducing the number of interpersonal contacts		Y N	Community
1	1-4	4. Frequently clean and disinfect personal surfaces (doorknobs, phones, keyboards, etc.)	Reduce the probability of indirect transmission by disinfecting fomites		Y N	Environmental
1	1-4	5. Remain home through the duration of respiratory illness	Reduce probability of transmission by preventing contacts between well and sick people		Y N	Personal
2	2-5	6. Voluntary isolation of sick persons	Reduce probability of transmission by preventing contacts between well and sick people	Health officers, medical providers, and public health personnel provide direct education to cases and contacts asking that they remain home for an established period of time.	Y N	
2	2-5	7. Voluntary quarantine of contacts of sick persons	Reduce probability of transmission in the event that the contact becomes contagious before symptoms developed.		Y N	
3	5-6,5	8. Involuntary isolation of sick persons	Reduce probability of transmission by preventing contacts between well and sick people	Health officers issue emergency detention orders or seek court orders for involuntary detention in order to involuntarily isolate or quarantine those who are uncooperative	Y N	Community
3	5-6,5	9. Involuntary quarantine of contacts of sick persons	Reduce probability of transmission in the event that the contact becomes contagious before symptoms develop		Y N	
4	5-7	10. Order cancellation of major public and large private gatherings	Reduce probability of transmission by reducing the number of the interpersonal contacts	Health officer orders to suspend all gatherings above a certain size with the intention to reduce risk of disease transmission if a subset of that population may be sick	Y N	
4	5-7	11. Order closure of schools, childcare facilities, workplaces, and public buildings	Reduce probability of transmission by reducing the number of the interpersonal contacts		Y N	
5	5,5-7	12. Prevent non-emergency travel outside of the home	Reduce probability of transmission by reducing the number of the interpersonal contacts	Health officer orders to halt non-emergency travel and remain indoors in order to protect those not yet sick.	Y N	
5	5,5-7	13. Establish a cordon sanitaire	Contain the disease within specific geographical boundaries.		Y N	

*Assessment levels are based on the following table (Table 2).

WA-KINGCO-20-0492-D-000009

Considerations for Implementing Community NPIs

- Transmissibility / Clinical severity
- Degree of spread
- State of the healthcare system (e.g., ventilator shortages)
- Effectiveness of the intervention
 - Little known about role of COVID-19 transmission in kids
 - Limited evidence on implementing social distancing measures in workplace and mass gatherings alone; some evidence supports implementing multiple social distancing measure in combination
- School closures
 - Kids on free and reduced lunch program
 - Healthcare workers staying home to care for kids
- Economic and social impacts
- Feasibility of implementation
- Public acceptance / ethical considerations

Authorities -- Local

- Local health officer and local board of health have authority to control spread of infectious diseases within their jurisdiction
 - This includes issuing orders to cancel events and to close schools and child care centers
- Local health officers are authorized to issue detention orders for the isolation or quarantine of individuals who are reasonably believed to be infected with or exposed to COVID-19.
 - Law enforcement officers have the authority to enforce a local health officer's order, including isolation or quarantine orders and other orders issued to control and prevent the spread of disease
- Key Stakeholders: local elected officials (such as mayor, city council, county council, and/or county executive), emergency managers, school and child care administrators, local law enforcement, impacted businesses, proprietors, cultural and religious leaders, event sponsors and event organizers, etc.

Authorities -- Local

- Local governments have police power to protect the public health under the US Constitution's 10th Amendment, granting authority to implement restrictions on private rights for the sake of public welfare, order, and security.
 - This might include restricting non-emergency travel outside the home and establishing cordon sanitaire
- Key Stakeholders: local elected officials (such as mayor, city council, county council, and/or county executive), emergency managers, school and child care administrators, local law enforcement, impacted businesses, proprietors, cultural and religious leaders, event sponsors and event organizers, etc.

Authorities -- State

- In an emergency or when a local health officer consents or does not act, the Secretary of Health may exercise the same authority as the local health officer to control and prevent disease.
 - This might include issuing orders to cancel events and to close schools and child care centers
- Governor has broad authority to proclaim state of emergency to preserve life, health, property, or the public peace (RCW 43.06.010).
 - Governor declared emergency could trigger limitations such as curfews, prohibitions of people on streets and open areas, limit use of streets, highways or public ways, or prohibiting travel
 - Governor may prohibit any activity to protect the public health and may suspend state statutes and rules that would hinder an emergency response
- Key Stakeholders: local elected officials (such as mayor, city council, county council, and/or county executive), private sector, emergency managers, local law enforcement, school superintendents, boards of education, health care, transportation agencies, etc.

Authorities -- Federal

- The federal government has independent authority when emergencies cross state and national borders.
- HHS Secretary may declare a public health emergency under 42 U.S.C. § 247d, which is a way to get Congress to fund a public health emergencies account, but declarations are often made without associated Congressional funding.
- The diseases subject to quarantine under federal law are determined by Executive Order. The most recent order published in the Federal Register includes severe acute respiratory syndromes and provides the basis for federal quarantine.

From: [Bogan, Sharon](#)
To: [Kay, Meagan](#)
Cc: [Duchin, Jeff](#); [Kawakami, Vance](#)
Subject: FOR APPROVAL_ KEY MESSAGES
Date: Sunday, March 1, 2020 3:07:51 PM
Attachments: [UPDATED CONTENT FOR KEY MESSAGES 3 pm.docx](#)

Meagan, Jeff and Vance,

These are the most important responses we need approval on. This content will be used for multiple messaging purposes.

PLEASE REVIEW, MAKE EDITS, AND APPROVE.

Thank you-

Sharon

UPDATED CONTENT FOR KEY MESSAGES

3.1.20 3:00 pm

1. **Guidance for contacts of presumed cases including Lifecare employees and residents:**

- If someone has respiratory illness and is an employee or resident of LifeCare, we are assuming they have COVID-19.
- We are not quarantining asymptomatic people regardless of their contact with COVID 19- cases (with the potential exception of people who entered LifeCare Kirkland).

Category 1: Contacts of the *asymptomatic* contacts of: any of the following: 1. confirmed cases, 2. PUIs, or 3. other LifeCare employees/residents **are not considered exposed.**

If you fall into this category and do develop symptoms, you should self-quarantine and contact your healthcare provider.

Example: Joni is a nurse at Lifecare. She is not sick. Mike lives with Joni. Mike does not need to self quarantine, nor does he need evaluation or testing for COVID-19.

If Joni gets sick, then Mike takes his temperature every day and watches himself carefully for any symptoms, but continues his life normally otherwise.

Joni should self-quarantine and call her healthcare provider.

Category 2: People who have entered the LifeCare Kirkland facility or for close contacts of LifeCare employees/residents who are sick.

They need to be self-monitoring – temperature checks daily, but they do not need to self-quarantine. If they develop any symptoms, they should immediately self-isolate and call their healthcare provider and Public Health: 206-296-4774

Example:

- Casey, (fake name) is a Lake Washington Technical student who went into LifeCare to clean. She is not sick. We do not yet have guidance on whether she needs to self-quarantine.
- Bob visited his grandmother at LifeCare. Bob's grandmother isn't sick. We do not yet have guidance on whether Bob needs to self-quarantine.
- Frank goes to lunch with his friend who is a LifeCare employee. The LifeCare employee now has symptoms and is a PUI. Self-monitor for 14 days. Go to work.

2.Can we confirm that community transmission is occurring? (We have been saying that specific cases are community transmission, but are we saying community transmission in King County?)

We have multiple (3) confirmed COVID-19 cases that currently do not have known contact with LifeCare, anyone who's been at LifeCare, or known travel. We are intensively investigating to understand the spread of the disease.djdjh;

3. Should employers and school administrators require healthcare provider documentation or a COVID-19 negative test before letting people enter?

Employers, and school administrators should not require any letter or documentation from employees' health care providers about their COVID-19 status. This will overwhelm the healthcare system and is not recommended as a measure to protect public health at this time.

4. Who should be tested for COVID-19? If we're not recommending wide-spread testing, why not?

We're not currently recommending widespread testing.

For members of the general public, we are only recommending testing for those who

have had close contacts with a lab confirmed case **and** have fever or cough or shortness of breath.

We anticipate testing guidance to change in the near term as more testing comes on-line at commercial laboratories.

More detail not for the public:

There are 3 categories of people recommended for testing:

1. People who are experiencing symptoms and are a close contact of a confirmed case.
2. People hospitalized with severe pneumonia with unknown cause.
3. People who have traveled in the last 14 days to a country with widespread or ongoing community spread of COVID-19, and have fever, cough or shortness of breath, contact your healthcare provider about potential testing. For more information, visit the CDC's webpage: <https://www.cdc.gov/coronavirus/2019-ncov/faq.html#symptoms>

If someone meets the first criteria, they should contact their healthcare provider (call, do not attend in-person) and call the Public Health Communicable Disease team: 206-296-4774

5. **Guidance on social distancing**

Should schools cancel assemblies, sporting events or gatherings? We do not have any formal CDC recommendations for avoiding gatherings or events, and we are not recommending cancelling events at this time. However, people who are at higher risk, such as those with underlying health conditions such as heart disease, lung disease or who are immune compromised, may want to consider ways to lower their risk such as limiting with large numbers of people. Talk to your doctor to make a plan based on your specific health conditions.

Social distancing clarification

People who are over 60 (**DO WE REALLY WANT TO SAY THAT PEOPLE OVER 60 should consider avoiding contact with large numbers of people?**)

People with underlying health conditions may want to consider ways to lower their risk, such as: avoiding close contacts with large numbers of people.

Sharon Bogan
Communications
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From: [Trish Perl](#)
To: [Duchin, Jeff](#)
Subject: FW: Concern re potential PPE shortages
Date: Sunday, March 1, 2020 1:53:00 PM
Attachments: [SuwantaratHCWriskCOID2015.pdf](#)
[setoSARSPrecautionsLancet2003.pdf](#)
[telemanSARSPrecautionsEpidemiolInfect2004.pdf](#)
[RaboudSARSriskHCPLOSOne2010.PDF](#)
[LauSarsPrecautionsEID2004.pdf](#)
[LoebSARSriskfactorsEID2004.pdf](#)
[jama_radonovich_2019_oj_190087.pdf](#)
[jama_talbot_2019_ed_190069.pdf](#)
[Quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection \(Johnson\).pdf](#)
[Jefferson_et_al-2011-Cochrane_Database_of_Systematic_Reviews.pdf](#)

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Jeff—so funny. Marci asked me the same thing and here is my long response to her. You look great on TV and sound good on NPR. Hang in there and keep up the good work. Let me know if you have questions. Trish

From: Trish Perl <Trish.Perl@UTSouthwestern.edu>
Date: Sunday, March 1, 2020 at 3:50 PM
To: Marci Layton <mLAYTON@health.nyc.gov>
Cc: Bob Pinner <rpw1@cdc.gov>, Ruth Lynfield <Ruth.Lynfield@state.mn.us>
Subject: Re: Concern re potential PPE shortages

Marci,

You are opening pandora's box and this is a long email for me. Happy to chat more about it and may want to do it with Jeff Duchin (see the second to last paragraph).

Sorting fact from emotion in these situations is the key issue. Based on SARS data risk of acquisition is associated with 1. Poor hand hygiene, 2. AGP, 3. Failure to wear elements of PPE and face shield is one of the more notable, 4. Not knowing how to put on PPE, 5. Duration in the room. I am trying to pull together the information from SARS and hence have inundated you with papers mainly so that you can look at the primary data. I have also included a meta-analysis from Jefferson in 2011 and an earlier BMJ metanalysis. What is nice is you get a risk reduction with each element of PPE and IPC practices and then an overall risk reduction of 91% with the bundled PPE and practices.

Mask versus N95 metanalyses have been done and one is attached. I am not sure if you are aware of the Respect study so have attached the findings from that. Primary endpoint was flu but secondary was laboratory confirmed respiratory illness or infection so this is helpful and there was no difference. We are working on the secondary analysis for coronavirus that accounts for 35% of the infections in this cluster randomized clinical trial to see if we can detect differences although I am guessing we will have a number problem.

With all this bla bla what do I think. 1. Hand hygiene matters; 2. Face shield, gowns and gloves

matter; 3. Mask matters but it is not clear one is better than the other for routine care. It is very clear in the setting of AGP N-95 should be used. 4. The environment must be cleaned. It is the bundle of PPE (faceshield, gowns and gloves and a mask/N95 that works) **with very good HH and cleaning**. My gut feeling is that we should be pushing source control in hospital just not at the entry to emergency rooms and masking the patients (see attached paper about source control). Likely face shield with medical mask is fine for most outpatient settings—the only thing that gives me pause is the duration of time HCW spend with nursing home patients and from the SARS work a cut off of 4 hours was where risk increased. So they need a break and more breaks than we likely normally allow if you go the route of less protection.

The harsh reality is that with the PPE shortages, I would much rather see a good bundle with a medical mask than reuse of masks and all the potential contamination with the virus (which we know from the briefing documents Bob shared last week) or giving people equipment they are not familiar with. I think the risks are much higher.

Jeff Duchin has been talking to me about the same issues partly because of your argument but also because in SNH/LTCF and offices no one is fit tested and they do not know how to use them. When people are unfamiliar with equipment mistakes are made (this is nicely documented) and honestly we are running out of masks. The Dallas VA which is the second largest in the country has no masks. I just heard and don't know whether it is true that the N95's in the stock pile have issues because the elastic head bands have disintegrated---I feel like we have an army with no guns or ammunition (not sure what the correct metaphor is).

I can talk to the current president of SHEA, David Henderson but he is a huge N95 and PAPR fan and will probably dominate the decision making whether fact based or not. I will reach out to him as I have no idea what SHEA is doing. Actually Jan Patterson, Connie Price and I were laughing as we have the most experience with these infections and SHEA has not asked us anything.

Have a great afternoon.

Trish

Let me know if you need anything else and happy to chat – cell is 410 615 1331.

From: Marci Layton <mlayton@health.nyc.gov>

Date: Sunday, March 1, 2020 at 12:23 PM

To: Trish Perl <Trish.Perl@UTSouthwestern.edu>

Cc: Bob Pinner <rwp1@cdc.gov>, Ruth Lynfield <Ruth.Lynfield@state.mn.us>

Subject: Concern re potential PPE shortages

EXTERNAL MAIL

Trish = as we start to see more community transmission in US, we are really concerned about PPE shortages, as means if you follow current CDC guidance for COVID-19 for fit tested N95s, that

everyone who presents for care with fever and resp illness will need to be seen in full PPE – not sustainable wrt supplies and means many outpatient settings wont be able to manage

this was also an issue during Spring wave of H1N1 when CDC guidance also stricter than WHO

In NYC, we would like to scale back to droplet UNLESS patient undergoing a potential aerosol generating procedure (luckily CDC changed earlier guidance that considered NP swab aerosol generating)

Do you know if SHEA is raising this concern yet to CDC as DHQP views SHEA as key partner
thanks

Sent from the New York City Department of Health & Mental Hygiene. This email and any files transmitted with it may contain confidential information and are intended solely for the use of the individual or entity to whom they are addressed. This footnote also confirms that this email message has been swept for the presence of computer viruses.

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Risks to healthcare workers with emerging diseases: lessons from MERS-CoV, Ebola, SARS, and avian flu

Nuntra Suwantararat^{a,b} and Anucha Apisarnthanarak^c

Purpose of review

Several viral diseases have emerged and impacted healthcare systems worldwide. Healthcare personnels (HCPs) are at high risk of acquiring some emerging infections while caring for patients. We provide a review of risk factors, evidence of infection in HCPs, and prevention strategies with Middle East respiratory syndrome coronavirus, Ebola virus disease (Ebola), severe acute respiratory syndrome (SARS), and avian influenza.

Recent findings

HCP-related infections with Middle East respiratory syndrome coronavirus, Ebola, and SARS have been reported among 1–27%, 2.5–12%, and 11–57% of total cases, respectively. The case fatality rate of Ebola in HCPs has been reported up to 73%. The WHO guidelines for the global surveillance of SARS were developed in 2004 and used as a template for other emerging diseases preparedness. Risks to HCPs with emerging diseases are related to inappropriate and insufficient infection control measures during an initial encounter, at the beginning of outbreak and with an overwhelming number of patient cases. To date, there are no reports of avian influenza transmission to HCPs from affected cases.

Summary

Early and rapid detection of suspected infected patients with communicable diseases along with appropriate infection control practice, education, national and global preparedness guidelines would help to prevent disease transmission to HCPs.

Keywords

avian influenza, Ebola, emerging diseases, healthcare personnel, Middle East respiratory syndrome coronavirus, severe acute respiratory syndrome

INTRODUCTION

Over the past 15 years, Middle East respiratory syndrome coronavirus (MERS-CoV), Ebola virus disease (Ebola), severe acute respiratory syndrome (SARS), and avian influenza have emerged and impacted care and practice in healthcare systems globally [1–4]. Healthcare personnels (HCPs) are at high risk of acquiring emerging infections while caring for patients. Several cases of these emerging diseases in HCPs have been reported [1–3]. The severity of the outbreak and risk of infection in HCPs was different based on viral characteristics and mode of transmissions [5^{••}]. Local researchers and international collaboration, such as the WHO and the Centers for Disease Control and Prevention (CDC), have previously reported evidence for transmission, infection control implications, prevention strategies and recommendations. In order to prevent HCPs from acquiring these emerging infections, we summarize

the literature to date for risk factors for transmission of these infections to HCPs, and the effective infection prevention strategies for these recent emerging diseases.

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Correspondence to Anucha Apisarnthanarak, MD, Thammasat University Hospital, Pathumthani 12120, Thailand. E-mail: anapisarn@yahoo.com

Nuntra Suwantararat, MD, Division of Medical Microbiology, Johns Hopkins University School of Medicine, Meyer B1-193 600 N. Wolfe St., Baltimore, MD 21287, USA. Tel: +1 410 955 5077; fax: +1 410 614 8087; e-mail: nuntras@yahoo.com, nsuwant1@jhmi.edu

Curr Opin Infect Dis 2015, 28:349–361

DOI:10.1097/QCO.0000000000000183

KEY POINTS

- HCPs are at risk to viral emerging infectious diseases with a high number of patients.
- Unaware and atypical presentations of infectious diseases, inappropriate and insufficient infection control measures, and an overwhelming number of patients are circumstances that commonly increase the risk of emerging infectious disease transmission to HCPs.
- Early and rapid detection of suspected patients along with appropriate infection control practice, and national and global preparedness guidelines would help to prevent emerging infectious disease transmission to HCPs.
- Education programs, drills to use personal protective equipment appropriately and surveillance programs for HCPs with disease exposure are additional effective prevention strategies.

MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS

MERS-CoV is a novel betacoronavirus that causes a spectrum of illness including severe respiratory distress with high mortality [6¹¹,7^{8,9}]. The virus was first isolated in September 2012 from a patient with fatal pneumonia in Saudi Arabia (KSA) [10]. The earliest identified human cases were traced back to March 2012 from clusters of severe respiratory illness among HCPs in Jordan [11]. As of 20 March 2015, 1075 laboratory-confirmed cases of human infection with MERS-CoV have been reported, including 404 related deaths. The majority of cases (>85%) were from KSA. The affected countries in the Middle East include Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, KSA, United Arab Emirates, Yemen, Algeria, and Tunisia; in Europe where cases have presented after exposure in the Gulf area: Austria, France, Germany, Greece, Italy, The Netherlands, Turkey, the United Kingdom; in Asia: Malaysia, Philippines; and in the United States [12]. Previous studies suggest that bats and camels are the natural reservoirs of MERS-CoV [13,14]. Multiple transmission routes are suspected with limited human-to-human transmission [5¹¹,6¹¹,7¹¹].

RISK FACTORS AND EVIDENCE OF INFECTION IN HEALTHCARE PERSONNELS

To date, four large outbreaks of MERS-CoV have been reported in healthcare facilities in Jordan (April 2012), Al-Hasa, KSA (April–May 2013), and KSA (majority from Jeddah) and United Arab Emirates (April–May 2014) [1,6¹¹,8,11,15¹¹]. More than 50%

of HCP-affected cases were nurses [6¹¹,11]. The most important risk to a HCP developing infection was insufficient infection control measure, especially because of unrecognized cases at the onset of the outbreak or because of patients presenting atypically [1,6¹¹,8,11,15¹¹,16¹¹,17¹¹]. Moreover, the seasonal changes increased community cases and infection control capacity in the affected hospitals (Table 1) [1,6¹¹,15¹¹,18].

Depending on the outbreak between 1 and 27% of HCPs have developed MERS-CoV nosocomially (Table 1) [1,6¹¹,8,11,15¹¹,16¹¹,19]. For the first outbreak in Jordan, Al-Abdallat *et al.* [16¹¹] used serologic assays to determine antibody responses to MERS-CoV infection among potentially affected HCPs at the three hospitals that were the epicenter of this outbreak. Of 57 HCPs at the initial hospital, six HCPs (10%) had confirmed evidence of MERS-CoV infection by the presence of antibody. Infection control practices were insufficient with an absence of physical barriers between the ICU beds and isolation rooms. There was no evidence of MERS-CoV infection among HCPs at the other two receiving transfer hospitals and the infection control practices were not considered insufficient [16¹¹]. From the second outbreak in Al-Hasa, a total of 23 cases were reported, including 15 deaths (65%). Only two HCPs were, however, identified [7¹¹]. Memish *et al.* [17¹¹] reported rare secondary transmission to HCPs in healthcare facilities in KSA between October 2012 and September 2013. Of 1695 HCP contacts of laboratory-confirmed MERS-CoV cases, only 19 (1.12%) tested positive [17¹¹]. The more recent outbreak in Jeddha demonstrates a high risk of transmission in which 402 laboratory-confirmed MERS-CoV cases were reported and included 114 deaths [1,19]. Of these, 109 cases (27%) were HCPs. The majority of HCPs developed asymptomatic or mild symptoms (63 cases) and moderate symptoms (35 cases). Only seven cases developed severe illness and four deaths were reported [19]. No evidence of genetic variations was identified among the MERS-CoV isolates from the Jeddha outbreak [20¹¹]. Therefore, the WHO concluded that the increase in 128 cases among HCPs was most likely related to inadequate infection control measures [1,6¹¹,15¹¹,19,20¹¹].

INFECTION CONTROL IMPLEMENTATION AND PREVENTION STRATEGIES

After an increase of MERS-CoV cases in 2014, the WHO developed the first infection control guidelines based on available knowledge about MERS-CoV and SARS [1,15¹¹,19,20¹¹]. Strategies to rapidly identify MERS-CoV cases and develop proactive and

Table 1. Number of total and HCP-affected cases of recent emerging infectious diseases; risk factors and infection prevention and control recommendations

Emerging diseases	Year and country of the first outbreak	Number of total cases	Number of death (% of total cases)	Number of HCPs (% of total cases)	Risks of infection to HCPs	Infection control recommendation
MERS-CoV	2012, Jordan	1075 ^a	404 (38%)	N/A (1–27%)	Multiple transmission routes but limited human-to-human transmission Insufficient infection control measures (not recognized early in outbreak, patients with atypical presentations) Seasonal changes (increased community cases) Asymptomatic infection in HCPs	Use standard/contact/droplet precautions with eye protection Use airborne precautions when performing aerosol-generating procedures Use airborne isolation room for hospitalized patient if available Employ strategies to rapidly identify and isolate suspected cases Monitor HCPs and excluded from work 14 days after exposures Follow global preparedness guidelines Perform disease surveillance Follow laboratories standards when handling patient specimens
Ebola virus disease	2013–2014, West Africa (recent outbreak)	24666 ^b	10179 ^c (41%)	852 ^d (3.5%)	Poor healthcare infrastructure Exposure to infected bodily fluids (vomit, diarrhea, blood) Initial presentation mimics other diseases (malaria, typhoid fever, cholera, heart failure) Limited PPE supplies Inappropriate PPE use or contamination, especially when doffing (removal process)	Use standard and barrier/isolation precautions Practice adequate, appropriate use, training and drill on PPE Use designated healthcare facilities and Ebola patient treatment units Separate entrances and egresses for Ebola treatment units Use designated persons at the exit of Ebola treatment unit to observe HCPs while doffing PPE

(Continued)

Table 1 (Continued)

Emerging diseases	Year and country of the first outbreak	Number of total cases	Number of death (% of total cases)	Number of HCPs (% of total cases)	Risks of infection to HCPs	Infection control recommendation
SARS	2002, China	80% ^a (no report of new cases since May 2004)	774 (10%)	1706 ^f (21%)	Inadequate PPE training Possible environmental contamination (shared toilet facilities)	Monitor HCPs and with high-risk exposures exclude from work for 21 days Follow global preparedness guideline Perform proactive disease surveillance Follow laboratories standards when handling patient specimens
					Primary transmitted by infected respiratory droplets and body secretions, close contact, environmental contamination High-risk patient care procedures (airway and respiratory related procedures) 'Super-spreader' phenomenon	Use standard/contact/droplet precautions with eye protection Use airborne precautions for aerosol generating procedures and isolation rooms Practice PPE use, donning and doffing Cohort patients and use designated hospitals for SARS patient treatment
					Insufficient infection control measures (not recognized early in outbreak, patients with atypical presentations) Inconsistent use of PPE, reuse of N95 respirators and other masks Lack of adequate infection control training HCP fatigue and stress	Provide the appropriate and adequate numbers of HCPs for patient care Monitor HCPs and exclude from work for 14 days after significant exposure Follow global preparedness guideline Perform proactive disease surveillance Follow laboratories standards when handling patient specimens

Avian influenza A/H5N1-H7N9	1997 and 2003, Hong Kong; 2013, China	784 ^g	429 (55%)	None	HCPs are at low occupational risk for acquisition of H5N1 infection ⁱ	Use standard/contact/droplet precautions with eye protection
		571 ^h	212 (37%)	None	Potential for pandemic influenza outbreak Human-to-human transmission of avian influenza A has occurred only via intimate contact without the use of barrier and in household clusters	Use airborne precautions and isolation room Follow pandemic avian influenza preparedness plans, especially in developing countries
					Employ strategies to rapidly create temporary isolation facilities, restrict access to exposed HCPs, screen and identify cases early by ID specialists Monitor infection-control practices Monitor HCPs and exclude from work 7 days (H5N1) and 10 days (H7N9) after exposure Perform proactive disease surveillance Follow laboratories standards when handling patient specimens Use adjuvanted vaccine for preventing avian influenza A (H5N1) for people with high-risk exposure in pandemic if indicated.	

HCPs, healthcare personnel; ID, infectious disease; MERS-CoV, Middle East respiratory syndrome coronavirus; N/A, not available; PPE, personal protective equipment; SARS, severe acute respiratory syndrome.

^aLaboratory-confirmed cases of human infection with MERS-CoV as of 20 March 2015.

^bLaboratory-confirmed/probable/suspected cases of human infection with Ebola in Guinea, Liberia, and Sierra Leone as of 18 March 2015.

^cNumber of fatal cases among hospitalized patients in Guinea (51%), Liberia (48%), and Sierra Leone (73%) as of 18 March 2015.

^dNumber of HCPs-affected cases with Ebola in Guinea (5.1%), Liberia (3.9%), and Sierra Leone (2.5%) as of 18 March 2015.

^eProbable cases of human infection with SARS as of 31 December 2003.

^fNumber of HCWs-affected cases with SARS as of 31 December 2003, in range 11–57%.

^gLaboratory-confirmed cases of human infection with avian influenza A (H5N1) as of 3 March 2015.

^hLaboratory-confirmed cases of human infection with avian influenza A (H7N9) as of 23 February 2015.

ⁱData obtained from avian influenza A (H5N1), Thailand outbreak in 2005 (Apisarnthanarak *et al.* [18]).

effective surveillance are critical to prevent disease transmission. Hospitals should have established policies and procedures for the rapid identification of suspected MERS-CoV cases and implementation of appropriate infection control measures [1,15²²,20²²,21²²]. HCPs should use standard precautions when in contact with all patients, regardless of their diagnosis, and use droplet precautions when providing care to patients with symptoms of acute respiratory infection. Contact precautions and eye protection should be used when caring for probable or confirmed cases of MERS-CoV infection. Although MERS-CoV has unclear mode of transmission, an airborne infection isolation room should be used for hospitalized patients when available. Airborne precautions should also be used when performing aerosol-generating procedures [5²²,20²²,21²²]. Moreover, a policy to follow HCPs after contact suspected MERS-CoV patients to determine furlough or work releases and to perform serological surveillance should be considered (Table 1, Fig. 1) [20²²,21²²,22–29].

EBOLA VIRUS DISEASE

In 1976, Ebola virus disease (Ebola) first reported causing hemorrhagic fever with high mortality in two simultaneous outbreaks, one in Nzara, Sudan, and the other in Yambuku, Democratic Republic of Congo (previously called Zaire), Central Africa [30²²]. Other Ebola outbreaks were reported and involved 1–400 patients and primarily reported in remote forested areas [31²²]. In December 2013, the Zaire strain of Ebola likely emerged in a small village in Guinea, West Africa but the disease was not recognized or identified as Ebola until March 2014 [30²²]. It spread rapidly causing the largest and longest outbreak of Ebola in Africa [2,31²²]. As of 18 March 2015, a total of 24 666 Ebola cases in Guinea, Liberia, and Sierra Leone, including 10 179 deaths, were reported. Case fatality among hospitalized patients is 31–66% in the three intense-transmission countries. Six countries (Mali, Nigeria, Senegal, Spain, the United Kingdom, and the United States) have reported imported cases from the affected West African countries [2]. Human-to-human transmission of Ebola is mainly because of contact with the infected bodily fluids (vomit, diarrhea) from symptomatic patients. The average incubation period for the disease is 8–10 days (range 2–21 days) [31²²,32²²,33²²,34²²].

RISK FACTORS AND EVIDENCE OF INFECTION IN HEALTHCARE PERSONNELS

A total of 852 HCPs (3.5%) have been reported to the WHO during this outbreak that includes 492 deaths

(Table 1). The case fatality rate among HCPs ranges between 44% and 73% [2]. Matanock *et al.* [35²²] reported 10 clusters of Ebola involving 97 HCPs working in non-Ebola treatment units in Liberia. The majority of affected HCPs were nurses (35%), and followed by physicians (15%). Risks of infection in HCPs were related to direct contact with patient bodily fluid, limited personal protective equipment (PPE), shared or reused equipment, lack of toilets, and isolation facilities. In four of the clusters, the source patients were initially thought to have other diseases (e.g., dysentery, cholera, Lassa fever, or heart disease). In one case a patient with gram-negative bacteremia who subsequently developed Ebola may have acquired the disease from an infected HCP who died 10 days prior to the patient-developing symptoms. They shared the same office and restroom until 3 days before the colleague died [36].

In Lagos, Nigeria, a symptomatic air traveler whose sister had just died from Ebola in Liberia was the index case. The patient reported to hospital staff that he had malaria and protective precautions were not used. A total of nine HCPs became infected, four of whom died [30²²]. In the United States, four laboratory-confirmed cases of Ebola have been reported. Three of them were HCPs, including two nurses who provided intensive care to the index case [2,37,38²²]. The first patient (index case) had arrived the United States from Liberia 5 days earlier. He was seen at Dallas County, emergency department with fever, abdominal pain, and headache and placed in a private room under standard, contact, and droplet precautions. The patient was treated for possible sinusitis and discharged home. He returned to the hospital by ambulance with persistent fever, abdominal pain, and new onset diarrhea. The patient was confirmed Ebola infection and finally died. A total of 179 contacts (149 HCPs, 20 community contacts, and 10 persons with contact in the same ambulance) were interviewed. There was no evidence of infection among other HCPs, patients' household, or community contacts [38²²].

INFECTION CONTROL IMPLEMENTATION AND PREVENTION STRATEGIES

The uncontrolled Ebola outbreak in West Africa impacts not only an emergency need for improving infection control practice in the three intense-transmission countries but also a global preparedness [30²²,39]. The WHO provides preparedness tools such as the Ebola preparedness checklist and outbreak investigation protocol [2]. Nigeria successfully controlled the Ebola outbreak (19 cases, 7 deaths)

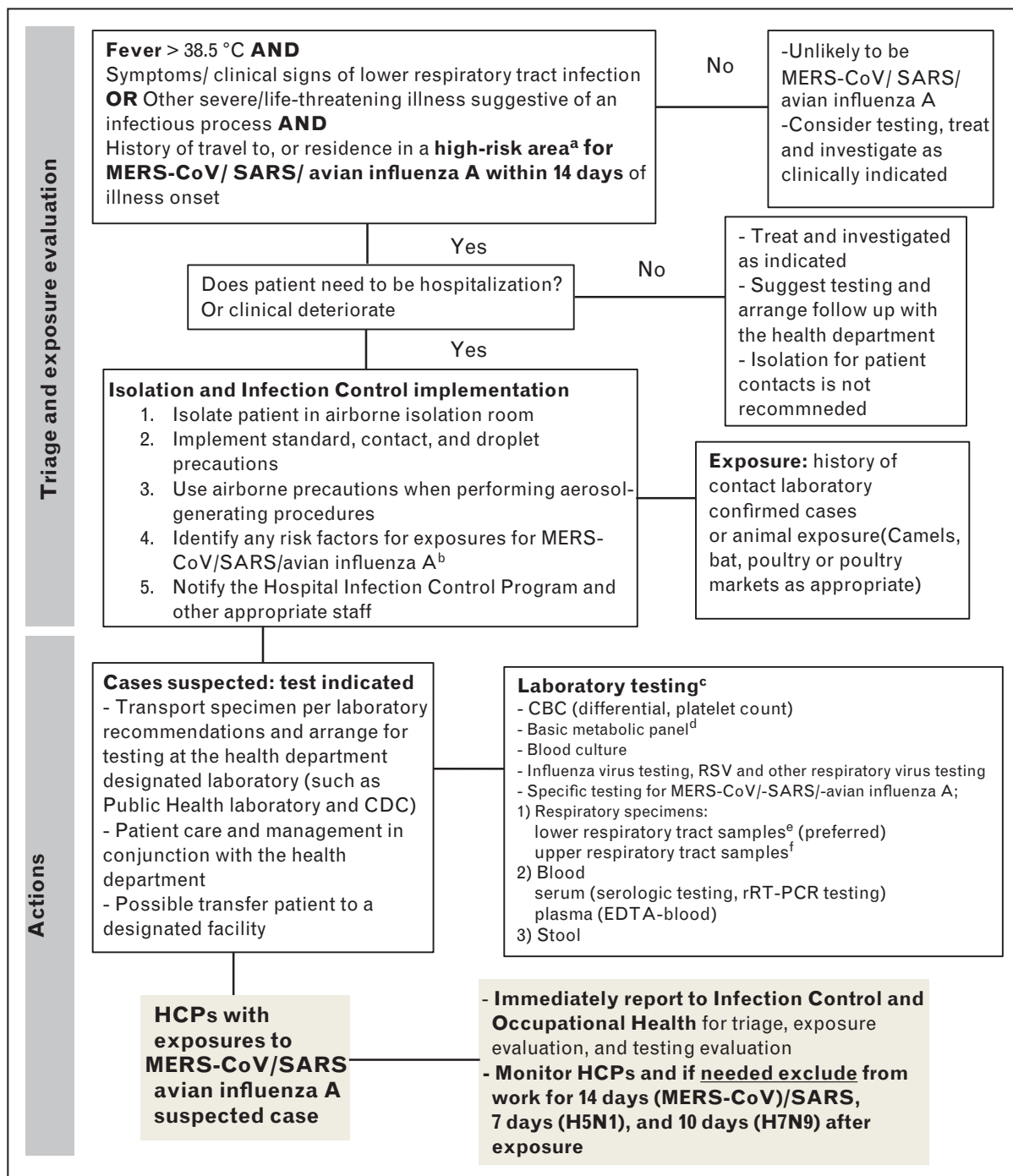


FIGURE 1. Algorithm for evaluation and infection control recommendation of suspected patient, and HCP exposure to patient with MERS-CoV/SARS/avian influenza A. CDC, The Centers for Disease Control and Prevention; HCPs, healthcare personnel; MERS-CoV, Middle East respiratory syndrome coronavirus; rRT-PCR, real-time reverse transcription polymerase chain reaction; RSV, respiratory syncytial virus; SARS, severe acute respiratory syndrome.^aHigh-risk area for MERS-CoV/SARS/avian influenza A [21^{••},22–28]. ^bRisk of exposures for MERS-CoV/SARS/avian influenza A [21^{••},22–28]. ^cLaboratory testing for suspected patient with MERS-CoV/SARS/avian influenza A [29]. ^dSodium, potassium, chloride, bicarbonate, calcium, blood urea nitrogen, creatinine, and glucose concentrations. ^eBronchoalveolar lavage, tracheal aspirate, and pleural fluid. ^fNasopharyngeal and oropharyngeal swabs.

within 3 months. It was contributed by the government supports for isolation, designated facilities, and contact tracing linked all cases back to the air traveler from Liberia [30¹¹]. The Dallas Ebola cluster highlights many important issues including the need to rapidly identify patients with Ebola, monitor potentially large numbers of community and healthcare contacts, assess infection control practices and conduct training sessions, develop protocols to safely transport suspected Ebola patients to hospitals, and designate facilities for patients with confirmed Ebola [38¹²]. The Centers for CDC provides guidance on PPE to be used by HCPs during management of patients with Ebola in US hospitals [40¹³] and also on compliance with select agent regulations for laboratories handling patient specimens suspected to contain Ebola virus [41¹⁴]. Furthermore, the risk of Ebola transmission to HCPs is also associated with infected bodily fluid exposure, especially during the PPE removal process (doffing). Thus, the exit of the Ebola patient treatment unit should be separate from the entrance. It is created to reduce cross-contamination between the PPE donning and doffing. A dedicated person at the exit is very important for guiding the HCPs and observing the exposure during PPE doffing. Even with PPE, HCPs are still at risk if the contaminated cloths with infectious bodily fluids are not appropriately removed. Therefore, HCPs should be trained to appropriately don and doff PPE and to use infection prevention practices (Table 1, Fig. 2) [42¹⁵,43,44]. In addition, studies that define how Ebola virus is transmitted and identify vaccines and antiviral therapy are critically needed. Recently, a replication defective recombinant chimpanzee adenovirus type 3-vec-tored Ebola virus vaccine, encoding the glyco-protein from Zaire and Sudan species that offers protection in the nonhuman primate model, was rapidly advanced into a phase 1, dose-dependent study and clinical trials among humans are in progress [45].

SEVERE ACUTE RESPIRATORY SYNDROME

SARS is caused by a novel coronavirus, found in November 2002 in Guangdong Province, China. It rapidly spread to other countries [3,46,47] causing 8096 infections, and 774 deaths between 1 November 2002 and 31 December 2003 [3]. SARS is highly contagious and transmitted primarily by respiratory droplets and other bodily secretions [46–49]. Transmission was documented in eight countries (number of probable SARS cases), including China (5327), Hong Kong (1755), Canada (251),

Mongolia (9), Philippines (14), Singapore (238), Taiwan (346), and Vietnam (63). Other countries that reported SARS cases without community transmission include Australia (6), China Macao (1), France (7), Germany (9), India (3), Indonesia (2), Italy (4), Kuwait (1), Malaysia (5), New Zealand (8), Ireland (1), South Korea (3), Romania (1), Russia (1), South Africa (1), Spain (1), Sweden (5), Switzerland (1), Thailand (9), the United Kingdom (4), and the United States (29) [3].

RISK FACTORS FOR AND EVIDENCE SUPPORTING SARS INFECTION IN HEALTHCARE PERSONNELS

SARS was the first global occupational disease in the millennium with a high number of HCP-affected cases [46]. At the end of the SARS outbreak, over 1706 HCP-affected cases were reported to WHO; from China (1002 cases, 19% of total cases), Canada (109 cases, 43%), France (two cases, 29%), Germany (one case, 11%), Hong Kong (386 cases, 22%), Philippines (four cases, 29%), Singapore (97 cases, 41%), Taiwan (68 cases, 20%), Thailand (one case, 11%) and Vietnam (36 cases, 57%) (Table 1) [3]. Risk of infection in HCPs was related to performing high-risk patient care procedures (especially airway and respiratory related procedures), inappropriate or insufficient infection control measures such as inconsistent use of PPE, reuse of N95 respirators, fatigue, and lacking of adequate infection control training [23,46–52]. The strongest predictor of SARS transmission from patients to HCPs was linked to aerosolization of secretions, while caring for SARS patients immediately prior to and during intubation [53]. Another important risk to HCPs acquiring SARS infection was possibly associated with the super-spreader. This phenomenon as reported in SARS outbreaks was associated with patients who transmitted to a large number of contacts and had a higher attack rate among those contacts [54,55]. Fisher *et al.* [56] reported four patients with atypical presentations of SARS, which were a source of nosocomial SARS outbreak in a nondesignated SARS patient treatment hospital in Singapore. Initially, the patients were diagnosed with congestive cardiac failure or bacterial pneumonia. Two patients, who were not isolated for 12 h, led to 10 documented infections (five HCPs) in 100 contacts [56]. However, super-spreader phenomenon was not associated with transmission from HCPs [23,54,55]. Early detection of suspected cases, frequent hand washing, and less opportunity for close contact might have contributed to lower rates of transmission from HCPs [54,55]. Moreover, the impact of SARS

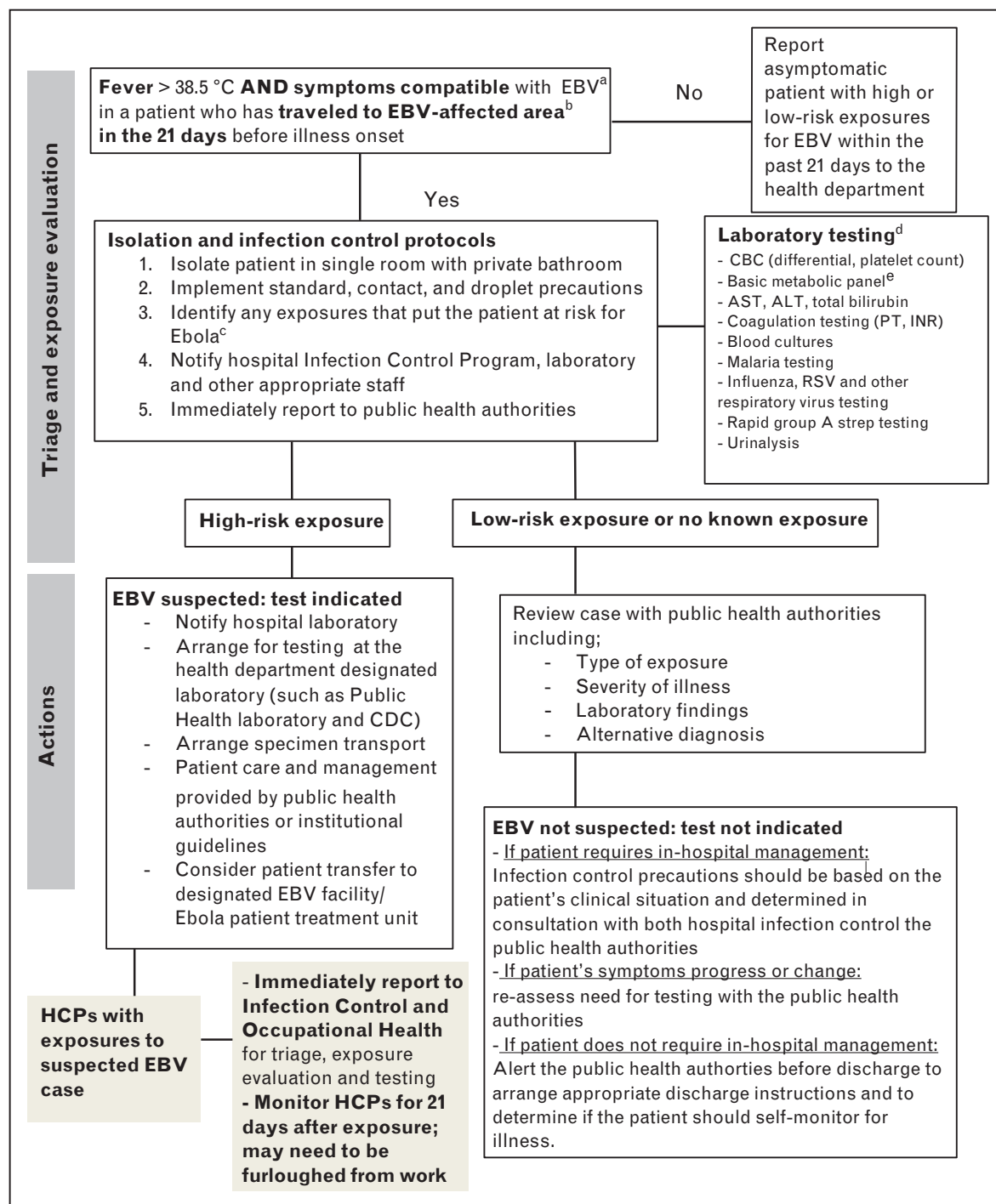


FIGURE 2. Algorithm for evaluation and infection control recommendation of suspected patient, and HCP exposure to patient with Ebola virus disease. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CDC, The Centers for Disease Control and Prevention; HCPs, healthcare personnel; INR, international normalized ratio; PT, prothrombin time; RSV, respiratory syncytial virus. ^aSevere headache, myalgia, vomiting, diarrhea, abdominal pain, and unexplained hemorrhage. ^bEbola-affected area [34^{***}]. ^cRisk of exposures for Ebola virus disease [34^{***},43]. ^dLaboratory testing for suspected patient with Ebola virus disease [44]. ^eSodium, potassium, chloride, bicarbonate, calcium, blood urea nitrogen, creatinine, and glucose concentrations.

among HCPs went beyond the physical challenges of caring for many patients at the height of the outbreak, the acute respiratory failure but also had substantial psychological impact [23,24].

INFECTION CONTROL IMPLEMENTATION AND PREVENTION STRATEGIES

The diffuseness of the SARS outbreak and the widespread scientific collaboration supported a climate

that advanced knowledge in several areas, including linking epidemiological and genetic information to trace the outbreak origins, effective contact tracing methods and outbreak investigation, and relevant and needed infection control practices. The appropriate uses of N95 mask, PPE, and isolation policy were updated and revised (Table 1, Fig. 1) [36,37,38[•],39,40^{••},41^{••}]. Training was recognized as a key component of using PPE. The WHO established guidelines for the global surveillance of SARS in 2004, which has subsequently used for global preparedness in other outbreaks such as MERS-CoV, Ebola, and avian influenza [21^{••},22,24,34^{••},57]. The WHO guideline defined high risk-procedures and enhanced appropriate nurse to patient ratios and other strategies to prevent HCP infection [22]. The SARS outbreak leads to notable improvements in several countries including China where the local public health infrastructure, responsibility, and policies were developed and enhanced [57]. The success of the multifactorial control measures was likely associated with having both cohorting in designated SARS patient treatment hospital, adequate infection control measures, and improved training [46–50,58]. Thus, the education programs for HCPs regarding appropriate use of N95 mask, PPE, and HCP adherence would decrease SARS transmission and should apply to other emerging diseases.

AVIAN INFLUENZA

Avian influenza routinely circulates in poultry and is caused by a RNA virus of the Orthomyxoviridae family. The first human avian influenza A (H5N1) outbreak occurred in Hong Kong in 1997 followed by an additional case in 2003 [4,59]. As of 3 March 2015, 784 laboratory-confirmed human cases of avian influenza A (H5N1) virus infection, including 429 deaths, have been reported from 16 countries (number of cases), including Azerbaijan (8), Bangladesh (7), Cambodia (56), Canada (1), China (47), Djibouti (1), Egypt (227), Indonesia (197), Iraq (3), Laos (2), Myanmar (1), Nigeria (1), Pakistan (3), Thailand (25), Turkey (12), and Vietnam (127). Currently, the number of influenza A (H5N1) virus outbreaks in poultry and human infection has increased in Egypt [4]. In March 2013, a novel avian influenza A (H7N9) was described in China [60,61]. As of 23 February 2015, a total of 571 laboratory-confirmed cases of human infection with avian influenza A (H7N9) virus, including 212 deaths, has been reported from four countries (number of cases), including China (469), Taiwan (4), Hong Kong (12), Malaysia (1), and Canada (2) [62]. In most of the human H5N1 and H7N9 virus exposure

to poultry or poultry markets is described. Although rare, human-to-human transmission of avian influenza (H5N1) has occurred via intimate contact such as among household contacts in which barrier precautions were not used [63–65]. Transmission has not occurred from casual, social contact.

RISK FACTORS AND EVIDENCE OF INFECTION IN HEALTHCARE PERSONNELS

To date, there are no reports of avian influenza transmission to HCPs (Table 1) [4,62]. Moreover, data lack that show efficient transmission to high-risk groups such as HCPs. Apisarnthanarak *et al.* [18] reported no evidence of seroconversion among 25 HCPs exposed to a patient with H5N1 virus infection cared for at a tertiary care hospital in Thailand. These data suggested that the risk to HCPs for occupational acquisition of H5N1 virus infection remains low. However, as avian influenza is associated with high case fatality in humans (more than 50%), high burden of virus circulating in poultry and its potential for genetic resortment, the pandemic potential of avian influenza, and risks for transmission to HCPs should be considered [4,23,62,66,67].

INFECTION CONTROL IMPLEMENTATION AND PREVENTION STRATEGIES

In order to prevent nosocomial transmission of avian influenza to HCPs and patients, planning for pandemic avian influenza should be considered along with heightened protective measures (Table 1, Fig. 1) [4,23,62,66,67]. The WHO encourages all countries to continue avian influenza surveillance, including surveillance for severe acute respiratory illness, reporting of human infections, and continue national health preparedness actions [4,62]. The key points in controlling avian influenza outbreaks are associated with the rapid responses of the central and regional health and agricultural authorities and the education and performance of HCPs [68,69]. The pandemic avian influenza preparedness plans in developing countries should be aligned with their resources and the setting. Planning should include the following: healthcare administrative support, mechanisms to rapidly create temporary isolation facilities, systems to restrict exposed HCPs, involvement of infectious disease specialists who can screen and identify cases early, provide for continuous monitoring to ensure adherence to optimal infection-control practices, and support regular feedback of compliance data to HCPs (Table 1) [70,71]. The virus should be closely monitored for any human-to-human transmission and pandemic potential

[66,67,70,71]. In China and since the SARS outbreak, the emergence of the novel avian influenza A (H7N9) infection leads to the continued improvement of the government's awareness and capacity to respond to health emergencies. The rapid communication and disclosure of information, the ability to detect and confirm an emerging virus within 1 month after the outbreak, and the capacity to collect clinical and disease information are major improvements [72]. Finally, to facilitate ongoing prevention efforts, improved vaccine and antiviral drugs need to be developed. In November 2013, the US Food and Drug Administration approved the first monovalent, adjuvant vaccine for the prevention of avian influenza A (H5N1) for people 18 years of age and older who are at increased risk of exposure to this virus. This vaccine is not intended for commercial availability. If avian influenza A (H5N1) develops the capability to spread efficiently from person to person, the vaccines will be critical to help counter the spread of influenza disease during a pandemic [73]. Vaccine for H7N9 is not currently available.

CONCLUSION

HCPs remain key members of our response but at increased risk to exposure of emerging infectious diseases, especially during the early part of epidemics when cases are unrecognized and diagnostic tests delayed or during situations in which healthcare facilities are significantly understaffed later in the outbreak. Knowledge deficits, unrecognized disease, insufficient infection control measures, poor compliance with recommended practices, and overwhelming numbers of patient cases during outbreaks increase the risks for nosocomial transmission to HCPs. Prevention of transmission requires an understanding of viral characteristics and the mechanisms of transmission, options for prophylaxis, treatment, and vaccines. Moreover, early and rapid detection of suspected cases along with appropriate infection control practices, education, national, and global preparedness guidelines are important preventive strategies.

Acknowledgements

This study was supported by National Research University Project of the Thailand Office of Higher Education Commission (to A.A.).

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. WHO. Global Alert and Response (GAR). Middle East respiratory syndrome coronavirus (MERS-CoV): summary of current situation, literature update and risk assessment as of 5 February 2015. http://www.who.int/csr/disease/coronavirus_infections/mers-5-february-2015.pdf?ua=1. [Accessed 8 February 2015]
2. WHO. Global Alert and Response (GAR). Ebola situation report as of 18 March 2015. http://apps.who.int/iris/bitstream/10665/156273/1/roadmap_sitrep_18Mar2015_eng.pdf?ua=1&ua=1. [Accessed 24 March 2015]
3. WHO. Global Alert and Response (GAR). Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 (based on data as of 31 December 2003). http://www.who.int/csr/sars/country/table2004_04_21/en/. [Accessed 8 February 2015]
4. WHO. Global Alert and Response (GAR). Cumulative number of confirmed human cases for avian influenza A (H5N1) reported to WHO, 2003–2015 as of 3 March 2015. http://www.who.int/influenza/human_animal_interface/EN_GIP_20150303cumulativeNumberH5N1cases.pdf?ua=1. [Accessed 24 March 2015]
5. Branch-Elliman W, Savor Price C, McGeer A, Perl TM. Protecting the front-line: designing an infection prevention platform for preventing emerging respiratory viral illnesses in healthcare personnel. *Infect Control Hosp Epidemiol* 2015; 36:336–345.
- This review provides the data behind current theories of respiratory virus transmission and key elements of the prevention program.
6. Maltezou HC, Tsiodras S. Middle East respiratory syndrome coronavirus: ■ implications for healthcare facilities. *Am J Infect Control* 2014; 42:1261–1265.
- This review provides the clinical and epidemiology data of MERS-CoV outbreak focusing on healthcare-associated transmission and infection control strategies.
7. Al-Tawfiq JA, Zumla A, Memish ZA. Coronaviruses: severe acute respiratory ■ syndrome coronavirus and Middle East respiratory syndrome coronavirus in travelers. *Curr Opin Infect Dis* 2014; 27:411–417.
- This article compares MERS-CoV with SARS-CoV regarding recent virological, clinical, epidemiological data, travel advice, and guidelines.
8. Assiri A, McGeer A, Perl TM, *et al.* Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med* 2013; 369:407–416.
9. de Groot RJ, Baker SC, Baric RS, *et al.* Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. *J Virol* 2013; 87:7790–7792.
10. Zaki AM, van Boheemen S, Bestebroer TM, *et al.* Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med* 2012; 367:1814–1820.
11. Hijawi B, Abdallat M, Sayaydeh A, *et al.* Novel coronavirus infections in Jordan, April 2012: epidemiological findings from a retrospective investigation. *East Mediterr Health J* 2013; 19:S12–S18.
12. WHO. Global Alert and Response (GAR). Middle East respiratory syndrome coronavirus (MERS-CoV): summary of current situation, literature update and risk assessment as of 20 March 2015. <http://www.who.int/csr/don/20-march-2015-mers-saudi-arabia/en/>. [Accessed 24 March 2015]
13. Memish ZA, Mishra N, Olival KJ, *et al.* Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. *Emerg Infect Dis* 2013; 19:1819–1823.
14. Briesse T, Mishra N, Jain K, *et al.* Middle East respiratory syndrome coronavirus quasispecies that include homologues of human isolates revealed through whole-genome analysis and virus cultured from dromedary camels in Saudi Arabia. *MBio* 2014; 5:e01146–e1214.
15. Memish ZA, Al-Tawfiq JA. Middle East respiratory syndrome coronavirus ■ infection control: the missing piece? *Am J Infect Control* 2014; 42:1258–1260.
- The editorial review article provides additional insight into the MERS-CoV outbreak focusing on infection control insufficiency aspect.
16. Al-Abdallat MM, Payne DC, Alqasrawi S, *et al.* Hospital-associated outbreak ■ of Middle East respiratory syndrome coronavirus: a serologic, epidemiologic, and clinical description. *Clin Infect Dis* 2014; 59:1225–1233.
- A retrospective seroepidemiologic investigation of the first MERS-CoV outbreak in Jordan provides more clinical and epidemiological data on HCP-affected cases and serological evidence that supports the problem regarding infection control insufficiency.
17. Memish ZA, Al-Tawfiq JA, Makhdoom HQ, *et al.* Screening for Middle East ■ respiratory syndrome coronavirus infection in hospital patients and their healthcare worker and family contacts: a prospective descriptive study. *Clin Microbiol Infect* 2014; 20:469–474.
- A prospective surveillance study of MERS-CoV from 1695 HCP contacts in Saudi Arabia reported only 1% infection rate.
18. Apisarnthanarak A, Erb S, Stephenson I, *et al.* Seroprevalence of anti-H5 antibody among Thai healthcare workers after exposure to avian influenza (H5N1) in a tertiary care center. *Clin Infect Dis* 2005; 40:e16–e18.

19. WHO. Global Alert and Response (GAR). Middle East respiratory syndrome coronavirus (MERS-CoV): summary of current situation, literature update and risk assessment as of 11 June 2014. http://www.who.int/csr/disease/coronavirus_infections/MERS-CoV_summary_update_20140611.pdf?ua=1. [Accessed 8 February 2015]
20. Memish ZA, Assiri A, Alhakeem R, *et al*. Middle East respiratory syndrome coronavirus, MERS-CoV. Conclusions from the 2nd Scientific Advisory Board Meeting of the WHO Collaborating Center for Mass Gathering Medicine, Riyadh. *Int J Infect Dis* 2014; 24:51–53.
A summary of recent virological, epidemiology data, and infection control recommendations on MERS-CoV from the WHO.
21. CDC. Interim infection prevention and control recommendations for hospitalized patients with Middle East respiratory syndrome coronavirus (MERS-CoV) on 14 May 2014. <http://www.cdc.gov/coronavirus/mers/downloads/MERS-Infection-Control-Guidance-051414.pdf>. [Accessed 28 February 2015]
- The recent infection control recommendations on MERS-CoV from the CDC.
22. WHO. Global Alert and Response (GAR). Guidelines for the global surveillance of severe acute respiratory syndrome (SARS) (October 2004). http://www.who.int/csr/resources/publications/WHO_CDS_CSR_ARO_2004_1.pdf?ua=1. [Accessed 15 February 2015]
23. Chan LY, Wong JT, Li PK, *et al*. Risk of transmission of severe acute respiratory syndrome to household contacts by infected healthcare workers and patients. *Am J Med* 2004; 116:559–560.
24. WHO. Interim recommendations for infection control in health-care facilities caring for patients with known or suspected Avian Influenza (21 May 2004). <http://www.cdc.gov/flu/avian/professional/pdf/infectcontrol.pdf>. [Accessed 28 February 2015]
25. Public Health England. MERS-CoV/avian influenza primary care algorithm (May 2014). http://webarchive.nationalarchives.gov.uk/20140714084352/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317141285220. [Accessed 28 February 2015]
26. Public Health England. MERS-CoV algorithm (February 2015). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/401035/Algorithm_case_v23-02Feb2015.pdf. [Accessed 28 February 2015]
27. Public Health England. Avian influenza A/H5N1 algorithm (March 2012). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/358675/Case_management_of_suspected_human_case.pdf. [Accessed 28 February 2015]
28. Public Health England. Avian influenza A/H7N9 algorithm (July 2013). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/358673/Investigation_and_management_of_possible_human_cases_of_avian_influenza_A_H7N9_flow_diagram_July_new.pdf. [Accessed 28 February 2015]
29. CDC. Interim guidelines for collecting, handling, and testing clinical specimens from patients under investigation (PULs) for Middle East respiratory syndrome coronavirus (MERS-CoV): version 2. <http://www.cdc.gov/coronavirus/mers/downloads/guidelines-clinical-specimens.pdf> [Accessed 26 March 2015]
30. WHO. Global Alert and Response (GAR). One year into the Ebola epidemic: a deadly, tenacious and unforgiving virus. <http://www.who.int/csr/disease/ebola/one-year-report/ebola-report-1-year.pdf?ua=1>. [Accessed 8 February 2015]
A recent summary and review of several aspects of Ebola from WHO.
31. WHO. Ebola Response Team. Ebola virus disease in West Africa: the first 9 months of the epidemic and forward projections. *N Engl J Med* 2014; 371:1481–1495.
This article provides a summary of epidemiological evidence and prevention strategies of Ebola outbreak in West Africa.
32. Baize S, Pannetier D, Oestereich L, *et al*. Emergence of Zaire Ebola virus disease in Guinea. *N Engl J Med* 2014; 371:1418–1425.
The first summary of a recent Ebola outbreak in Guinea.
33. Schieffelin JS, Shaffer JG, Goba A, *et al*. Clinical illness and outcomes in patients with Ebola in Sierra Leone. *N Engl J Med* 2014; 371:2092–2100.
The first summary of clinical data on a recent EVD in Sierra Leone.
34. CDC. Ebola Virus Disease (EVD) information for clinicians in U.S. healthcare settings. <http://www.cdc.gov/vhf/ebola/healthcare-us/preparing/clinicians.html>. [Accessed 28 February 2015]
The information and infection control recommendation on Ebola from the CDC.
35. Matanock A, Arwady MA, Ayscue P, *et al*. Ebola virus disease cases among healthcare workers not working in Ebola treatment units: Liberia, June–August, 2014. *MMWR Morb Mortal Wkly Rep* 2014; 63:1077–1081.
This article provides possible risks to HCPs with Ebola in Liberia and further preventive strategies.
36. Kreuels B, Wichmann D, Emmerich P, *et al*. A case of severe Ebola virus infection complicated by gram-negative septicemia. *N Engl J Med* 2014; 371:2394–2401.
37. Lyon GM, Mehta AK, Varkey JB, *et al*. Clinical care of two patients with Ebola virus disease in the United States. *N Engl J Med* 2014; 371:2402–2409.
38. Chevalier MS, Chung W, Smith J, *et al*. Ebola virus disease cluster in the United States, Dallas County, Texas, 2014. *MMWR Morb Mortal Wkly Rep* 2014; 63:1087–1088.
The epidemiological study from the first Ebola cluster in the United States provides critical suggestions on outbreak investigation and preventive plans.
39. Briand S, Berthet E, Cox P, *et al*. The international Ebola emergency. *N Engl J Med* 2014; 371:1180–1183.
40. CDC. Guidance on personal protective equipment to be used by healthcare workers during management of patients with Ebola virus disease in U.S. Hospitals, including procedures for putting on (donning) and removing (doffing) (20 October 2014). <http://www.cdc.gov/vhf/ebola/healthcare-us/hospitals/infection-control.html>. [Accessed 15 February 2015]
The recommendations for HCPs focusing on PPE use for caring for Ebola patients.
41. CDC. Interim guidance regarding compliance with select agent regulations for laboratories handling patient specimens that are known or suspected to contain Ebola virus (19 November 2014). <http://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/select-agent-regulations.html>. [Accessed 15 February 2015]
The guideline and recommendations for clinical laboratories regarding suspected Ebola patients' specimens management including specimen transportation, specimen processing, recommended instruments, and waste management.
42. Fischer WA 2nd, Hynes NA, Perl TM. Protecting healthcare workers from Ebola: personal protective equipment is critical but is not enough. *Ann Intern Med* 2014; 161:753–754.
This article emphasizes critical points regarding the PPE contamination with Ebola patients and provides further preventive suggestions such as entrance and exit of the Ebola treatment unit and PPE doffing observation.
43. CDC. Ebola virus disease, algorithm for evaluation of the returned traveler. <http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf>. [Accessed 28 February 2015]
44. CDC. Guidance for U.S. laboratories for managing and testing routine clinical specimens when there is a concern about Ebola Virus Disease. <http://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/safe-specimen-management.html>. [Accessed 26 March 2015]
45. Ledgerwood JE1, DeZure AD, Stanley DA, *et al*. Chimpanzee adenovirus vector Ebola vaccine: preliminary report. *N Engl J Med* 2014. [Epub ahead of print]
46. Low JG, Wilder-Smith A. Infectious respiratory illnesses and their impact on healthcare workers: a review. *Ann Acad Med Singapore* 2005; 34:105–110.
47. Ofner-Agostini M, Gravel D, McDonald LC, *et al*. Cluster of cases of severe acute respiratory syndrome among Toronto healthcare workers after implementation of infection control precautions: a case series. *Infect Control Hosp Epidemiol* 2006; 27:473–478.
48. Lai TS, Yu WC. The lessons of SARS in Hong Kong. *Clin Med* 2010; 10:50–53.
49. Koh D, Sng J. Lessons from the past: perspectives on severe acute respiratory syndrome. *Asia Pac J Public Health* 2010; 22 (3 Suppl):132S–136S.
50. Shigayeva A1, Green K, Raboud JM, *et al*. Factors associated with critical-care healthcare workers' adherence to recommended barrier precautions during the Toronto severe acute respiratory syndrome outbreak. *Infect Control Hosp Epidemiol* 2007; 28:1275–1283.
51. Chen NH, Wang PC, Hsieh MJ, *et al*. Impact of severe acute respiratory syndrome care on the general health status of healthcare workers in Taiwan. *Infect Control Hosp Epidemiol* 2007; 28:75–79.
52. Reynolds MG, Anh BH, Thu VH, *et al*. Factors associated with nosocomial SARS-CoV transmission among healthcare workers in Hanoi, Vietnam, 2003. *BMC Public Health* 2006; 6:207.
53. Raboud J, Shigayeva A, McGeer A, *et al*. Risk factors for SARS transmission from patients requiring intubation: a multicentre investigation in Toronto, Canada. *PLoS One* 2010; 5:e10717.
54. Centers for Disease Control and Prevention (CDC). Severe acute respiratory syndrome Singapore, 2003. *MMWR Morb Mortal Wkly Rep* 2003; 52:405–411.
55. Shen Z, Ning F, Zhou W, *et al*. Superspreading SARS events, Beijing, 2003. *Emerg Infect Dis* 2004; 10:256–260.
56. Fisher DA, Lim TK, Lim YT, *et al*. Atypical presentations of SARS. *Lancet* 2003; 361:1740.
57. WHO. Interim guidance for infection control within healthcare settings when caring for confirmed cases, probable cases, and cases under investigation for infection with novel Influenza A viruses associated with severe disease. <http://www.cdc.gov/flu/avianflu/h7n9-infection-control.htm>. [Accessed 28 February 2015]
58. Yao L1, Chen E, Chen Z, Gong Z. From SARS to H7N9: the mechanism of responding to emerging communicable diseases has made great progress in China. *Biosci Trends* 2013; 7:290–293.
59. Pang X, Zhu Z, Xu F, *et al*. Evaluation of control measures implemented in the severe acute respiratory syndrome outbreak in Beijing, 2003. *JAMA* 2003; 290:3215–3221.
60. Gao HN, Lu HZ, Cao B, *et al*. Clinical findings in 111 cases of influenza A (H7N9) virus infection. *N Engl J Med* 2013; 368:2277–2285.
61. Li Q, Zhou L, Zhou M, *et al*. Epidemiology of human infections with avian influenza A(H7N9) virus in China. *N Engl J Med* 2014; 370:520–532.
62. WHO. Global Alert and Response (GAR). Background and summary of human infection with avian influenza A(H7N9) virus: as of 31 January 2014. http://www.who.int/influenza/human_animal_interface/20140131_background_and_summary_H7N9_v1.pdf. [Accessed 15 February 2015]
http://www.who.int/influenza/human_animal_interface/influenza_h7n9/Risk_Assessment_H7N9_23Feb2015.pdf?ua=1
63. Katz JM, Lim W, Bridges CB, *et al*. Antibody response in individuals infected with avian influenza A (H5N1) viruses and detection of anti-H5 antibody among household and social contacts. *J Infect Dis* 1999; 180:1763–1780.

64. Kandun IN, Wibisono H, Sedyaningsih ER, *et al.* Three Indonesian clusters of H5N1 virus infection in 2005. *N Engl J Med* 2006; 355:2186–2194.
65. Ungchusak K, Auewarakul P, Dowell SF, *et al.* Probable person-to-person transmission of avian influenza A (H5N1). *N Engl J Med* 2005; 352:333–340.
66. Bartlett JG. Planning for avian influenza. *Ann Intern Med* 2006; 145:141–144.
67. Martinello RA. Preparing for avian influenza. *Curr Opin Pediatr* 2007; 19:64–70.
68. Sarikaya O1, Erbaydar T. Avian influenza outbreak in Turkey through health personnel's views: a qualitative study. *BMC Public Health* 2007; 7:330.
69. Manabe T, Pham TP, Kudo K, *et al.* Impact of education and network for avian influenza H5N1 in human: knowledge, clinical practice, and motivation on medical providers in Vietnam. *PLoS One* 2012; 7:e30384.
70. Apisarnthanarak A, Warren DK, Fraser VJ. Issues relevant to the adoption and modification of hospital infection-control recommendations for avian influenza (H5N1 infection) in developing countries. *Clin Infect Dis* 2007; 45:1338–1342.
71. Apisarnthanarak A, Mundy LM. Infection control for emerging infectious diseases in developing countries and resource-limited settings. *Infect Control Hosp Epidemiol* 2006; 27:885–887.
72. Wang Y. The H7N9 influenza virus in China: changes since SARS. *N Engl J Med* 2013; 368:2348–2349.
73. FDA, News release, FDA approves first adjuvanted vaccine for prevention of H5N1 avian influenza on 22 November 2013. <http://www.fda.gov/News/Events/Newsroom/PressAnnouncements/ucm376444.htm>. [Accessed 16 February 2015]

Research letters

Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS)

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We did a case-control study in five Hong Kong hospitals, with 241 non-infected and 13 infected staff with documented exposures to 11 index patients with severe acute respiratory syndrome (SARS) during patient care. All participants were surveyed about use of mask, gloves, gowns, and hand-washing, as recommended under droplets and contact precautions when caring for index patients with SARS. 69 staff who reported use of all four measures were not infected, whereas all infected staff had omitted at least one measure ($p=0.0224$). Fewer staff who wore masks ($p=0.0001$), gowns ($p=0.006$), and washed their hands ($p=0.047$) became infected compared with those who didn't, but stepwise logistic regression was significant only for masks ($p=0.011$). Practice of droplets precaution and contact precaution is adequate in significantly reducing the risk of infection after exposures to patients with SARS. The protective role of the mask suggests that in hospitals, infection is transmitted by droplets.

Lancet 2003; **361**: 1519–20

On March 12, 2003, WHO issued a worldwide alert for severe acute respiratory syndrome (SARS).¹ The hospital authority, which oversees all public hospitals in Hong Kong, had requested cases to be reported centrally since early February, in response to media reports of pneumonia outbreaks in Guangdong Province, People's Republic of China.² At that time, droplets precautions³ and rigorous universal precautions³ or standard precautions³ were recommended for the care of patients with SARS. Here we report findings of a case-control study assessing the effectiveness of droplets precautions for prevention of nosocomial transmission.

We defined SARS as fever of 38°C or higher, radiological infiltrates compatible with pneumonia, and two of: chills, new cough, malaise, and signs of consolidation. We excluded patients who had known pathogens, radiological evidence of lobar consolidation, or who responded to antibiotics within 48 h.

Exposure to the virus was defined as coming within 0.91 m (3 feet) of an index patient with symptoms of SARS when providing care. Infected hospital staff were those who acquired

SARS 2–7 days after exposure, with no exposure to cases outside the hospital.

For this study, index patients were selected only when there was documented clustering, indicating recent spread of infection. We could identify infected staff because since early February, notification of staff with SARS was mandatory in hospital-authority hospitals. We tested sera taken from index patients and infected hospital staff during the acute phase of the infection and during convalescence for antibodies to the corona-like virus⁴ associated with SARS using an indirect immunofluorescence test.⁴

We excluded one hospital that had a large nosocomial outbreak because a drug nebuliser was used on an index patient with SARS for longer than 10 days. Droplets precautions have never been recognised as an effective infection control measure for such aerosol-generating procedures⁵ and assessment of its efficacy seems inappropriate in the presence of such an apparent confounder.

A questionnaire was given to all infected and non-infected staff listed on the current roster in the clinical regions providing care for index patients with SARS. The names of index patients were listed on the questionnaire and the staff were asked if they had cared for these patients. Those who replied affirmatively were asked to indicate whether they had used mask, gloves, gowns, and hand-washing during patient care, selecting one of three responses: yes, most of the time, or no. These levels of response were to ensure that no indicated a definite lapse in practice. Staff who used masks were asked whether it was a paper mask, surgical mask, or N95 mask. The survey, which started on March 15, was done by the hospital's infection-control nurses and all responses were collected by March 24. Statistical analysis was done with SPSS version 10, with either χ^2 or Fisher's exact test for univariate analysis, whereas we used forward stepwise selection (Waldesian) for logistic regression.

We identified 11 index patients from five hospitals. None was nursed in negative-pressure rooms for the duration of illness. In three of the five hospitals, 13 hospital staff were

	Sex	Occupation	Unit	Protective measures during exposure
1	Female	Nurse	Emergency	*Paper mask/gloves/hand-washing
2	Female	Nurse	Medicine	Hand-washing
3	Female	Nurse	Medicine	Hand-washing
4	Female	Nurse	Medicine	Hand-washing
5	Female	Nurse	Medicine	Nil
6	Male	Nurse	Medicine	*Paper mask/hand-washing
7	Male	Doctor	Medicine	Gloves
8	Male	Doctor	Medicine	Hand-washing
9	Female	Health-care assistant	Medicine	Gloves/hand washing
10	Female	Health-care assistant	Medicine	Hand-washing
11	Female	Health-care assistant	Medicine	Hand-washing
12	Male	Health-care assistant	Medicine	Hand-washing
13	Female	Domestic staff	Medicine	Gloves

*2-layered paper mask.

Table 1: Demographic profile of infected hospital staff

	Infected Staff (n=13)	Non-infected staff (n=241)	p*	Odds ratio (95% CI) [†]
Protective measures[‡]				
Masks [§]	2 (15%)	169 (70%)	0.0001	13 (3–60)
Paper mask	2	26	0.511¶	
Surgical mask	0	51	0.007¶	
N95	0	92	0.0004¶	
Gloves	4 (31%)	117 (48%)	0.364	2 (0.6–7)
Gowns	0 (0%)	83 (34%)	0.006	NC
Hand-washing	10 (77%)	227 (94%)	0.047	5 (1–19)
All measures	0 (0%)	69 (29%)	0.022	NC

NC=not calculatable. *Two-tailed. †Odds ratio of staff with specific protection not getting infected. ‡“Yes” and “most of the time” were grouped together. §Total cases 254 by forward stepwise (Waldesian) logistic regression using 0.05 as entry probability and 0.10 as removal probability. Forward and backward stepwise regression result in same model with mask in the model (p=0.011). ¶Comparing proportion of infected over non-infected staff, with those without mask (11 infected and 72 non-infected).

Table 2: Protective measures reported by infected and non-infected staff

reported to have SARS after exposure to an index case. One infected staff member had no exposure to any admitted patient with SARS and was classified as a community-acquired infection. All index patients and infected staff in the study, except for one, showed a four-fold rise in the number of antibodies to corona-like virus.

356 completed questionnaires were returned, covering 85% of the staff on roster. Non-responders were mostly those on leave or night shift, which is rotated among the staff. We excluded 102 staff who had no contact with index patients (table 1), and omitted at least one of the four measures queried. Two who were using a mask reported only paper masks.

Staff who used masks, gowns, and handwashing were less likely to develop SARS than those who did not use them, but the association for gloves was not significant (table 2). None of the 69 staff reporting use of all four measures became infected. By contrast, all 13 infected staff had omitted at least one of the measures (p=0.0224). However logistic regression of the four measures with forward stepwise selection showed that only use of masks was significant in the final model (table 2).

The staff who wore surgical masks and N95 masks were significantly associated with non-infection (table 2), but this was not seen for paper masks.

That use of masks and hand-washing was associated with non-infection, and that no staff became infected when they used all four measures, suggest that precautions against droplets and contact are adequate for prevention of nosocomial SARS, where no aerosolisations are expected. The surgical and N95 masks were both effective in significantly reducing the risk of infection, which together with the finding that 30% of non-infected staff did not use masks (table 2) supports that transmission is not airborne. The finding that paper masks did not significantly reduce the risk is not unexpected. Such masks, being easily wet with saliva, are never recommended as a precaution against droplets.³

In any survey, recall bias is a concern. However, it probably had little effect since the associations shown are clear and the information requested was about simple concrete behaviour and events that took place recently. Masks seem to be essential for protection, since only this measure was significant in stepwise logistic regression. Thus, in hospital, the other three measures add no significant protection to the mask. This finding fits well with droplets transmission because droplets are generated at the face level making the mask crucial for protection.

Contributors

W H Seto is the main investigator and was involved in all aspects of the study. D Tsang, R W H Yung, T K Ng, and M Ho helped in the survey, and T Y Ching coordinated the infection-control nurses. L M Ho did the statistical analysis, and J S M Peiris organised the laboratory tests and supervised the writing of the report. The Expert Group advised on the clinical aspects of the report.

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Conflict of interest statement
None declared.

Acknowledgments

We thank the staff of the Infection Control Units who assisted in the study, and the hospital authority of Hong Kong for help and assistance. Research funding was received from Public Health Research Grant A95357, and the National Institute of Allergy and Infectious Diseases, USA.

- 1 WHO. WHO issues global alert about cases of atypical pneumonia: cases of severe respiratory illness may spread to hospital staff. Geneva: World Health Organization, March 12, 2003. www.who.int/mediacentre/releases/2003/pr22/en/print.html (accessed April 1, 2003).
- 2 Rosling L, Rosling M: Pneumonia causes panic in Guangdong province. *BMJ* 2003; **326**: 416.
- 3 US Centers for Disease Control: Guideline for isolation precautions in hospitals. *Am J Infect Control* 1996; **24**: 24–52.
- 4 Peiris JSM, Lai ST, Poon LLM, et al: Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet* 2003; **361**: 1319–25.
- 5 US Centers for Disease Control. Infection control precautions for aerosol-generating procedures on patients who have suspected severe acute respiratory syndrome. March 20, 2003. <http://www.cdc.gov/ncidod/sars/aerosol/infectioncontrol.htm> (accessed March 29, 2003).

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Haemorrhagic-fever-like changes and normal chest radiograph in a doctor with SARS

Eugene B Wu, Joseph J Y Sung

A 33-year-old doctor contracted severe acute respiratory syndrome presenting with features of disseminated intra-vascular coagulopathy without changes in the chest radiograph initially. A CT scan of his chest showed marked lung changes. His condition improved with intravenous methylprednisolone 500 mg daily and ribavirin 1.2 g orally thrice daily. The case illustrates the importance of a break in fever between the viraemic and lung inflammatory phases of the illness that

Factors associated with transmission of severe acute respiratory syndrome among health-care workers in Singapore

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(Accepted 9 June 2004)

SUMMARY

Between 1 and 22 March 2003, a nosocomial outbreak of Severe Acute Respiratory Syndrome (SARS) occurred at the Communicable Disease Centre in Tan Tock Seng Hospital, Singapore, the national treatment and isolation facility for patients with SARS. A case-control study with 36 cases and 50 controls was conducted of factors associated with the transmission of SARS within the hospital. In univariate analysis, contact with respiratory secretions elevated the odds ratio to 6·9 (95% CI 1·4–34·6, $P=0\cdot02$). Protection was conferred by hand washing (OR 0·06, 95% CI 0·007–0·5, $P=0\cdot03$) and wearing of N95 masks (OR 0·1, 95% CI 0·03–0·4, $P=0\cdot001$). Use of gloves and gowns had no effect. Multivariate analysis confirmed the strong role of contact with respiratory secretions (adjusted OR 21·8, 95% CI 1·7–274·8, $P=0\cdot017$). Both hand washing (adjusted OR 0·07, 95% CI 0·008–0·66, $P=0\cdot02$) and wearing of N95 masks (adjusted OR 0·1, 95% CI 0·02–0·86, $P=0\cdot04$) remained strongly protective but gowns and gloves had no effect.

INTRODUCTION

Singapore was one of the countries most affected in the first outbreak of severe acute respiratory infection (SARS), with a total of 238 cases occurring between 1 March and 5 May 2003 [1], out of a global total of 8098 probable cases that occurred worldwide between 1 November 2002 and 31 July 2003 [1].

The epidemiological and microbiological evidence thus far indicates that the aetiological agent, now designated the SARS coronavirus (SARS-CoV) [2–4], spreads predominantly from person-to-person. Infection mainly occurs either via the projection of virus-bearing respiratory droplets onto mucous membranes of the eyes, nose and mouth across a short (arbitrarily

defined as 1 m) distance, i.e. droplet transmission [5, 6], or via direct or indirect (involving fomites) contact with an infected source patient, i.e. contact transmission [6]. Contact transmission is especially likely among health-care workers (HCWs). Spread by fomites depends on the survivability of the virus in the environment, which for SARS has been demonstrated to be as long as a few days [7]. An unusual route of transmission was implicated by epidemiological investigation of an outbreak in a Hong Kong apartment block, in which it was hypothesized that exhaust fans causing back-flow of air through a faulty sewage system may have been responsible for the widespread circulation of virus-bearing faecal droplets throughout the building [8]. The subsequently reported clinical presentation of these cases, however, supports possible faecal–oral transmission as an alternative hypothesis [4].

Apart from ‘superspreaders’, for which phenomenon the specific host and/or environmental factors

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responsible remain to be elucidated [7], the infectiousness of SARS is in general less than that of most other respiratory infections. Despite numerous unprotected exposures, no transmission occurred among HCWs in the United States [9]. Estimates of the basic reproduction ratio R_0 , average around 3 [7], compared to estimates of 11–18 for measles [10, 11] and up to 30 for influenza [12, 13]. Case-fatality ratios ranged from 0% to over 50%, with the overall case fatality estimated at approximately 15% [7]. In Singapore, the case-fatality ratio was 13.6% [14].

A hallmark of the SARS outbreak in affected countries was the amplification of transmission that occurred within health-care settings [7]. The occurrence of hospital and nursing-home clusters involving staff and patients caused much alarm. Initial perceptions of infectiousness were coloured by the apparent efficiency and unpredictability of nosocomial transmission of SARS [7, 15]. Several high-profile fatalities among HCWs both locally and internationally [16, 17] also led to unduly grim perceptions of its virulence. Scientific studies were urgently undertaken to ascertain the risk level associated with various therapeutic settings and procedures and inform recommendations on the use of personal protective equipment (PPE) by HCWs [18].

This report presents results of a case-control study of the risk and protective factors for nosocomial transmission of SARS in Tan Tock Seng Hospital (TTSH), Singapore in an outbreak which affected a total of 44 HCWs.

Chronology of events

On 6 March 2003, the Ministry of Health, Singapore was notified of a cluster of atypical pneumonia in three patients with a preceding history of travel to Hong Kong [8]. The health authorities having been alerted by the World Health Organization (WHO), these and subsequent patients were isolated at a central location, the Communicable Disease Centre (CDC) at TTSH. On 22 March, TTSH, Singapore's second largest general hospital, was designated as the central referral, screening and treatment centre for SARS. The CDC is a specialist facility with a national role, staffed by experts in clinical infectious diseases, hospital infection control and public health.

The nosocomial outbreak in TTSH began shortly after the admission on 1 March of the first index patient (case 1), a 23-year-old female who had returned from a visit to Hong Kong. She was managed initially as

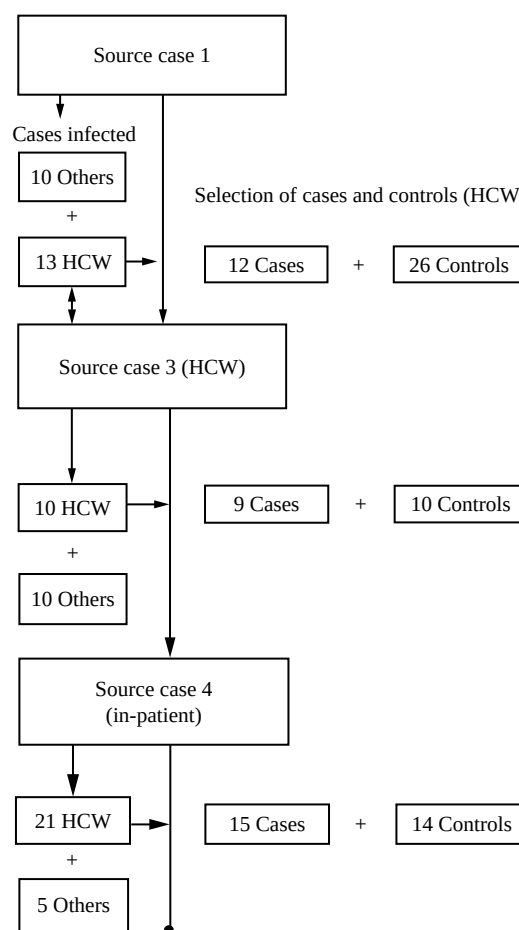


Fig. Source cases for SARS transmission among health-care workers (HCW) and selection of cases and controls in the study.

for straightforward community-acquired pneumonia. After 5 days, a deterioration in her condition, which coincided with recognition of a second index case (case 2), raised suspicions that led to her being isolated 5 days after admission. Shortly after, clusters of cases emerged in three separate wards, all traceable to case 1. She had already infected 23 cases, including 13 HCWs, before she was isolated. No secondary cases arose from case 2. Case 3, a secondary case to case 1, was admitted to another ward where she infected a total of 20 persons, including 10 HCWs before she was isolated 3 days later. An in-patient (case 4) who shared a cubicle with case 3 was subsequently transferred to a coronary care unit when her clinical condition deteriorated. Before her isolation 8 days later, she had infected a total of 26 persons, including 21 HCWs. Over 21 days, secondary and tertiary transmission occurred within the hospital from source cases 1, 3 and 4, involving a total of 44 HCWs and 25 patients (Fig.).

Enhanced personal protective measures

By the end of the first week of March, HCWs were employing N95 masks for personal protection when nursing case 1 and her contacts. These are health-care particulate respirators with at least 95% filtration efficiency against non-oily, solid and liquid aerosols [17]. By the end of week 2 PPE against contact, droplet and respiratory transmission had been adopted by HCWs attending patients in areas involved in SARS screening or treatment (intensive care unit, emergency department and communicable disease wards). By 22 March 2003, N95 masks were required when treating any patient in the hospital. Beginning 6 April 2003, the wearing of gloves, gowns and N95 masks was enforced for contact with all patients in the hospital, with visors additionally advised for procedures with a risk of splashing. On 25 April 2003, goggles were made mandatory for all patient contact. Later, a requirement of positive air purifying respirators (PAPR) for high-risk or aerosol-generating procedures was also imposed. Beyond 22 March 2003, no further intra-hospital transmission occurred.

MATERIALS AND METHODS

Subjects

HCWs with probable SARS admitted between 1 and 31 March 2003 were recruited as cases. Diagnosis was based on WHO's criteria of documented fever (temperature $>38^{\circ}\text{C}$), presence of cough, shortness of breath or breathing difficulty, and a significant history of exposure to a SARS patient not more than 10 days prior to onset of symptoms, plus radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR) [20]. HCWs in whom an alternative diagnosis was eventually established were excluded from the list of probable SARS cases and also from the study. All cases included were subsequently confirmed by a positive serology result performed at the national referral laboratory.

We initially selected as controls all HCWs from SARS-affected wards who reported exposure to patients with probable SARS during the same period but who remained well. To establish exposure, respondents were asked if they had cared for any person on the list of probable SARS patients. Exposure was deemed to be definite where there was a history of being within close physical proximity (1 m) of a patient subsequently confirmed with SARS. For all

patients not subsequently confirmed by serology, controls were excluded from final analysis.

Epidemiological investigation and data collection

Telephone interviews with cases and controls were carried out using a closed questionnaire by staff experienced in epidemiological investigations from the Department of Clinical Epidemiology of TTSH.

Information collected included demographic data (age, gender and ethnic group), occupation, history of medical conditions and vaccinations within the previous 5 years and history of performing procedures with transmission risk (date, place, type, duration and frequency). Incubation periods were estimated by ascertaining from subjects the date of onset of their first symptom and dates of first and last exposure. In cases with exposure to more than one SARS case, the source of infection was assigned based on the most likely range of incubation of 2–10 days. Subjects were questioned on their compliance with recommendations for personal protection, i.e. wearing of N95 masks, gloves, gown and consistent hand washing after patient contact.

Statistical analysis

For statistical analyses, differences in proportions observed between cases and controls were compared using χ^2 or Fisher's exact test. Probability (P) values of less than 0.05 were considered significant. Factors found to be significant in univariate analysis were included in forward logistic regression analysis. Potentially confounding covariates were selected among those where P values were <0.2 in the univariate analysis. Statistical analyses were performed using SPSS version 11.5 (SPSS Inc., Chicago, IL, USA) software.

RESULTS

Descriptive epidemiology

Of the 44 cases generated by source cases 1, 3 and 4 during the period under study, 36 (82%) were successfully recruited, six were too ill to be interviewed and two died before they could be interviewed. A total of 50 HCWs working in the same wards as the cases, with history of exposure but who did not develop disease, were included in the control group.

The demographic and epidemiological characteristics showed that the two groups were comparable

Table 1. *Univariate analysis of demographic and epidemiological characteristics*

	Cases (<i>n</i> = 36)		Controls (<i>n</i> = 50)		Crude OR (95 % CI)	<i>P</i> value*
	<i>n</i>	(%)	<i>n</i>	(%)		
Gender						
Female	32	(88.9)	49	(98.0)	6.1 (0.7–57.3)	0.16
Male	4	(11.1)	1	(2.0)		
Ethnic group						
Chinese	20	(55.6)	17	(34.0)	2.4 (1.0–5.9)	0.04
Non-Chinese	16	(44.4)	33	(66.0)		
Age group (years)						
<30	23	(63.9)	28	(56.0)	1.4 (0.3–1.7)	0.5
30+	13	(36.1)	22	(44.0)		
Presence of comorbid condition	6	(16.7)	9	(18.0)	0.9 (0.3–3.2)	0.9
History of vaccination in previous 5 years	19	(52.8)	26	(54.0)	1.03 (0.4–2.7)	0.9
Category of health-care worker						
Doctors and nurses	26	(72.2)	39	(78.0)	0.7 (0.3–1.9)	0.5
Other health-care workers	10	(27.8)	11	(22.0)		

* Using χ^2 or Fisher's exact test.Table 2. *Univariate analysis of factors associated with transmission of SARS to health-care workers*

	Cases (<i>n</i> = 36)		Controls (<i>n</i> = 50)		Crude OR (95 % CI)	<i>P</i> value*
	<i>n</i>	(%)	<i>n</i>	(%)		
Distance to source of infection						
<1 m	32	(88.9)	45	(90.0)	0.9 (0.2–3.6)	0.9
Duration of exposure (min)						
60+	21	(58.3)	24	(48.0)	0.7 (0.3–1.6)	0.4
Wearing of N95 mask	3	(8.3)	23	(46.0)	0.1 (0.03–0.4)	0.001
Wearing of gloves	10	(27.8)	22	(44.0)	0.5 (0.2–1.2)	0.1
Wearing of gown	5	(13.9)	13	(26.0)	0.5 (0.1–1.4)	0.2
Touched patients	29	(80.6)	40	(80.0)	1.0 (0.4–3.0)	0.9
Touched patients' personal belongings	28	(77.8)	43	(86.0)	0.6 (0.2–1.7)	0.3
Contact with respiratory secretions	8	(22.2)	2	(4.0)	6.9 (1.4–34.6)	0.02
Performed venepuncture	30	(83.3)	40	(80.0)	0.8 (0.3–2.4)	0.7
Performed/assisted in intubation	2	(5.6)	4	(8.0)	1.5 (0.4–5.4)	0.6
Performed suction of body fluids	8	(22.2)	11	(22.2)	1.01 (0.4–2.8)	1
Administered oxygen	7	(19.4)	10	(20.0)	1.0 (0.3–2.8)	1
Hand washing after each patient	27	(75.0)	46	(92.0)	0.06 (0.007–0.5)	0.03

* Using χ^2 or Fisher's exact test.

except for a higher proportion of Chinese than non-Chinese in cases (Table 1).

Univariate analysis

Compared to the control population, a small and marginally significant elevation of the crude odds ratio (OR) for SARS was found for Chinese compared with

non-Chinese (OR 2.4, 95 % CI 1.0–5.9, $P=0.048$) (Table 1). Contact with respiratory secretions substantially and significantly increased the odds of SARS (OR 6.9, 95 % CI 1.4–34.6, $P=0.02$) (Table 2). A very large reduction in odds was achieved by consistent hand washing after patient contact (OR 0.06, 95 % CI 0.007–0.5, $P=0.03$). A large and highly significant reduction in odds was also achieved by the

Table 3. *Multivariate analysis of factors associated with transmission of SARS to health-care workers*

Covariate	Adj. OR*	95% CI	P value
Gender			
Male	2.9	0.2–34.0	0.4
Ethnic group			
Chinese	2.0	0.7–6.1	0.2
Non-Chinese†			
Wearing of N95 mask	0.1	0.02–0.9	0.04
Wearing of gloves	1.5	0.3–7.2	0.6
Wearing of gowns	0.5	0.4–6.9	0.6
Hand washing after each patient	0.07	0.008–0.7	0.02
Contact with respiratory secretions	21.8	1.7–274.8	0.017

* Adjusted odds ratio by forward-enter logistic regression.

† Reference category.

wearing of N95 masks when attending to patients (OR 0.1, 95% CI 0.03–0.4, $P=0.001$) (Table 2). Wearing of latex gloves (OR 0.5, 95% CI 0.2–1.2, $P=0.1$) and gowns (OR 0.5, 95% CI 0.1–1.4, $P=0.2$) each halved the odds of infection, although both failed to achieve statistical significance.

Logistic regression analysis

The best fit was obtained by forward-entering the following covariates into the regression model: gender, ethnic group, wearing of N95 masks, wearing of gloves, wearing of gowns, hand washing after each patient contact, and contact with patients' respiratory secretions. The results (Table 3) show that contact with patients' respiratory secretions was independently and significantly associated with a greatly increased odds of infection (adjusted OR 21.8, 95% CI 1.7–274.8, $P=0.017$). Conversely, hand washing after patient contact was strongly protective (adjusted OR 0.07, 95% CI 0.008–0.66, $P=0.02$), but wearing of gloves and gowns had no demonstrable effect. Wearing of N95 masks during each patient contact was also strongly protective, with an adjusted OR of 0.1 (95% CI 0.02–0.86, $P=0.04$).

DISCUSSION

In this study, no adjustment was made for the effect of 'superspreaders' – who featured strongly in the Singapore outbreak – nor for any decrease in infectiousness over successive generations of cases: all

exposures were treated as equivalent, regardless of timing within the outbreak or source of infection. An inherent limitation of this study was that viral load measurements were not available for any of the patients in TTSH. Data on times of first and last exposure were also incomplete: time of first and last exposure were missing for 78 (83%) and 65 (69%) out of 94 subjects. Variations in viral load may explain the wide range of infectiousness observed across patients and across outbreaks. Fluctuations in viral load and shedding during the clinical course may be associated with varying infectiousness during the clinical course of SARS. However, we encountered difficulty in our study with obtaining precise exposure history from subjects, some of whom had tended more than one patient, and all of whom had imperfect recall of an extremely stressful period. We felt this would have limited the value of any analysis of transmission risk by time of illness of the source patient or time of exposure of the contact patient. Although we analysed for differences in risk between long and short exposure durations and small and large distances from source, the failure to detect any effect is not surprising given the undoubted subjectivity and imprecision with which study subjects generally estimate time and distance.

It is unlikely that ORs of this magnitude could result primarily from recall bias relating to protective measures. Given the climate of anxiety and uncertainty that prevailed, it is likely that performance of risky procedures and omissions of PPE would have been equally salient to both cases and the controls. Moreover, the study was conducted almost contemporaneously with the outbreak, whereas confirmatory serology was only available later, thus minimizing the information bias to which retrospective studies are otherwise susceptible.

In this study, a history of contact with respiratory secretions from an infected patient was associated with a 22-fold increased odds of infection for the attending HCW. Hand washing after attending patients was found to be strongly protective with a 15-fold amelioration of odds. The finding that wearing of gloves and gowns separately halved the odds of infection in univariate analysis yet failed to achieve statistical significance in multivariate analysis may be attributed to insufficient sample size. We also believe that, whereas this study accepted at face value subject responses on donning gloves and gowns, there exists broad variation in actual compliance to proper infection control technique, which we were unable to

elucidate in this study. In the study by Seto et al. in Hong Kong [18], protection from gloves also failed to achieve statistical significance, but both gowns and hand washing were found to be protective. Much emphasis is presently given to droplet spread as the principal route of transmission for SARS, and to droplet precautions as the main protective measure. This study provides evidence for contact, both direct and indirect, with respiratory secretions or body fluids, as an additional major risk factor in the hospital setting. While the wearing of gloves and gowns should not be downplayed, this is a timely reminder of the importance of hand washing, as espoused by Semmelweis in the 19th century [21], albeit this time with the focus shifted to self-protection.

Consistent with the finding of the Hong Kong study, we found that wearing a mask was associated with a ten-fold lower odds of SARS. Although the local recommendation was for N95 use, this finding may simply attest to its effectiveness as a barrier to droplet spread rather than to the importance of airborne spread. Prolonged aerosol-generating procedures such as nebulization were not performed for any of the index cases, and there was no significant difference in the distribution of suctioning, intubation and oxygen administration between cases and controls. Within our study, given the 15-fold protective effect observed for hand washing, an OR of 0.1 seems almost negligible. However, this estimate of effect is not very different from the Hong Kong study, where failure to wear a mask was associated with an increased OR for SARS of 13.

Given that the index cases in Singapore were ethnic Chinese who had travelled to Hong Kong, the slightly higher odds of SARS we observed for Chinese over non-Chinese HCWs is most plausibly attributed to the tendency of patients to seek to communicate in their mother tongue, rather than to any genetic predisposition.

In summary, these results provide confirmation that personal protective measures against droplet spread and contact with body fluids are effective against the nosocomial spread of SARS. Although SARS is viewed as being primarily spread by droplet transmission, this study additionally provides evidence that direct and indirect contact with respiratory and body fluids of patients is also an important, if underrated, risk factor. It provides a timely reminder of the importance of the long-advocated but oft-neglected practice of hand washing between patient encounters.

ACKNOWLEDGEMENTS

The authors thank Nursing Officer Molly Wee, Staff Nurse Ai Kiau Soh and Mrs Phyllis Chew from the Department of Clinical Epidemiology, Tan Tock Seng Hospital, for their dedicated efforts in conducting the interviews.

REFERENCES

1. World Health Organization. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Geneva: World Health Organization, 26 September 2003 (http://www.who.int/csr/sars/country/table2003_09_23/en/). Accessed January 2004.
2. Ksiazek TG, Erdman D, Goldsmith CS, et al. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003; **348**: 1953–1966.
3. Drosten C, Gunther S, Preiser W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 2003; **348**: 1967–1976.
4. Peiris and colleagues. Novel coronavirus and severe acute respiratory syndrome. *Lancet* 2003; **361**: 1312–1314.
5. Chin JS (ed.). Control of communicable diseases in man, 17th edn. Washington, DC: American Public Health Association, 2000.
6. CDC. Guidelines for isolation precautions in hospitals. Atlanta, GA: Centers for Disease Control and Prevention, 1997 (<http://www.cdc.gov/ncidod/hip/ISOLAT/Isolat.htm>). Accessed January 2004.
7. WHO. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). Geneva: World Health Organization, 2003 (<http://www.who.int/csr/sars/en/WHOconsensus.pdf>). Accessed January 2003.
8. WHO environmental health team report on Amoy Gardens (<http://www.info.gov.hk/info/ap/who-amoye.pdf>). Accessed May 2004.
9. Park BJ, Peck AJ, Kuehnert J, et al. Lack of SARS transmission among healthcare workers, United States. *Emerg Infect Dis* 2004; **10**: 244–248.
10. Giesecke J. Modern infectious disease epidemiology, 2nd edn. Stockholm: Arnold, 2002.
11. Anderson RM, May RM. Infectious diseases of humans: dynamics and control. Oxford: Oxford, 1991.
12. Hill AN, Longini IM. The critical vaccination fraction for heterogeneous epidemic models. *Math Biosci* 2003; **181**: 85–106.
13. Bonabeau E, Toubiana L, Flahault A. The geographical spread of influenza. *Proc R Soc Lond B* 1998; **265**: 2421–2425.
14. Ministry of Health, Singapore. Information for healthcare professionals. Singapore: Ministry of Health, 2003 (www.moh.gov.sg/sars/information/healthcare.html#epidemiology). Accessed January 2004.

15. Cable News Network. Canada: SARS knows no boundaries, April 2003 (<http://edition.cnn.com/2003/HEALTH/04/22/sars.canada/>). Accessed January 2004.
16. WHO. Dr Carlo Urbani of the World Health Organization dies of SARS. Geneva: World Health Organization, 2003 (<http://www.who.int/mediacentre/notes/2003/np6/en/>). Accessed January 2004.
17. Ministry of Health, Singapore. MOH SARS press releases. Singapore: Ministry of Health, 2003 (http://app.moh.gov.sg/sars/news/update_details.asp?id=1&mid=6580). Accessed January 2004.
18. Seto WH, Tsang D, Yung RWH, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003; **361**: 1519–1520.
19. CDC. NIOSH guide to the selection and use of particulate respirators certified under 42 CFR 84. Atlanta, GA: Centers for Disease Control and Prevention, 1996 (<http://www.cdc.gov/niosh/userguid.html>). Accessed January 2004.
20. WHO. Case definitions for surveillance of severe acute respiratory syndrome (SARS). Geneva: World Health Organization, 2003 (<http://www.who.int/csr/sars/case-definition/en/>). Accessed January 2004.
21. Daniels IR. Historical perspectives on health. Semmelweis: a lesson to relearn? *J R Soc Health* 1998; **118**: 367–370.

Risk Factors for SARS Transmission from Patients Requiring Intubation: A Multicentre Investigation in Toronto, Canada

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Abstract

Background: In the 2003 Toronto SARS outbreak, SARS-CoV was transmitted in hospitals despite adherence to infection control procedures. Considerable controversy resulted regarding which procedures and behaviours were associated with the greatest risk of SARS-CoV transmission.

Methods: A retrospective cohort study was conducted to identify risk factors for transmission of SARS-CoV during intubation from laboratory confirmed SARS patients to HCWs involved in their care. All SARS patients requiring intubation during the Toronto outbreak were identified. All HCWs who provided care to intubated SARS patients during treatment or transportation and who entered a patient room or had direct patient contact from 24 hours before to 4 hours after intubation were eligible for this study. Data was collected on patients by chart review and on HCWs by interviewer-administered questionnaire. Generalized estimating equation (GEE) logistic regression models and classification and regression trees (CART) were used to identify risk factors for SARS transmission.

Results: 45 laboratory-confirmed intubated SARS patients were identified. Of the 697 HCWs involved in their care, 624 (90%) participated in the study. SARS-CoV was transmitted to 26 HCWs from 7 patients; 21 HCWs were infected by 3 patients. In multivariate GEE logistic regression models, presence in the room during fiberoptic intubation (OR = 2.79, $p = .004$) or ECG (OR = 3.52, $p = .002$), unprotected eye contact with secretions (OR = 7.34, $p = .001$), patient APACHE II score ≥ 20 (OR = 17.05, $p = .009$) and patient $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 59 (OR = 8.65, $p = .001$) were associated with increased risk of transmission of SARS-CoV. In CART analyses, the four covariates which explained the greatest amount of variation in SARS-CoV transmission were covariates representing individual patients.

Conclusion: Close contact with the airway of severely ill patients and failure of infection control practices to prevent exposure to respiratory secretions were associated with transmission of SARS-CoV. Rates of transmission of SARS-CoV varied widely among patients.

Citation: Raboud J, Shigayeva A, McGeer A, Bontovics E, Chapman M, et al. (2010) Risk Factors for SARS Transmission from Patients Requiring Intubation: A Multicentre Investigation in Toronto, Canada. PLoS ONE 5(5): e10717. doi:10.1371/journal.pone.0010717

Editor: Joel Mark Montgomery, U.S. Naval Medical Research Center Detachment/Centers for Disease Control, United States of America

Received: March 11, 2009; **Accepted:** April 19, 2010; **Published:** May 19, 2010

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Funding: This research was funded by a contract from the Ontario Ministry of Health and Long Term Care. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

On March 7, 2003, a son of Canada's index SARS case was admitted to a hospital in Toronto with a diagnosis of community-acquired pneumonia. Because he and other family members were not identified as infected with SARS CoV until March 13,

infection was transmitted to patients, volunteers, visitors and health care workers in this community hospital, and subsequently in other hospitals and the community throughout Greater Toronto Area (GTA). Over the next three months, SARS-CoV would be transmitted to 375 persons in Toronto, 271 (72%) of whom acquired their infections in health care settings.[1–3] The

healthcare workers at greatest risk of acquiring SARS were those caring for critically ill SARS patients, and transmission was documented despite the use of recommended personal protective equipment. [3–7]

During and after the outbreak, considerable controversy evolved regarding how HCWs using precautions became infected, and what care activities and/or behaviours posed the greatest risk of transmission. We conducted a retrospective cohort study designed to identify risk factors associated with transmission of SARS-CoV from patients requiring intubation to HCWs involved in their care. In particular, we wanted to assess the risk of SARS-CoV transmission associated with adherence to infection control precautions and with performance of “high-risk” procedures in a setting in which adjustment for potential patient-related characteristics was possible.

Methods

Ethics Statement

Patient clinical details were obtained through review of health records which was conducted for a study of clinical presentation and management of SARS. The study was approved by the IRB of each hospital where patients were treated. Individual consents were not obtained which is the practice for chart review studies in which individual patient identifying information is not required. All patients in the SARS outbreak were given a unique identifying number and all data were coded with this unique number. There was no information collected that could identify the patient personally.

HCWs blood samples were obtained through a seroprevalence study, which was part of the public health investigation and received IRB approval at each hospital where HCWs were enrolled. HCWs provided consent for blood samples.

Approvals for both studies were obtained from The Mount Sinai Hospital Research Ethics Board as well as the Research Ethics Boards/Committees of the following institutions: Sunnybrook Health Center, North York General Hospital, The Scarborough Hospital, Rouge Valley Health Care, Humber River Regional Hospital, Markham Stouffville Hospital, St. Michael's Hospital, St. Joseph's Health Center, Southlake Regional Health Center, Toronto East General Hospital, University Health Center, and Lakeridge Health Center.

HCWs were interviewed as part of a public health investigation into the transmission of SARS-CoV. HCWs were invited to participate and consent was implied by willingness of HCWs to be interviewed about their experiences. No IRB approval was required as these interviews occurred as part of the public health outbreak investigation which is a legislated responsibility of the Ontario public health units.

Identification and Classification of Patients and HCWs

Patients. SARS patients requiring intubation were identified by reviewing outbreak line lists from the Province of Ontario, local public health units, and hospitals. All cases in the Toronto outbreak who met the clinical and epidemiologic criteria for SARS [8] and who required intubation were included. Clinical criteria for SARS included fever $>38^{\circ}\text{C}$, one or more respiratory symptoms, radiological evidence of pneumonia or respiratory distress syndrome and no alternative diagnosis; or having an unexplained acute respiratory illness resulting in death between March 5, 2003 and June 12, 2003. [8] Epidemiological criteria included: visiting a setting that was associated with a SARS cluster or having cared for, lived with or had face-to-face contact with a person known to have SARS in the 10 days prior to onset of symptoms.

All patients in whom SARS was suspected had multiple clinical specimens tested by culture and PCR for SARS-CoV, including nasal swabs, nasopharyngeal swabs, throat swabs, sputum/endotracheal secretions, conjunctival swabs, stool, urine and, if available, bronchoalveolar lavage and post-mortem lung and other tissue samples. [9] If possible, acute and convalescent serum were also obtained. Patients were classified as laboratory confirmed, probable, unclassifiable or not a case of SARS-associated coronavirus (CoV) disease, based on laboratory testing. Laboratory confirmed cases were those with SARS-CoV antibodies detected in serum obtained after the onset of symptoms by tests conducted in two different reference laboratories, SARS CoV isolated by cell culture from a clinical and/or autopsy specimen, SARS-CoV RNA detected by reverse transcription polymerase chain reaction (RT-PCR) from an autopsy specimen with compatible histological findings, or SARS-CoV RNA detected by RT-PCR from at least two different specimens by two different reference laboratories. [9] Probable cases were those in whom a convalescent serum specimen was not available for testing and other laboratory criteria for SARS were not met, but who had clinically compatible disease and at least one household contact who was a laboratory confirmed case of SARS. Cases were unclassifiable if they did not meet criteria for laboratory confirmed disease, and either had no household contacts, or contacts without laboratory confirmed disease. Patients were classified as not having SARS if antibodies to SARS-CoV could not be detected in serum obtained more than 28 days after symptom onset.

HCWs. All HCWs who provided care to intubated SARS patients during treatment or transportation, or who entered the room of such patients from 24 hours prior to intubation until 4 hours after intubation were eligible for this study, and approached for consent to participate. They were identified by review of patient charts, work schedules, assignments and on-call schedules, and by asking individuals being interviewed to recall which other staff members were present.

We reviewed outbreak line lists and interviewed HCWs to identify those with fever or respiratory symptoms with onset from 1 to 14 days after each work shift with identified patients. Participating HCWs were also asked to submit a convalescent serum sample for SARS-CoV antibody testing. HCWs were classified as SARS if they had antibodies to SARS-CoV detected in their convalescent serum, or if they met the SARS outbreak case definition [8] and did not have serology performed. They were classified as not having SARS if they had negative serology or if they did not have serology done and had no fever or respiratory symptoms. They were deemed unclassifiable if they had SARS compatible symptoms that did not meet the case definition and convalescent serology was not available.

Staff were asked about their history of travel to areas affected by SARS, care provided to any possible SARS patients, and household and other contact with potential SARS cases, including other HCWs. For symptomatic HCWs, we recorded potential exposures in the period from 24 hours to 12 days before onset of illness using outbreak contact tracing data, interviews and work assignments. For HCWs who were SARS-CoV seropositive without symptoms, we reviewed all potential exposures which occurred during the outbreak period.

A high risk exposure to SARS was defined as being in the same room as or involved in the transport of a SARS patient either during the 24 hours prior to the patient requiring intubation, or at any time when adequate precautions had not been implemented. Adequate precautions were defined as the patient being in a negative pressure room and gown, gloves, mask (surgical mask or, N95 or higher respirator) and eye protection (goggles, safety glasses or face shield) being worn.

Cohorts for analysis. The primary analysis was restricted to patients with laboratory-confirmed SARS, and HCWs who were either asymptomatic or had laboratory confirmed disease and whose only high risk exposure was contact with intubated patients. A secondary analysis included probable and laboratory confirmed SARS patients and all infected HCWs. Because there were no significant differences between the two analyses, only the results of the primary analysis are presented here.

Measurements

Patients. A standardized data collection form was used for chart review, and included: age, sex, underlying chronic conditions, date of symptom onset, duration of illness at the time of intubation, date of hospital and ICU admission, date of discharge, outcome; documented vomiting, diarrhea, incontinence, agitation, and combativeness during the 24 hours prior to intubation, acute physiology and chronic health evaluation II score during the same period (APACHE II) [10], lowest PaO_2 to FiO_2 (P/F ratio) ratio during the first 24 hours in the ICU and maximum inspired oxygen requirement (FiO_2) on the second day of hospital admission. We also recorded whether attending physicians suspected that the patient had SARS at the time of intubation.

Details of the intubation procedures were obtained from medical records and interviews with the staff member who performed the intubation. These included: method of intubation (fiber optic, laryngoscopic, nasopharyngeal, or tracheotomy), patient combativeness, number of attempts required, experience of person performing the procedure, and whether manual intubation was required before and/or after intubation. Intubations were classified as difficult if more than one attempt was required, if fiber optic visualization or any adjuvant device for difficult airway was required, or if the patient was combative. HCWs performing intubations were considered experienced if they had more than three years of experience and performed more than one intubation per month, or if they had more than one year of experience and performed more than one intubation per week.

Procedures and activities performed during the defined exposure period were documented. These included: airway management procedures (oxygen therapy, bronchoscopy, non-invasive positive pressure ventilation, manual ventilation, suctioning, type of mechanical ventilation, nebulizer treatment) and cardiopulmonary resuscitation and defibrillation and other care activities (chest x-ray; electrocardiogram; chest tube insertion; insertion of central venous, peripheral or arterial catheters; insertion of urinary catheter or nasogastric tube; collection of blood, urine, stool, or sputum samples).

HCWs. A structured questionnaire was administered to HCWs through a face-to-face interview or by telephone interview if a respondent was in quarantine or had left their job. HCWs were asked about occupation, years of experience in their current occupation, age, sex, history of smoking and underlying chronic conditions.

All non-demographic variables were assessed separately for each eligible shift. An eligible shift was defined as one in which a HCW provided care for one patient during that patient's defined exposure period. When HCWs worked two shifts during one exposure period, data from these two shifts were combined for the analysis.

For each shift, questions were asked about the number of room entries, cumulative time spent in a patient room, and type and duration of contact with a patient. We also assessed level of involvement (performed, assisted or observed) in and the amount of time the HCW spent in the patient's room during 34 patient care activities, as well as the HCW's presence in the patient's room

while the patient was receiving non-invasive ventilation, oxygen therapy, and mechanical ventilation. Copies of charts were provided to interviewees to assist in recall.

Type of personal protection equipment (PPE) -gloves, gown, goggles or face shield, surgical mask, N95 or higher respirator, and frequency of its use (never, sometimes, most of the time and always) during the shift were assessed. We also asked about PPE use separately during involvement in patient care activities and categorized HCWs' sequence of removal of PPE based on the potential risk of self-contamination of mucous membranes. [11]

Participants were asked whether they had received SARS-specific infection control training prior to their eligible shift. Infection control training was categorized as active (face-to-face teaching) or passive (written instructions only). Exposure incidents that occurred during the eligible shift were recorded, including needle stick injuries and exposure of skin or mucous membranes to patient's body fluids, blood, secretions or mucous membranes.

Laboratory tests. Laboratory testing was conducted in collaboration with the Ontario Laboratory Working Group for the Rapid Diagnosis of Emerging Diseases, the Central Ontario Public Health Laboratory, the SARS autopsy investigation, the British Columbia Centre for Disease Control, and the Canadian National Microbiology Laboratory. Detection of IgG antibody to SARS-CoV was performed by using an enzyme-linked immunosorbent assay (ELISA) or immunofluorescent assay (IFA) as previously described. [9]

Statistical Methods

Demographic and clinical characteristics were summarized with counts and percentages for categorical variables and with medians and interquartile ranges for ordinal and continuous variables. These characteristics were compared between patients who did and did not transmit SARS-CoV and between HCWs who did and did not develop SARS with chi square or Fisher's exact tests for categorical variables and Wilcoxon rank sum tests for ordinal and continuous variables.

Two statistical methods were used to identify factors associated with SARS-CoV transmission: Classification and regression trees (CART) [12] and Generalized Estimating Equation (GEE) models. [13] CART is a non-parametric method of identifying predictor variables by using binary recursive partitioning: subsets of patients are formed by examining each possible cut point of each variable to identify the cut point that resulted in maximum discrimination between subgroups of patients with respect to the probability of acquiring SARS. CART analyses were conducted twice: with and without allowing patient specific covariates to be predictor variables.

GEE logistic regression models were used to identify predictor variables while adjusting for correlation among responses from HCWs caring for the same patient. Correlation within HCW shifts caring for a single patient was assumed to follow the exchangeable correlation structure. Correlation among shifts worked by the same HCW was not modeled. Covariates which had a p value <0.10 in univariate GEE logistic regression models were considered as candidates for entry into the multivariable GEE model.

Results

Fifty-six (15%) of 360 SARS patients who received treatment in one of 20 Ontario hospitals required intubation. Eleven patients were excluded from the primary analysis: seven had probable SARS, one patient was unclassifiable and three patients had at

least one specimen positive by PCR, but did not have detectable antibodies to SARS CoV at ≥ 28 days after symptom onset. Thus, 45 patients were classified as having laboratory confirmed SARS and were included in the primary analysis as potential index cases for the exposed HCWs.

Overall, 624 (90%) of 697 HCWs who were identified as having provided care to the 45 laboratory confirmed SARS patients consented to participate, could be classified as having had SARS or not, and had no other high risk exposures. They worked a total of 786 eligible shifts. Interviews were completed at a median of 4.2 months (range 0.2–10 months) after the eligible shift. 111 (17.8%) HCWs were involved in the care of more than one intubated SARS patient, with a maximum of 8 eligible patients cared for by the same HCW. The median number of participating HCWs involved in the care of each SARS patient during the relevant time period (24 hours prior to intubation until 4 hours post-intubation) was 15 (range 6 to 30).

Of the 624 participating HCWs, 26 contracted SARS; all survived and none required intubation. SARS-CoV transmission to HCWs was attributable to 7 of the 45 laboratory confirmed SARS patients. Transmission to 22 HCWs could be definitively

attributed to a single patient, with 6 patients transmitting to 1, 1, 2, 5, 6 and 7 HCWs respectively. The remaining four HCWs who acquired SARS had cared for more than one SARS patient during the high risk period, making it difficult to precisely identify which patient was the source of infection. For the primary analysis, we assumed a 'most likely scenario' for assigning transmission to one patient. Three of the infected staff members cared for two patients whose intubations were a few hours apart. Since one patient was the source of infection for five other individuals; we assumed in the primary analysis that this patient had also transmitted SARS-CoV to these 3 HCWs. The fourth HCW was involved in the care of two intubated patients; transmission was assumed to have occurred on the shift that involved emergency intubation and cardiac resuscitation.

No patient characteristics were statistically significantly different between patients who did and did not transmit SARS-CoV (Table 1). HCWs who contracted SARS were more likely to be paramedics ($p < .01$) and had less infection control training ($p < .009$) than other workers (Table 2). They were less likely to always wear goggles ($p < 0.01$) or a gown ($p = .02$) while in the patient's room, and more likely to have used less effective methods

Table 1. Demographic and clinical characteristics of SARS patients requiring intubation in the Toronto outbreak by presence or absence of transmission to HCWs.

	No Transmission of SARS to HCWs N = 38	SARS Transmission to at least one HCW N = 7	p value	All N = 45
Patient Characteristics at Admission				
Age, years ^a	59 (45, 72)	63 (47, 75)	0.64	61 (47, 72)
Sex, number (%) male	17(45%)	5 (71%)	0.24 ^b	22 (49%)
Chronic underlying illness ^c	15(39%)	3(43%)	0.99 ^b	18 (40%)
Diabetes	12(32%)	3(43%)	0.67 ^b	15(33%)
Immunosuppression	3(8%)	1(14%)	0.50 ^b	4(9%)
PaO ₂ /FiO ₂ ratio ^a	84 (67, 116)	85 (51, 112)	0.64	84 (59, 112)
FiO ₂ on day 2 of hospitalization ^a	0.38 (0, 0.95)	0.4 (0, 1)	0.78	0.4 (0, 0.95)
Apache II score (1 st 24 h ICU) ^a	16 (14, 20)	21 (11, 22)	0.20	16 (14,21)
Patient transmitted SARS prior ^d	15(39%)	4(57%)	0.43 ^b	19 (42%)
Patient Characteristics at Intubation				
Day of illness at time of intubation ^a	9(7, 13)	7(7, 9)	0.20	9(7, 12)
Diarrhea 24 hours prior to intubation	18(47%)	1(14%)	0.21 ^b	19 (42%)
Vomiting 24 hours prior to intubation	7(18%)	1(14%)	0.99 ^b	8(18%)
Copious secretions at intubation	14(37%)	1(14%)	0.40 ^b	15(33%)
Combative during intubation	7(18%)	1(14%)	0.99 ^b	8(18%)
Intubated in negative pressure room	33(87%)	6(86%)	0.99 ^b	39(87%)
Patient recognized as SARS at time of intubation	33 (87%)	6(86%)	0.99 ^b	39 (87%)
Characteristics of Intubation				
Intubation difficult	12(32%)	3(43%)	0.67 ^b	15(33%)
Intubation performed during night shift	7(18%)	1(14%)	0.99 ^b	8(18%)
Primary intubator experienced	32(84%)	6(86%)	0.99 ^b	38(84%)
Intubation emergent	0(0%)	1(14%)	0.16 ^b	1(2%)
Patient Outcome				
Deceased	18 (47%)	5 (71%)	0.40 ^b	23 (51%)

^aValues are given as median (lower quartile, upper quartile).

^bFisher's exact test.

^cChronic underlying illness is defined as having one or more of diabetes, chronic renal failure, chronic liver disease, chronic obstructive pulmonary syndrome, coronary artery disease, congestive heart failure, active cancer, HIV/AIDS, transplantation.

^dTransmission occurred from patient to household or hospital contact prior to study period (starting 24 hours prior to intubation).

doi:10.1371/journal.pone.0010717.t001

Table 2. Characteristics of health care workers who provided care to intubated SARS patients in Toronto, by SARS acquisition status.

	HCWs who did not develop SARS N = 598	HCWs who developed SARS N = 26	p value	All N = 624
Age, years ^a	40 (34, 48)	38.5 (33, 44)	0.21	40 (34, 47)
Sex, number (%) male	145 (24%)	10 (38%)	0.10	155 (25%)
Had chronic disease ^b (N = 609)	36 (6%)	1 (4%)	0.99 ^c	37 (6%)
Position	73 (12%)	4 (15%)	0.55 ^c	77 (12%)
Staff physician	14 (2%)	2 (8%)	0.14 ^c	16 (3%)
Medical resident/intern	272 (45%)	11 (42%)	0.75	283 (45%)
Registered nurse	85 (14%)	4 (15%)	0.78 ^c	89 (14%)
Respiratory therapist	66 (11%)	1 (4%)	0.34 ^c	67 (11%)
Radiology technologist	38 (6%)	0 (0%)	0.39 ^c	38 (6%)
Housekeeper	25 (4%)	1 (4%)	0.99 ^c	26 (4%)
Personal service assistant	14 (2%)	0 (0%)	0.99 ^c	14 (2%)
Laboratory technician/technologist	0 (0%)	3 (12%)	<0.01 ^c	3 (0.5%)
Paramedic/emergency medical technician	2 (0.3%)	0 (0%)	0.99 ^c	2 (0.3%)
Pharmacist	2 (0.3%)	0 (0%)	0.99 ^c	2 (0.3%)
Ward clerk	2 (0.3%)	0 (0%)	0.99 ^c	2 (0.3%)
Porter	1 (0.2%)	0 (0%)	0.99 ^c	1 (0.2%)
Physiotherapist/occupational therapist	4 (0.7%)	0 (0%)	0.99 ^c	4 (0.6%)
Other				
Total hours worked in 7 days prior to study period ^a (N = 565)	37.5(32, 48) (N = 545)	40(36, 55) (N = 20)	0.15	38(32, 48)
Always wore goggles while in patient room	451(75%)	13(50%)	<0.01	464 (74%)
Always wore gloves while in patient room	555 (93%)	23 (88%)	0.43 ^c	578 (93%)
Always wore gown while in patient room	541 (90%)	20 (77%)	0.04 ^c	561 (90%)
Respiratory protection while in patient room	49 (8%)	3 (12%)	0.04 ^d	52 (8%)
➤ None	25 (4%)	5 (19%)		30 (5%)
➤ Surgical mask	496 (83%)	18 (69%)		514 (82%)
➤ N95 or equivalent	28 (5%)	0 (0%)		28 (4%)
➤ Higher protection than N95 (e.g., N95 plus Stryker hood, PAPRs)				
Personal protective equipment removal ^e	41 (7%)	3 (12%)	0.56 ^d	44 (7%)
➤ None used	192 (32%)	11 (42%)		203 (33%)
➤ No hand hygiene performed	290 (48%)	8 (31%)		298 (48%)
➤ No hand hygiene before removing face protection, hand hygiene at the end	14 (2%)	0 (0%)		14 (2%)
➤ Hand hygiene before removing face protection, no hand hygiene at the end	61 (10%)	4 (15%)		65 (10%)
➤ Hand hygiene before removing face protection, plus hand hygiene at the end				
Infection control training	173 (29%)	16 (62%)	0.009 ^d	189 (30%)
➤ None	9 (2%)	0 (0%)		9 (1%)
➤ Other (information from colleagues)	136 (23%)	2 (8%)		138 (22%)
➤ Email or written instructions	127 (21%)	2(8%)		129 (21%)
➤ Group sessions	153 (26%)	6 (23%)		159 (25%)
➤ Individual face to face instruction				

^aValues are given as median (lower quartile, upper quartile).^bChronic underlying illness is defined as having one or more of diabetes, chronic renal failure, chronic liver disease, chronic obstructive pulmonary syndrome, coronary artery disease, congestive heart failure, active cancer, HIV/AIDS, transplantation.^cFisher's exact test.^dCochran-Armitage test for trend.^esee reference 11.

doi:10.1371/journal.pone.0010717.t002

of respiratory protection while in a patient's room ($p = .04$). They were more likely to have participated in administering non-invasive ventilation ($p < 0.01$), and to have performed ECGs ($p < 0.01$), fiber optic intubation ($p < 0.01$) or manual ventilation before intubation ($p < 0.01$) than HCWs who did not develop SARS (Table 3).

In the CART analysis allowing individual patients to be entered as covariates, patient covariates were the top four splitting variables according to the deviance at each node (Figure 1). Twenty-three of the 26 HCWs who acquired SARS were involved in the care of one of these four patients. The results of this analysis

did not change when only HCWs with exposures to single patients were considered, or when we altered the assumptions regarding which patient infected the four HCWs with exposures to two patients. If patients were not included as predictor variables (Figure 2), then the first splitting variable was whether the patient P/F ratio was >35.5 or <35.5 (3% vs 42% contracted SARS). Among the 605 HCWs involved in the care of patients with P/F ratio >35.5 , the most predictive variable was whether or not the HCW wore eye protection (1% of HCWs infected wearing eye protection vs 8% infected not using eye protection). It should be noted that the single patient with P/F ratio <35.5 was the patient

Table 3. HCW participation in patient care procedures, by SARS acquisition status.

	HCWs who did not develop SARS N = 598	HCWs who developed SARS N = 26	p value	All N = 624
Potential HCW exposure to respiratory secretions^a				
Non-invasive ventilation	99 (17%)	10 (38%)	<0.01	109 (17%)
High flow oxygen	106 (18%)	2 (8%)	0.29 ^b	108 (17%)
Mechanical ventilation	227 (38%)	9 (35%)	.73	236 (38%)
HCW involvement in intubation^a				
Intubation (including fiber optic intubation)	132 (22%)	12 (46%)	<0.01	144 (23%)
Suctioning before intubation	106 (18%)	7 (27%)	0.29 ^b	113 (18%)
Suctioning after intubation	155 (26%)	10 (38%)	0.16	165 (26%)
Manual ventilation before intubation	108 (18%)	10 (38%)	0.02 ^b	118 (19%)
Manual ventilation after intubation	114 (19%)	6 (23%)	0.61	120 (19%)
Procedures with potential exposure to respiratory secretions^a				
Cardiac compressions	8 (1%)	1 (4%)	0.32 ^b	9 (1%)
Bronchoscopy	10 (2%)	0 (0%)	0.99 ^b	10 (2%)
Chest physiotherapy	47 (8%)	1 (4%)	0.71 ^b	48 (8%)
Defibrillation	3 (1%)	1 (4%)	0.15 ^b	4 (1%)
Collection of sputum sample	38 (6%)	4 (15%)	0.09 ^b	42 (7%)
Nebulizer treatment	9 (2%)	0 (0%)	0.99 ^b	9 (1%)
Manipulation of oxygen mask	280 (47%)	17 (65%)	0.06	297 (48%)
Insertion of NG tube	45 (8%)	2 (8%)	0.99 ^b	47 (8%)
Procedures with potential exposure to stool or urine^a				
Collection of stool sample	17 (3%)	2 (8%)	0.19 ^b	19 (3%)
Emptying urine bag or taking urine sample	137 (23%)	4 (15%)	0.37	141 (23%)
Emptying bed pan	48 (8%)	1 (4%)	0.71 ^b	49 (8%)
Other procedures^a				
Insertion of central venous line	53 (9%)	3 (12%)	0.72 ^b	56 (9%)
Insertion of urinary catheter	38 (6%)	3 (12%)	0.24 ^b	41 (7%)
Insertion of peripheral IV access line	138 (23%)	7 (27%)	0.65	145 (23%)
Venipuncture/arterial blood gas	160 (27%)	7 (27%)	0.99	167 (27%)
Chest tube insertion	12 (2%)	0 (0%)	0.99 ^b	12 (2%)
ECG	98 (16%)	11 (42%)	<0.01 ^b	109 (17%)
Bathing a patient	133 (22%)	4 (15%)	0.41	137 (22%)
Feeding a patient	87 (15%)	1 (4%)	0.16 ^b	88 (14%)
Transporting a patient	93 (16%)	7 (27%)	0.17 ^b	100 (16%)
Taking oral temperature	71 (12%)	2 (8%)	0.76 ^b	73 (12%)
Administering oral medication	111 (19%)	3 (12%)	0.45 ^b	114 (18%)
Housekeeping activities^a				
Cleaning equipment	150(25%)	7(27%)	0.83	157 (25%)
Cleaning room	81(14%)	2(8%)	0.56 ^b	83 (13%)
Cleaning bathroom	41(7%)	1(4%)	0.99 ^b	42 (7%)
Changing bedding	171(29%)	7(27%)	0.85	178 (29%)

^aFor these potential risk factors, health care workers were considered exposed if they reported being in the room while the patient was receiving the therapy.

^bFisher's exact test.

doi:10.1371/journal.pone.0010717.t003

who was the first splitting variable in the CART analysis with individual patients included.

In univariate GEE models (Table S1), patient characteristics associated with transmitting SARS-CoV were: P/F ratio ≤ 59 , gender, death due to SARS, APACHE II score ≥ 20 , presence of diarrhea within 24 hours of intubation, any chronic underlying

illness disease, and diabetes mellitus (when underlying illnesses were considered separately). HCW characteristics associated with acquiring SARS included eye/mucous membrane exposure to blood/body fluids, performing intubation, and presence in the room for any of cardiac compressions, defibrillation, ECG, intubation, manual ventilation, manipulation of oxygen mask or

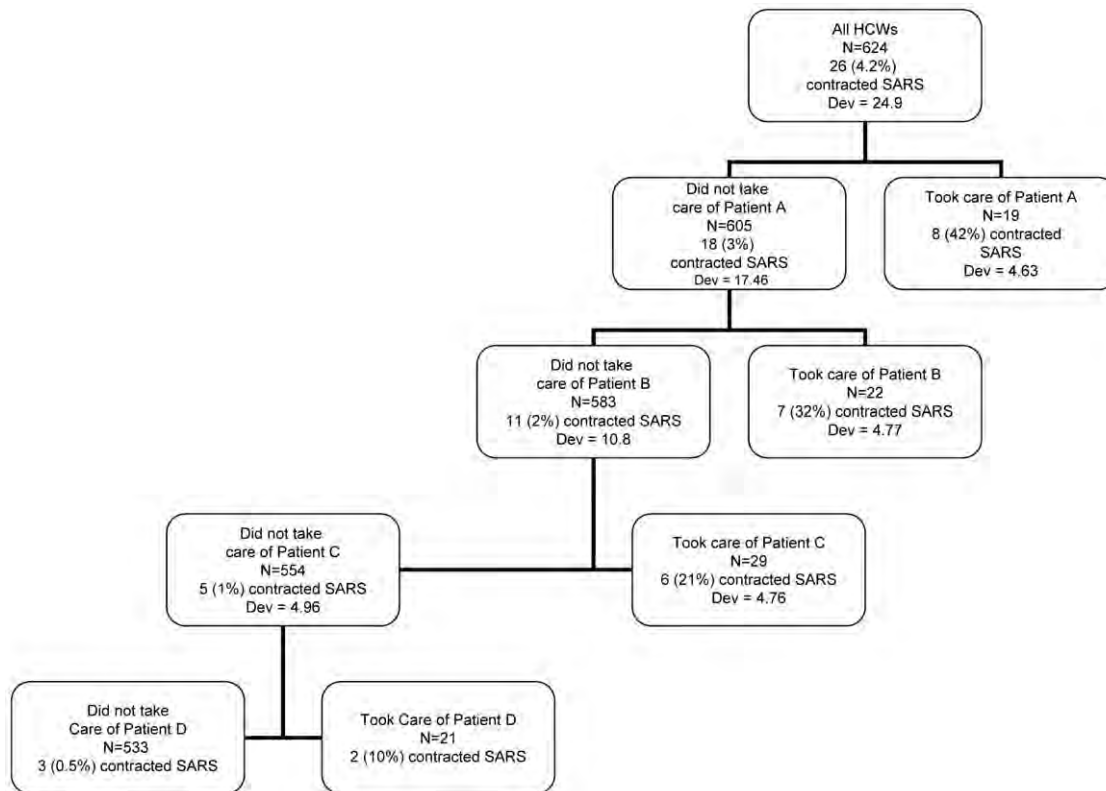


Figure 1. Classification and regression tree analysis of risk factors for SARS transmission, allowing patient-specific covariates.
doi:10.1371/journal.pone.0010717.g001

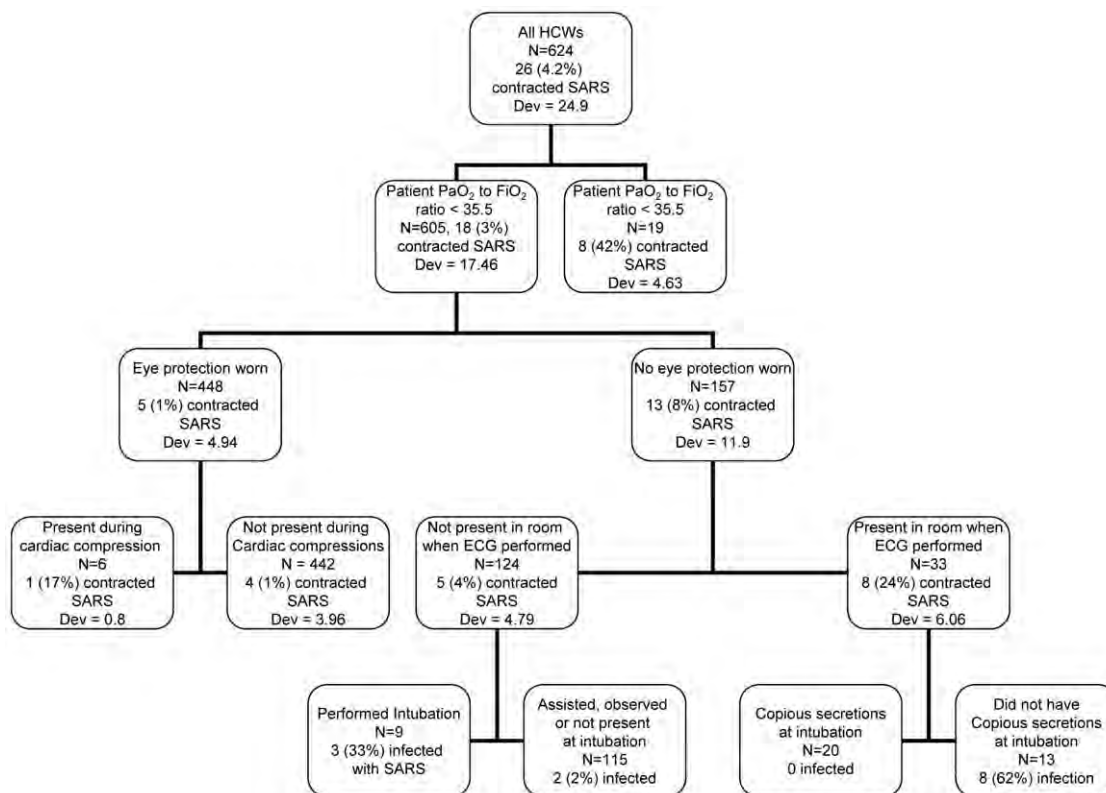


Figure 2. Classification and regression tree analysis of risk factors for SARS transmission, not allowing patient specific covariates.
doi:10.1371/journal.pone.0010717.g002

tubing, collection of sputum or stool samples, or transporting the patient. In the multivariate GEE logistic regression model (Table 4), the independent predictors were eye or mucous membrane exposure to body fluids (OR = 7.34, $p = .001$), patient APACHE II score ≥ 20 (OR = 17.05, $p = .0009$), patient P/F ratio ≤ 59 (OR = 8.65, $p = .001$), presence during ECG (OR = 3.52, $p = .002$), and presence during intubation OR = 2.79, $p = .004$).

Discussion

This study is the most detailed assessment to date of the risks of SARS acquisition associated with HCW involvement in medical procedures, their infection control practices and the demographic and clinical characteristics of SARS patients. [4–6,14–19] Amongst this group of HCWs caring for SARS patients immediately prior to and during intubation, the strongest predictor of SARS transmission from patient to HCW was whether or not the patient under care was a “superspreader”. Twenty-three of the 26 HCWs who became infected with SARS were infected by four of 45 patients. Lack of adherence to infection control procedures was also associated with transmission of SARS-CoV; however, individual patient characteristics beyond superspreader status were not.

The substantial heterogeneity in the number of secondary infections created by each case for many sexually transmitted and vector-borne diseases has led to the general rule that 20% of patients are associated with 80% of new cases. Although heterogeneity in individual patient transmission in diseases spread by direct contact and respiratory droplets is less well recognized, it has been clearly described for measles [20], rubella [21,22], *Staphylococcus aureus* [23], and tuberculosis [24–26], as well as for SARS-CoV in previous publications. [1,4,27–30] Understanding this heterogeneity is important, because modeling studies demonstrate that the models incorporating variability in transmission differ substantially from standard outbreak models, and, in these models, individually-targeted interventions are much more effective than untargeted interventions. [31,32] “Superspreading” appears to be a normal feature of disease transmission, and one that must be understood if we are to effectively prevent the spread of respiratory infection. The presence of heterogeneity in transmission also makes the interpretation of observational cohort data about risk factors for transmission difficult: our analysis illustrates the substantial potential impact of confounding in such cohorts. Observational cohort data may have very limited value for assessing transmission of influenza unless patient transmission heterogeneity can be taken into account.

Our findings with respect to HCW activity risk factors are similar to those of other studies assessing HCW risks unadjusted for patient factors, but illustrate the complexity of analyses of

cohort studies in these settings. [15–19] The factors associated with SARS in other analyses are somewhat different, but essentially all are related to procedures that bring workers into proximity with a patient’s airway for prolonged periods of time, or with unprotected faces. In keeping with data from Teleman et al. [16] our highest estimated HCW risk in GEE models was eye or mucous membrane exposure to body fluids (OR = 7.3), while in CART analysis, the primary HCW related risk factor was whether or not eye protection was worn. This should not be interpreted as meaning that conjunctival contact in particular is a primary mode of spread of SARS CoV: when exposure to droplet spray occurs, is it generally not possible to distinguish exposure to eyes versus other mucous membranes. Absence of eye protection results in exposure of facial skin, and transmission could subsequently be from facial skin to hand to other mucous membrane. It is also possible that absence of eye protection is a marker for reduced adherence to other precautionary measures for which adherence is not adequately captured by self-report.

The range of different types of healthcare providers infected emphasizes that healthcare worker safety is not an issue limited to one profession, or to those workers with less education or control over their workplace situation. The finding in our study and those of others that a relatively small amount of education was associated with significant increases in adherence to precautions and reductions in infection also highlights the fact that, at least in some situations, education alone is enough to provide significant safety benefits. [11,16] Where possible, hospital planners should consider building plans for “just-in-time” training into pandemic and outbreak responses.

CART and GEE logistic regression were complementary techniques for identifying HCW and patient characteristics most associated with transmission of SARS-CoV. Advantages of CART include the ability to identify interactions between variables by identifying specific combinations of variables which place HCWs at higher risk of acquiring SARS, modeling of nonlinear relationships between the dependent and independent variables, ability to handle numerical data that is highly skewed and categorical data with either ordinal or non-ordinal structures and its ease of interpretation. While logistic regression models are not as flexible in handling this variety of data, they yield odds ratios and p values, which are useful for quantifying risk and measuring the statistical significance of relationships between variables. The CART analyses were comparable with logistic regression GEE models with respect to sensitivity, specificity, and positive and negative predictive values.

There are several limitations to this study. Although we used patient charts to enhance recall, and validated our questionnaire [33,34], HCW recall of various exposures may have been imperfect due to the stress of caring for SARS patients and the

Table 4. Multivariate Generalized Estimating Equation logistic regression model of the probability of transmitting SARS from patient to health care worker.

Parameter	OR	95% CI	p value
HCW’s eye/mucous membranes exposed to body fluids	7.34	(2.19, 24.52)	.001
Patient APACHE II score ≥ 20	17.05	(3.20, 90.75)	.009
HCW present during ECG	3.52	(1.58, 7.86)	.002
HCW present during intubation	2.79	(1.40, 5.58)	.004
Patient PaO ₂ to FiO ₂ ratio ≤ 59	8.65	(2.31, 32.36)	.001

HCW = health care worker.

doi:10.1371/journal.pone.0010717.t004

time from exposure to interview, may have been biased by HCW outcomes, or may themselves have introduced biases if some were more accurate or complete than others. While our assumption that patients who were known to have infected other HCWs also infected the three HCWs whose source of infection was unclear had the potential to overestimate the superspreader phenomenon, secondary analyses confirmed our findings. While we might speculate that presence in the room during an ECG identified as a risk factor because other variables incompletely adjusted for duration of time in the room when a patient is deteriorating rapidly, we do not have a satisfactory explanation for why this variable is associated with SARS-CoV transmission. Finally, since the greatest risk of transmission of SARS-CoV occurred in the cohort of HCWs caring for the patient with the lowest PaO₂ to FiO₂ (P/F) ratio, the superspreader effect was confounded with the P/F ratio effect, and it is not possible to conclude that low patient P/F ratio is associated with SARS-CoV transmission.

Although some authors have assumed that all viral respiratory infections have the same relative modes of transmission, such that identified risk factors and/or interventions that prevent transmission for one can be assumed to be true for others [35], it is not clear that knowledge about risk factors for SARS coronavirus infection can be directly applied to other diseases such as influenza. It is clear, however, that, during the SARS outbreak, HCW exposures to body fluids occurred frequently and adherence to recommended precautions was often incomplete, putting

HCWs at significant risk of infection. Thus, research into the incidence of and risk factors for influenza transmission in acute care hospital settings, and into interventions effective in minimizing transmission, is urgently needed.

Supporting Information

Table S1 Univariate GEE logistic regression models of the probability of transmission of SARS from patient to HCW, for care provided from 24 hours before to four hours after intubation, Toronto, 2003.

Found at: doi:10.1371/journal.pone.0010717.s001 (0.23 MB DOC)

Acknowledgments

We are grateful to the many HCWs, patients and families whose collaboration made this research possible.

Author Contributions

Conceived and designed the experiments: AM EB MC DG BH SEL MBL LCM MO SP DR DS SS AS TES MV DZ KAG. Performed the experiments: AS AM BH DR DS MV KAG. Analyzed the data: JR AS AM BH LCM SS KAG. Wrote the paper: JR AS AM EB BH SEL MO SP DR DS AS TES MV. Obtained funding: DZ.

References

- Varia M, Wilson S, Sarwal S, McGeer A, Gournis E, et al. (2003) Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *CMAJ* 169: 285–92.
- Svoboda T, Henry B, Shulman L, Kennedy E, Rea E, et al. (2004) Public health measures to control the spread of the severe acute respiratory syndrome during the outbreak in Toronto. *N Engl J Med* 350: 2352–61.
- McDonald LC, Simor AE, Su JJ, Maloney S, Ofner M, et al. (2004) SARS in healthcare facilities, Toronto and Taiwan. *Emerg Infect Dis* 10: 777–81.
- Scales DC, Green K, Chan AK, Poutanen SM, Raboud JM, et al. (2003) SARS exposure in an intensive care unit: level of exposure and syndrome development in health care workers. *Emerg Infect Dis* 9: 1205–10.
- Loeb M, McGeer A, Henry B, Ofner M, Rose D, et al. (2004) SARS among critical care nurses, Toronto. *Emerg Infect Dis* 10: 251–5.
- Yin WW, Gao LD, Lin WS, Du L, et al. (2004) Effectiveness of personal protective measures in prevention of nosocomial transmission of severe acute respiratory syndrome. *Zhonghua Liu Xing Bing Xue Za Zhi* 25: 18–22.
- Ofner-Agostini M, Gravel D, McDonald LC, Lem M, Sarwal S, et al. (2006) Cluster of cases of severe acute respiratory syndrome among Toronto HCWs after implementation of infection control precautions: a case series. *Infect Control Hosp Epidemiol* 27: 473–8.
- Public Health Agency of Canada. National Case Definitions for the SARS Outbreak Period. Available at: <http://www.phac-aspc.gc.ca/sars-sras/sarscasedef-eng.php>. Accessed June 29, 2008.
- Tang P, Louie M, Richardson SE, Smieja M, Simor A, et al. (2004) Interpretation of diagnostic laboratory tests for severe acute respiratory syndrome: the Toronto experience. *CMAJ* 170: 47–54.
- Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. *Crit Care Med* 13: 818–829.
- Shigayeva A, Green K, Raboud JM, Henry B, Simor AE, et al. (2007) Factors associated with critical-care HCWs' adherence to recommended barrier precautions during the Toronto severe acute respiratory syndrome outbreak. *Infect Control Hosp Epidemiol* 28: 1275–83.
- Breiman L, Friedman J, Stone CJ, Olshen RA (1984) Classification and Regression Trees. Chapman and Hall.
- Zeger SL, Liang KY (1986) Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 42: 121–30.
- Ho AS, Sung JJY, Chan-Yeung M (2003) An outbreak of severe acute respiratory syndrome among hospital workers in a community hospital in Hong Kong. *Ann Int Med* 139: 564–7.
- Lau JTF, Fung KS, Wong TW, Kim JH, Wong E, et al. (2004) SARS transmission among hospital workers in Hong Kong. *Emerg Infect Dis* 10: 280–86.
- Teleman MD, Boudville IC, Heng BH, Zhu D, Leo YS (2004) Factors associated with transmission of severe acute respiratory syndrome among health-care workers in Singapore. *Epidemiol Infect* 132: 797–803.
- Reynolds MG, Anh BH, Thu VH, Montgomery JM, Bausch DG, et al. (2006) Factors associated with nosocomial SARS-CoV transmission among HCWs in Hanoi, Vietnam, 2003. *BMC Public Health* 207.
- Pei LY, Gao ZC, Yang A, Wei DG, Wang SX, et al. (2006) Investigation of the influencing factors on severe acute respiratory syndrome among health-care workers. *Beijing Da Xue Xue Bao* 38: 271–5.
- Ma, HJ, Wang HW, Fang LQ, Jiang QF, et al. (2004) A case-control study on the risk factors of severe acute respiratory syndromes among health-care workers. *Zhonghua Liu Xing Bing Xue Za Zhi* 25: 741–4.
- Paunio M, Peltola H, Valle M, Davidkin I, Virtanen M, et al. (1998) Explosive school-based measles outbreak: intense exposure may have resulted in high risk, even among revaccinees. *Am J Epidemiol* 148: 1103–10.
- Hattis RP, Halstead SB, Herrman KL, Witte JJ (1973) Rubella in an immunized island population. *JAMA* 223: 1019–21.
- Marks JS, Serdula MK, Halsey NA, Gunaratne MV, Craven RB, et al. (1981) Saturday night fever: a common-source outbreak of rubella among adults in Hawaii. *Am J Epidemiol* 114: 574–83.
- Sheretz RJ, Reagan DR, Hampton KD, Robertson KL, Streed SA, et al. (1996) A Cloud Adult: The Staphylococcus aureus-Virus Interaction Revisited. *Annals Internal Medicine* 124: 539–547.
- Brooks SM, Lassiter NL, Young EC (1973) A pilot study concerning the infection risk of sputum positive tuberculosis patients on chemotherapy. *Am Rev Respir Dis* 108: 799–804.
- Riley RL, Mills CC, O'Grady F, Sultan LU, Wittstadt F, et al. (1962) Infectiousness of air from a tuberculosis ward. Ultraviolet irradiation of infected air: comparative infectiousness of different patients. *Am Rev Respir Dis* 85: 511–25.
- Riley RL, Mills CC, Nyka W, Weinstock N, Storey PB, et al. (1995) Aerial dissemination of pulmonary tuberculosis. A two-year study of contagion in a tuberculosis ward, 1959. *Am J Epidemiol* 142: 3–14.
- Wang ShX, Li YM, Sun BC, Zhang SW, Zhao WH, et al. (2006) The SARS outbreak in a general hospital in Tianjin, China – the case of superspreader. *Epidemiol Infect* 134: 786–791.
- Kwok KO, Leung GM, Lam WY, Riley S (2007) Using models to identify routes of nosocomial infection: a large hospital outbreak of SARS in Hong Kong. *Proc R Soc B* 274: 611–617.
- Shen Z, Ning F, Zhou W, He X, Lin C, et al. (2004) Superspreading SARS events, Beijing, 2003. *Emerg Infect Dis* 10: 256–60.
- Wang JX, Feng HY, Liu D, Zhang ZL, Shan AL, et al. (2003) Epidemiological characteristics of severe acute respiratory syndrome in Tianjin and the assessment of effectiveness on measures of control *Zhonghua Liu Xing Bing Xue Za Zhi* 24: 565–9.
- Woolhouse MEJ, Dye C, Etard J-F, Smith T, Charlwood JD, et al. (1997) Heterogeneities in the transmission of infectious agents: implications for the design of control programs. *PNAS* 94: 338–42.

32. Lloyd-Smith JO, Schreiber SJ, Kopp PE, Getz WM (2005) Superspreading and the effect of individual variation on disease emergence. *Nature* 438: 355–9.
33. Dimoulas P, Green KA, Shigayeva A, Aquino M, McGeer A, et al. (2005) Toronto SARS Hospital Investigation Team. Patient contact recall after SARS exposure. *Emerg Infect Dis* 11: 625–8.
34. Aquino M, Raboud JM, McGeer A, Green K, Chow R, et al. (2006) Accuracy of HCW recall and medical record review for identifying infectious exposures to hospitalized patients. *Infect Control Hosp Epidemiol* 27: 722–8.
35. Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, et al. (2008) Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. *BMJ* 336: 77–80.

SARS Transmission among Hospital Workers in Hong Kong

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Despite infection control measures, breakthrough transmission of severe acute respiratory syndrome (SARS) occurred for many hospital workers in Hong Kong. We conducted a case-control study of 72 hospital workers with SARS and 144 matched controls. Inconsistent use of goggles, gowns, gloves, and caps was associated with a higher risk for SARS infection (unadjusted odds ratio 2.42 to 20.54, $p < 0.05$). The likelihood of SARS infection was strongly associated with the amount of personal protection equipment perceived to be inadequate, having <2 hours of infection control training, and not understanding infection control procedures. No significant differences existed between the case and control groups in the proportion of workers who performed high-risk procedures, reported minor protection equipment problems, or had social contact with SARS-infected persons. Perceived inadequacy of personal protection equipment supply, infection control training <2 hours, and inconsistent use of personal protection equipment when in contact with SARS patients were significant independent risk factors for SARS infection.

The first large-scale outbreak of severe acute respiratory syndrome (SARS) occurred on or near March 12, 2003 in the Prince of Wales Hospital in Hong Kong (1). In this worldwide epidemic, hospital workers were one of the affected groups; as of May 31, 2003, a total of 384 (22.1%) of 1,739 suspected or confirmed cases reported in Hong Kong were hospital workers (2). In the initial phase of the epidemic, hospital workers did not take special protective measures. Thus, hospital workers accounted for 43.6% (68 of 156 cases) of those admitted to the Prince of Wales Hospital from March 11 to 25, 2003 (3). By May 25, 2003, a total of 453 confirmed SARS cases had been admitted to hospitals in the New Territories East cluster of the Hospital Authority in Hong Kong, which serves 1.3 million people and to which the Prince of Wales Hospital belongs. From March 28, 2003, to May 29, 2003, a total of 77 cases of

SARS infection among hospital workers had been reported by the 5 hospitals in the cluster.

A recent study concluded that the use of protective masks is an effective countermeasure against SARS (4). Nevertheless, even after these measures were implemented, there were approximately 300 more hospital workers in whom the disease developed. Limitations of that study were the small number of cases and potential confounding by the possible differences in the intensity of care given to the SARS patients between the case and control groups.

Breakthrough transmission continues despite implementing strict infection control measures. We investigated the factors associated with breakthrough transmission of the SARS virus among hospital workers infected in hospital settings.

Materials and Methods

Study Design

A 1:2 matched case-control design was used. All participants were working in wards with SARS inpatients, some of which also included non-SARS patients. The case group included all infected hospital workers in the five hospitals of the New Territories East cluster of the Hospital Authority in Hong Kong who were registered as SARS cases by the Department of Health's eSARS registry and were hospitalized during March 28 through May 25, 2003.

The SARS case definition criteria used by Hong Kong Hospital Authority is as follows: radiographic evidence of infiltrates consistent with pneumonia, and current fever $>38^{\circ}\text{C}$ or a history of such at any time in the preceding 2 days, and at least two of the following: history of chills in the past 2 days, new or increased cough or breathing difficulty, general malaise or myalgia, typical signs of consolidation, or known exposure. These criteria are equivalent with the World Health Organization's case definition for probable SARS. Suspected SARS cases are those that do not completely fulfill the above definition

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but were considered to be likely cases of SARS on the basis of clinical judgment. If no known history of exposure exists, patients are considered for exclusion if an alternative diagnosis can fully explain the clinical symptoms. Laboratory confirmation of SARS infection was also conducted by one or more of the following assays: reverse transcriptase-polymerase chain reaction (RT-PCR); culture from throat wash, urine, stool and nasal swab specimens taken at days 1, 3, and 5; or paired serologic assay from clotted blood taken at day 1 and 21.

Of 77 probable and suspected SARS cases, 72 (93.5%) participated in the study. As all staff was required to use protective masks from March 12, 2003, these hospital workers were presumed to have contracted the virus as a result of breakthrough transmission. An infection control nurse explained the purpose and logistics of the study to the study participants, obtained their verbal consent for participation, presented them with a structured questionnaire, and collected the completed questionnaire. SARS case-patients were asked to nominate as controls two colleagues who had been working in the same job position, in the same ward, and in proximity with the case-patient before he became ill. Medical and nursing staff (48 of 72 cases) self-administered the questionnaires while other staff (e.g., healthcare assistants and ward assistants) were interviewed by an infection control nurse. Out of the 72 cases, 57 nominated 114 controls who completed the questionnaire (114/144 = 79.2%); 15 cases did not nominate a control and hence 30 controls were randomly selected from the duty roster of the day before the case felt unwell, matching for job position (30/144 = 20.8%). Questionnaires were collected from 57 (79.2%) nominated controls. Nominated controls who did not return the questionnaire were replaced by controls randomly selected from the duty roster of the day before the case felt unwell, matching for job position (15/72 = 20.8%). Of the 144 controls completing the questionnaire, one was invalidated because she later became a suspected case. Controls showed neither influenzalike symptoms nor SARS-related symptoms during the study and had not been identified as a suspected SARS case as of August 15, 2003. No blood test was conducted to determine whether these persons were asymptomatic SARS cases. Another study that tested 674 healthcare workers who were working in the same hospital cluster found no asymptomatic or subclinical SARS. It can thereby be assumed that the control group had not contracted the virus (5).

Measurements

Questions were asked about the hospital worker's job position, whether the healthcare worker had been seconded from another unit, whether he/she had made physical contact with any SARS patients and if so, whether various high-risk procedures were performed to the SARS

patient (including intubation, suction, cardiopulmonary resuscitation).

Personal protection equipment use (N95 mask, surgical mask, gloves, goggles, gown, and cap) was examined under three different settings: when having direct contact with SARS patients, when having contact with "patients in general" (includes both SARS and non-SARS patients), and when there was "no patient contact." Information about the frequency of using different types of personal protection equipment (never, occasionally, most of the time, or all of the time) was asked for each of these three settings. A respondent was considered to be exposed to a particular risk if he or she had "never" or "occasionally" been using personal protection equipment rather than "most or all of the time." Those who had not been in contact with any SARS patients or patients in general were considered as not having been exposed to the particular risk. Respondents were asked whether they perceived the supply of such personal protection equipment items to be adequate or not (yes/no). Questions regarding the frequency of hand washing after making contact with SARS patients, patients in general and when there was no patient contact (never, occasionally, most of the time, all of the time) were also asked. In the analysis, frequency of using personal protection equipment and frequency of hand hygiene practice were coded into 2 categories: used inconsistently (i.e., "never or occasionally used") or used consistently ("used most or all of the time").

Study participants were also asked to assess whether the masks fit them (yes/no), whether their goggles were fogged (yes/no), and the frequency of touching protective masks (never, occasionally, most of the time, or always), and whether they had any problems complying with infection control procedures (yes/no). Respondents were asked whether they had ever made social contact with others who were later found to be SARS case-patients before SARS-related symptoms manifested (yes/no/not sure), within the 14-day period before the case's onset of symptoms. The questionnaire also asked about the respondent's exposure to infection control training (length of SARS infection control training) and whether they understood the infection control measures (yes/no). A trained research assistant contacted the respondents by telephone to follow up on any incomplete or unclear answers.

Statistical Methods

Unadjusted matched odds ratios calculated from conditional logistic regression methods (6) are summarized in Tables 1 to 4. A multivariate conditional logistic regression was fitted using a forward-stepwise procedure with all variables that were marginally significant ($p < 0.10$) in the unadjusted analyses as candidates for selection. Matched odds ratios and their exact 95% confidence intervals were

derived. LogXact for Windows version 4.1 was used for all calculations (7).

Results

Background Characteristics of Respondents

The 72 SARS-infected healthcare workers worked in five hospitals (distribution: 50% Alice Ho Miu Ling Nethersole Hospital, 40.3% from Prince of Wales Hospital, 2.8% from North District Hospital, 4.2% from Shatin

Hospital, and 2.8% from Taipo Hospital). The study sample was composed of nurses 59.7% (n = 43), healthcare assistants 23.6% (n = 17), medical officers 9.7% (n = 8), clerical staff (2.8%, n = 2), and workmen (4.2%, n = 3).

Use of Masks and Other Types of Protection Equipment

Almost 100% of the study respondents used either an N95 mask or surgical mask in all 3 settings (Table 1). The differences of the use of the N95 mask (most of those not

Table 1. Percentage of healthcare workers exposed to the risk of inconsistent use of different types of personal protection equipment in 3 clinical settings with SARS patients^a

Type of personal protection equipment	Controls (n = 143)	%	Case-patients (n = 72)	%	Matched OR (exact 95% CI)	p value (exact)
N95 or Surgical mask ^b						
Direct contact with SARS patient	0	0	1	1.4	2.00 (0.05 to ∞)	0.6667
Direct contact with patients in general ^c	1	0.7	2	2.8	4.00 (0.21 to 235.99)	0.5185
No patient contact ^d	3	2.2	4	5.7	2.43 (0.41 to 16.77)	0.4198
N95 ^b						
Direct contact with SARS patients	6	4.2	7	9.7	2.86 (0.70 to 13.71)	0.1683
Direct contact with patients in general ^c	5	3.6	3	4.2	1.28 (0.16 to 10.47)	1.0000
No patient contact ^d	14	10.2	12	17.1	1.83 (0.72 to 4.71)	0.2315
Goggles ^b						
Direct contact with SARS patients	12	8.4	23	31.9	6.41 (2.49 to 19.49)	<0.0001
Direct contact with patients in general ^e	7	5.1	16	22.2	6.93 (2.19 to 28.85)	0.0003
No patient contact ^f	19	13.9	21	30.0	3.50 (1.42 to 9.47)	0.0046
Gown ^b						
Direct contact with SARS patients	6	4.2	15	20.8	8.85 (2.46 to 48.28)	0.0002
Direct contact with patients in general ^c	2	1.4	12	16.7	11.54 (2.56 to 106.36)	0.0002
No patient contact ^f	16	11.7	19	27.1	3.42 (1.38 to 9.30)	0.0061
Gloves ^b						
Direct contact with SARS patients	2	1.4	11	15.3	20.54 (2.96 to 887.72)	0.0002
Direct contact with patients in general ^c	5	3.6	7	9.7	3.53 (0.77 to 21.85)	0.1211
No patient contact ^f	20	14.6	19	27.1	2.42 (1.05 to 5.81)	0.0374
Cap ^b						
Direct contact with SARS patients	8	5.6	17	23.6	7.30 (2.33 to 30.21)	0.0001
Direct contact with patients in general ^c	5	3.6	15	20.8	12.81 (2.92 to 116.75)	0.0001
No patient contact ^{g,f}	16	11.7	22	31.4	4.05 (1.68 to 10.76)	0.0009
No. of equipment inconsistently used with direct contact with SARS patients ^g						
0	129	90.2	45	62.5	1.00	
1–2	7	4.9	13	18.1	5.35 (1.79 to 18.53)	0.0015
≥3	7	4.9	14	19.4	7.84 (2.30 to 34.83)	0.0003
No. of equipment inconsistently used with direct contact with patients in general ^{e, g}						
0	127	92.0	52	72.2	1.00	
1–2	6	4.3	8	11.1	4.85 (1.01 to 31.86)	0.0479
≥3	5	3.6	12	16.7	10.83 (2.29 to 102.60)	0.0007
No. of equipment inconsistently used when there was no patient contact ^{g, h}						
0	113	82.5	46	65.7	1.00	
1–2	6	4.4	4	5.7	1.56 (0.28 to 7.97)	0.7721
≥3	18	13.1	20	28.6	3.40 (1.37 to 9.23)	0.0061

^aSARS, severe acute respiratory syndrome; CI, confidence interval; OR, odds ratio.

^bThose having no contact with patients were considered to be unexposed to the tabulated risk factor.

^cInformation on 4 controls missing.

^dInformation on 4 controls and 2 case-patients missing.

^eInformation on 5 controls missing.

^fInformation on 6 controls and 1 case-patients missing.

^gInformation on 6 controls and 2 case-patients missing.

^hIncluding N95, goggles, gown, gloves and cap.

Table 2. Percentage with inconsistent hand hygiene^a

Category	Controls (n = 143)		Case-patients (n = 72)		Matched OR (exact 95% CI)	p value (exact)
	n	%	n	%		
After direct contact with SARS patients	0	0	2	2.8	4.83 (0.38 to ∞)	0.2222
After direct contact with "patients in general" ^b	2	1.4	1	1.4	1.00 (0.02 to 19.21)	1.0000
When there was "no patient contact" ^c	3	2.1	10	14.3	6.38 (1.64 to 36.17)	0.0044

^aOR, odds ratio; CI, confidence interval; SARS, severe acute respiratory syndrome.^bInformation on 3 controls missing.^cInformation on 1 control and 2 case-patients missing.

wearing a N95 mask were wearing a surgical mask) were not statistically significant between cases and controls in any of the three settings ($p > 0.05$, Table 1).

When hospital workers were in direct contact with SARS patients, the case group was more likely to inconsistently use goggles (odds ratio [OR] = 6.41, $p < 0.0001$), gowns (OR = 8.85, $p = 0.0002$), gloves (OR = 20.54, $p = 0.0002$), and caps (OR = 7.30, $p = 0.0001$) than the control group. When in direct contact with patients in general, cases were more likely to inconsistently use goggle (OR = 6.93, $p = 0.0003$), gowns (OR = 11.54, $p = 0.0002$), and caps (OR = 12.81, $p = 0.0001$). When there was "no patient contact," cases had more than a twofold likelihood of inconsistently using goggles ($p = 0.0046$), gowns ($p = 0.0061$), gloves ($p = 0.0374$), or cap ($p = 0.0009$), compared to their matched controls. Having three or more personal protection equipment inconsistently used (including masks) was also a significant predictor of SARS infection for hospital workers in direct contact with SARS patients (OR = 7.84, $p = 0.003$); for those with direct contact with patients in general (OR = 10.83, $p = 0.0007$); and for those with no patient contact (OR = 3.4, $p = 0.006$) (Table 1).

More than 97% of both the cases and control group consistently reported to practice good hand hygiene after contacting SARS patients or "patients in general" therefore differences between the two groups were not statistically significant ($p = 0.22$, and $p = 1.00$, respectively, Table 2). There was, however, a statistically significant difference in the proportion of cases (14.3%) and controls

(2.1%) of hospital workers who reported inconsistent hand hygiene when there was "no patients contact" (OR = 6.38, 95% CI = 1.64, 36.2, $p = 0.0044$).

Perceived Inadequacy of Personal Protection Equipment Supply

A much higher percentage of SARS cases compared to controls reported a perceived inadequate supply of each of the 6 types of personal protection equipment (OR = 28.0, $p < 0.0001$ for surgical masks; OR = 5.19, $p = 0.0004$ for N95 masks; OR = 8.44, $p < 0.0001$ for gowns; OR = 29.3, $p < 0.0001$ for gloves; OR = 19.8, $p < 0.0001$ for goggles; OR = 52.4, $p < 0.0001$ for cap) (Table 3). Most notably, 44.4% of the cases reported that there was an inadequate supply of at least one item of the personal protection equipment, as compared to 14.0% of the controls (OR = 6.78, $p < 0.0011$); among SARS cases, 26% reported three or more personal protection equipment items as being in inadequate supply, compared to 1.4% of the controls (OR = 52.2, $p < 0.0001$).

SARS-Related Infection Control Training

The unadjusted results indicated that 50% of SARS cases did not receive any SARS infection control training (versus 28% of the controls) (Table 4). Those who underwent ≥ 2 hours of training (4.2% of cases and 25.2% of controls) were far less likely to have been infected with SARS (OR = 0.03, $p < 0.0001$). Of the SARS cases, 23.9% indicated that they did not understand the infection control

Table 3. Percentages with perceived inadequacy of personal protection equipment supply and breakthrough SARS infection among hospital workers^a

Type of personal protection equipment	Controls (n = 143)		Case-patients (n = 72)		Matched OR (exact 95% CI)	p value (exact)
	n	%	n	%		
Surgical mask	1	0.7	14	19.4	28.00 (4.26 to ∞)	<0.0001
N95 mask	13	9.1	20	27.8	5.19 (1.95 to 16.13)	0.0004
Gown	7	4.9	19	26.4	8.44 (2.77 to 34.37)	<0.0001
Gloves	2	1.4	12	16.7	29.34 (4.79 to ∞)	<0.0001
Goggles	5	3.5	22	30.6	19.81 (4.83 to 174.55)	<0.0001
Cap	4	2.8	21	29.2	52.41 (9.08 to ∞)	<0.0001
Any one of above as inadequate ^b	20	14.0	32	44.4	6.78 (2.86 to 18.51)	<0.0001
No. of items identified to be inadequate ^b						
0	123	86.0	40	55.6	1.00	
1–2	18	12.6	13	18.1	3.25 (1.17 to 9.80)	0.0209
3	2	1.4	19	26.4	52.24 (7.70 to 2280.07)	<0.0001

^aSARS, severe acute respiratory syndrome; OR, odds ratio; CI, confidence interval.^bIncluding N95 mask, goggle, gown, gloves and cap.

measures, compared with 8.5% of the controls (OR = 3.14, $p = 0.0065$). Duration of SARS training (<2 hrs versus ≥ 2 hours) was significantly associated with reported understanding of the infection control measures (OR = 7.29, $p = 0.001$). There was also a marginal statistically significant difference (OR = 0.27, $p = 0.057$) in the proportion who reported having received updated SARS information between case-patients (88.9%) and controls (96.5%).

Patient Care and Infection Control Measures

A higher but statistically nonsignificant percentage of the control group (73.4%) reported having direct contact with SARS patients as compared to the case group (62.5%). Three (4.2%) of 72 case-patients and 7 (4.9%) of 143 controls reported that they had no direct contact with patients in general ($p > 0.05$). Having performed high-risk procedures on SARS patients and being seconded from another unit were not significantly associated with risk of SARS infection (Table 4).

Table 4. Percentage distributions of variables related to training, patient care, social contact and mask compliance^a

Characteristic	Controls (n = 143)		Case-patients (n = 72)		Matched OR (exact 95% CI)	p value (exact)
	n	%	N	%		
Length of SARS infection control training						
None	40	28.0	36	50.0	1.00	
<2hrs	67	46.9	33	45.8	0.47 (0.18 to 1.14)	0.1028
≥ 2 hrs	36	25.2	3	4.2	0.03 (0.001 to 0.20)	<0.0001
Understood infection control measures ^b						
Yes	130	91.5	54	76.1	1.00	
No	12	8.5	17	23.9	3.14 (1.35 to 7.73)	0.0065
Acquired updated information						
No	5	3.5	8	11.1	1.00	
Yes	136	96.5	64	88.9	0.27 (0.06 to 1.04)	0.0574
High risk procedures with SARS patients ^c						
No	115	86.5	60	83.3	1.00	
Yes	18	13.5	12	16.7	1.22 (0.45 to 3.14)	0.8061
Direct contact with SARS patients						
No/Not sure	38	26.6	27	37.5	1.00	
Yes	105	73.4	45	62.5	0.57 (0.28 to 1.14)	0.1197
Direct contact with patients in general						
No/Not sure	7	4.9	3	4.2	1.68	1.000
Yes	136	95.1	69	95.8	(0.07 to 117.74)	
Seconded from another unit						
No	77	53.8	46	63.9	1.00	
Yes	66	46.2	26	36.1	0.60 (0.29 to 1.21)	0.1671
Social contact with SARS patients						
No/Not sure	95	66.4	55	76.4	1.00	
Yes	48	33.6	17	23.6	0.59 (0.28 to 1.19)	0.1592
Frequency of touching the N95 ^d						
Never/occasional	108	76.6	46	70.8	1.00	
Most of the time/Always	33	23.4	19	29.2	1.32 (0.63 to 2.74)	0.5205
General problems with mask ^e						
No	72	51.4	41	59.4	1.00	
Yes	68	48.6	28	49.6	0.66 (0.34 to 1.27)	0.2407
Problems with mask fit ^f						
No	73	51.0	36	52.1	1.00	
Yes	70	49.0	33	47.8	1.00 (0.51 to 1.95)	1.0000
Problems with fogging of goggles ^g						
No	67	47.2	40	60.1	1.00	
Yes	75	52.8	26	39.9	0.61 (0.31 to 1.17)	0.1520
Overall problems in general compliance ^h						
No	69	50.0	41	58.6	1.00	
Yes	69	50.0	29	41.4	0.58 (0.25 to 1.33)	0.2264

^aOR, odds ratio; CI, confidence interval; SARS, severe acute respiratory syndrome.

^bInformation on 1 control and 1 case-patient missing.

^cInformation on 10 controls with direct contact with SARS patients missing.

^dExcluded 2 controls and 6 case-patients who did not use N95 mask; information on 1 case-patient missing.

^eExcluded 1 case who did not use mask; information on 3 controls and 2 case-patients missing.

^fExcluded 1 case who did not use mask; information on 2 case-patients missing.

^gExcluded 3 cases who did not use goggles; information on 1 control and 3 case-patients missing.

^hExcluded 1 case who did not use any equipment; information on 5 controls and 1 case-patient missing.

There were no significant differences between the percentages of case-patients and controls who reported the following problems: general compliance problems, frequency of touching or adjusting the N95 mask, general problems with mask, problems with mask fit, and problems with fogging of goggles (Table 4).

Social Contact with SARS Cases

Approximately 23.6% of the SARS case-patients and 33.6% of the matched controls reported ever having social contact with someone who was later diagnosed with SARS before the onset of symptoms of the relevant case-patients ($p = 0.1592$) (Table 4).

Problems Encountered

Seven problems in the unadjusted analysis (Table 5) were significantly associated with risk for SARS infection. An indicator variable was constructed by counting the number of problems encountered by the study participants. Almost all (98.6%) of the case group encountered at least one problem (versus 79.9% in the control group). The risk increases greatly with the number of problems encountered (OR = 44.2 for 3 or more problems, $p < 0.0001$) (Table 5). Using a cut-off point of two or more problems to predict SARS infection gives a sensitivity and specificity of 0.681 and 0.691, respectively.

Multivariate Analysis

The results of the forward stepwise conditional logistic regression model using the seven significant variables as candidate variables indicate that the perceived inadequacy of personal protection equipment supply (adjusted OR = 4.27, 95% CI 1.66 to 12.54, $p = 0.0028$), SARS infection control training <2 hours or no training (adjusted OR = 13.6, 95% CI 1.24 to 27.50, $p = 0.002$), and inconsistent use of more than one type of personal protection equipment when having direct contact with SARS patients (adjusted OR = 5.06, 95% CI 1.91 to 598.92, $p = 0.02$) were significantly and independently associated with SARS infection among hospital workers.

Discussion

Breakthrough transmission was likely responsible for the SARS infection of these cases, as protective masks (primarily N95) were used consistently by almost all of the cases. All workers were required to wear protective masks from March 12, 2003. Using protective masks alone is, therefore, not sufficient to eliminate SARS transmission among hospital workers. Cases were less likely to have had direct contact with a SARS patient than controls, suggesting that direct physical contact with SARS patients was not necessary for breakthrough transmission to occur. It also suggests that modes of transmission other than droplets cannot be excluded. Consistent hand hygiene after contact with patients was almost universal and was not a significant factor predicting SARS transmission in our study, although hand hygiene appeared to be a risk factor in situations when there was no patient contact.

Data from all the three settings show that inconsistent use of gown, cap, and goggles were all very strongly associated with breakthrough transmissions. Personal protection equipment should be used consistently in all three settings. The high degree of collinearity in the use of the various types of personal protection equipment makes it difficult to ascertain which type of personal protection equipment is most important as a SARS countermeasure. Nevertheless, policy makers should be made aware that the supply of different types of personal protection equipment had often been seen as inadequate, and it is one of the very significant risk factors identified. The perception of inadequate supply was not verified by this study. These perceptions may reflect the actual situation or may be an inaccurate impression of the hospital workers. Caution is advised in interpreting these results. Nevertheless, at the time of the study, the media had reported frequent complaints about personal protection equipment supply shortages from hospital workers. The perception of inadequate personal protection equipment is likely to be associated with the personal protection equipment supply situation. Given the large differences in our results (OR > 5.0, $p < 0.001$), it is likely that personal protection equipment

Table 5: Percentage distribution of the number of problems encountered by the hospital worker^a

No. of problems encountered ^b	Controls			Case-patients			Matched OR (exact 95% CI)	p value (exact)
	n	%	Cumulative %	n	%	Cumulative %		
0	27	20.1	20.1	1	1.4	1.4	1.00	
1	65	48.5	68.6	21	30.4	31.8	8.47(1.37 to ∞)	0.0169
2	24	17.9	86.5	17	24.6	56.4	17.78(2.67 to ∞)	0.0010
≥3 ^{c,d}	18	13.4	100.0	30	43.5	100.0	44.15(7.02 to ∞)	<0.0001

^aExcluded nine controls and three cases that had at least one missing entry on one of the problems encountered.

^bThe seven problems are: 1) inconsistent use of at least 1 type of personal protection equipment when having contact with SARS patients, 2) with "patients in general," 3) when there was "no patient contact," 4) when SARS infection control training was less than 2 hours, 5) when the respondent reported not understanding SARS infection control procedures, 6) when at least one personal protection equipment was perceived to be in inadequate supply in the 3 settings, and 7) when hand hygiene was inconsistent when there was "no patient contact."

^cPercentages of the number of problems encountered in the control group: 3 problems (6.7%), 4 problems (4.5%), 5 (1.5%), 6 (0.7%), and 7 (0%).

^dPercentages of the number of problems encountered in the case group: 3 problems (10.1%), 4 (8.7%), 5 (13.0%), 6 (8.7%), and 7 (2.9%).

shortages were at least partially responsible for many of the SARS infections. As inadequate knowledge of SARS infection control ("did not understand procedures") is also a strong risk factor for breakthrough transmission, SARS infection control training must not be overlooked. In-depth, thorough training (≥ 2 hrs) is required.

Soon after the initial SARS outbreak, it was mandatory for all hospital workers to attend at least one 1-hour structured training session delivered by the infection control team, and the records of these sessions were collected and submitted to the Hospital Authority. These training sessions were conducted twice per day for the initial week from the middle of March and daily until the end of June. The content of these training sessions included basic knowledge of SARS and its clinical presentation, route of transmission, types and proper use of different personal protective equipment for different risk levels, the procedures for handling high risk specimens, environmental disinfection protocols, and commonly observed problems. The content of the training was regularly revised with updated information. Regular updates and attendance of the training sessions were strongly recommended. The unit supervisors were given more intensive training to train their staff. The findings of this study underscore the importance of in-depth training in SARS prevention among hospital workers.

The findings eliminate a number of speculated risk factors which include the following: performing particular high-risk procedures on SARS patients, having social contacts with people who were later found to have SARS cases, and experiencing various minor problems in using the mask. Performing high-risk procedures was not a significant factor, hence, it is speculated that this is due to a high degree of awareness and caution taken when performing these procedures with SARS patients.

It is found that those who encountered any of the seven identified problems had a greatly increased likelihood of contracting SARS. The number of problems encountered is a strong predictor of SARS infection. It is recommended that, after each day's work, health workers complete a checklist to be reviewed by management. No hospital staff should be exposed to SARS before receiving adequate training or before they have obtained a thorough understanding of the infection control procedures. The results of the multivariate analysis show that infection control training, personal protection equipment use, and perceived supply were independently associated with SARS infection risk among hospital workers.

This study has a number of limitations. As a case-control study, it is subject to recall bias. However, the recall period was usually within 1 week as all the case-

patients were interviewed while they were hospitalized. Hand hygiene data were self-reported and not audited. Nevertheless, since respondents were required to report the frequency of hand washing from a categorical response format rather than an open ended question, the responses should be reasonably reliable. Another possible bias may be the case group's attributing their infection to external factors (e.g., inadequate supplies) and the control group's doing the opposite. Given that the odds ratios obtained were strongly significant and consistent with one another, it is unlikely that this form of bias could account for all of the observed differences. The study, however, has a relatively large sample size, a high response rate, and has controlled for the exposure to other background confounding factors.

Acknowledgments

We thank C.K. Lee for his assistance with this project.

This study was supported by internal funding of the Faculty of Medicine, The Chinese University of Hong Kong.

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References

1. World Health Organization. WHO issues a global alert of cases of atypical pneumonia: Cases of severe respiratory illness may spread to hospital staff. [cited May 23, 2003]. Available from: URL: <http://www.who.int/mediacentre/releases/2003/pr22/en/print.html>
2. Hong Kong Government. Latest figures on Severe Acute Respiratory Syndrome (as of May 31st 2003). [cited May 31, 2003]. Available from: URL: <http://www.info.gov.hk/dh/diseases/ap/eng/infected.htm>
3. Tomlinson B, Cockram C. SARS: experience at Prince of Wales Hospital, Hong Kong. *Lancet* 2003;361:1486-7.
4. Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, Ho M, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003;361:1519-20.
5. Chan PKS, Ip M, Ng KC, et al. Seroprevalence of severe acute respiratory syndrome (SARS)-associated coronavirus infection among health care workers after a major outbreak of SARS in a regional hospital. *Emerg Infect Dis* In press 2004.
6. McFadden D. Conditional logit analysis of qualitative choice behavior. In: Zarembka, editor. *Frontiers in econometrics*. New York: Academic Press 1973:105-42.
7. Cytell Software Corporation. LogXact for Windows (4.1). 2000. Cambridge, MA.

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SARS among Critical Care Nurses, Toronto

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To determine factors that predispose or protect health-care workers from severe acute respiratory syndrome (SARS), we conducted a retrospective cohort study among 43 nurses who worked in two Toronto critical care units with SARS patients. Eight of 32 nurses who entered a SARS patient's room were infected. The probability of SARS infection was 6% per shift worked. Assisting during intubation, suctioning before intubation, and manipulating the oxygen mask were high-risk activities. Consistently wearing a mask (either surgical or particulate respirator type N95) while caring for a SARS patient was protective for the nurses, and consistent use of the N95 mask was more protective than not wearing a mask. Risk was reduced by consistent use of a surgical mask, but not significantly. Risk was lower with consistent use of a N95 mask than with consistent use of a surgical mask. We conclude that activities related to intubation increase SARS risk and use of a mask (particularly a N95 mask) is protective.

Severe acute respiratory syndrome (SARS) was first recognized in Canada in early March 2003 (1). Caused by a novel strain of coronavirus, the disease was reported in more than 8,400 people globally, with cases in Asia, Europe, and North America in 2003 (2–4). SARS is associated with substantial illness and death. The case-fatality rate has been estimated at 13% for patients <60 years and 43% for those ≥60 years (5). In Canada, disease transmission has occurred predominantly among healthcare workers within the healthcare setting (1). Preventing SARS transmission to healthcare workers is therefore an important priority (6).

Little is known about SARS risk factors for healthcare workers. Determining patient care activities that pose a high risk for infection and possible protective measures for healthcare workers may inform strategies for prevention and may elucidate SARS transmission. Recommended protective equipment for healthcare workers caring for

patients with SARS includes a particulate respirator mask (N95) and a goggle or face shield, gown, and gloves (7,8). One report from Hong Kong has suggested that surgical and N95 masks are protective (9), but few data exist to support the recommendations.

SARS poses a special challenge for healthcare workers who care for the critically ill. Many SARS patients are in critical care units. In a Toronto case series, 29 (20%) of 144 SARS patients were admitted to the intensive care unit (ICU) and 20 (69%) of these 29 received mechanical ventilation (10). The close interaction of staff and patients and the nature of invasive patient care activities, such as intubation and other procedures that involve potential exposure to respiratory secretions, raise important questions about the risk for healthcare workers working in critical care units.

To determine risk factors for SARS, we conducted a retrospective cohort study among nurses who worked in two critical care units in a Toronto hospital. We hypothesized that patient care activities (e.g., intubating, suctioning of endotracheal tubes, and administering nebulizers) that increase exposure to respiratory droplets are associated with an increased risk for SARS transmission and that masks protect against infection.

Methods

Study Setting and Population

Hospital A is a 256-bed community hospital that provides medical, surgical, obstetric, and pediatric care in the Greater Toronto Area. On March 7, 2003, the 42-year-old son (patient A) of the index patient in the Toronto SARS outbreak (1) was seen in the emergency department. He was admitted to the hospital's 10-bed ICU on March 8. Patient A stayed in the ICU until March 13, the date of his death due to SARS. On March 17, a 77-year-old man (patient B) who had been exposed to patient A in the emergency room on March 7 was admitted to the ICU. He stayed there until his death due to SARS on March 21. Patient C, another emergency room contact of patient A, was admitted to the hospital's 15-bed coronary care unit

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(CCU) on March 13. On March 16, he was transferred to another hospital's ICU, where he stayed until his death from SARS on March 29. Nurses who worked one or more shifts in hospital A's ICU from March 8 to 13 and from March 17 to 21 (i.e., when a SARS patient was in the unit) were included in the cohort. Similarly, nurses who worked one or more shifts from March 14 to March 16 in hospital A's CCU were included.

Measurements

We recorded the age, sex, and medical history of the nursing staff, including history of any respiratory illness, smoking, conditions that might result in immunosuppression, and use of immunosuppressive medications. Using a standardized data collection form, trained research nurses abstracted information regarding the patient care activities administered by the critical care nurses. To link particular nurses to activities performed in SARS patients' rooms, we identified nurses' signatures on patient charts by using a master list of signatures provided by the CCUs. Data collection included type and duration of patient care activities performed. The types of personal protection equipment (goggles, face shield, surgical mask, glove, gown, N95 mask) and the duration and frequency of using the equipment when caring for SARS patients were recorded. Information from the charts was then used to interview nurses about the specific care provided during their shifts. Information provided by the nurses was corroborated whenever possible by data from the charts.

Case Definition

We used Health Canada's case definition for suspected or probable SARS cases (11). A suspected case was described as fever ($\geq 38^{\circ}\text{C}$), cough or breathing difficulty, and one or more of the following exposures during the 10 days before onset of symptoms: close contact with a person with suspected or probable SARS, recent travel to an area with recent local SARS transmission outside Canada, recent travel or visit to an identified setting in Canada where SARS exposure might have occurred. A probable case was defined as a suspected SARS case with radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome or a suspected SARS case with autopsy findings consistent with pathologic features of respiratory distress syndrome without identifiable cause. The case definitions are in accordance with the World Health Organization's clinical case definitions (12). All three source patients met the definition for probable SARS cases. For this study, we assessed outcomes for each nurse from the first exposure to a source patient until 10 days (one incubation period) after the last exposure (March 8–April 3 for nurses in ICU and March 14–26 for nurses in CCU). Nurses who met the suspected

or probable case definition and the three SARS source patients (patients A, B, and C) were tested for antibodies against SARS-associated coronavirus by immunofluorescence (EUROIMMUN, Luebeck, Germany).

Statistical Analysis

Fischer's exact two-sided tests were used to assess risk factors. Exact confidence intervals (CI) were reported. A Kaplan-Meier survival curve was constructed. Data were analyzed by using EpiInfo 2000 (Centers for Disease Control and Prevention, Atlanta, GA) and SAS version 8.0 (SAS Institute Inc., Cary, NC).

Results

Forty-three nurses worked at least one shift in a critical care unit where there was a patient with SARS; 37 worked in ICU and 6 in CCU. Eight nurses were infected with SARS, four who worked only in the ICU, three who worked only in the CCU, and one ICU nurse who worked one shift in the CCU. All cohort nurses were female; the mean age was 41 years (range 27–65 years). Only two nurses had a history of respiratory illness (one asthma, one bronchitis). Illness onset for the eight nurses was March 16–21. The most common symptoms included fever (8 [100%] of 8), myalgia (7 [87.5%] of 8), cough (6 [75%] of 8) and chills (6 [75%] of 8). Five nurses (62.5%) had headaches, and four (50%) had shortness of breath. Of the eight nurses, four (probable SARS case-patients) had unilateral infiltrates on chest radiograph and four (suspected SARS case-patients) had normal chest radiographs. SARS diagnosis in these eight nurses and in the three SARS source patients was confirmed by serology.

Patient Care Activities

Relative infection risk for 23 patient care activities is shown in Table 1. None of the 11 nurses who did not enter a SARS patient's room became ill. Our analysis was thus limited to the 32 nurses who entered a SARS patient's room at least once. Three patient care activities were associated with SARS infection: intubating (relative risk [RR] 4.20, 95% CI 1.58 to 11.14, $p = 0.04$); suctioning before intubation (4.20 RR, 95% CI 1.58 to 11.14, $p = 0.04$); and manipulating an oxygen mask (9.0 RR, 95% CI 1.25 to 64.9, $p \leq 0.01$).

Personal Protective Equipment

Use of personal protective equipment and history of high-risk patient care activities among SARS-infected nurses are summarized in Table 2. Relative risk for SARS infection and use of personal protective equipment is summarized in Table 3. Three (13%) of 23 nurses who consistently wore a mask (either surgical or N95) acquired SARS compared to 5 (56%) of 9 nurses who did not consistently

Table 1. Relative risk of critical care nurses acquiring SARS by patient care activity

Patient care activity	SARS attack rate (No. cases/No. exposed or unexposed) (%)		Relative risk (95% CI)	p value
	Exposed	Unexposed		
Intubation	3/4 (75)	5/28 (18)	4.20 (1.58 to 11.14)	0.04
Suctioning before intubation	3/4 (75)	5/28 (18)	4.20 (1.58 to 11.14)	0.04
Suctioning after intubation	4/19(21)	4/13(31)	0.68 (0.21 to 2.26)	0.68
Nebulizer treatment	3/5(20)	5/27 (8)	3.24 (1.11 to 9.42)	0.09
Manipulation of oxygen mask	7/14 (50)	1/18 (6)	9.00 (1.25 to 64.89)	0.01
Manual ventilation	2/7 (29)	6/25 (24)	1.19 (0.30 to 4.65)	1.00
Mouth or dental care	5/21 (24)	3/11(27)	0.87 (0.25 to 2.99)	1.00
Insertion of a nasogastric tube	2/6 (33)	6/26 (23)	1.44 (0.38 to 5.47)	0.62
Insertion of an indwelling urinary catheter	2/2 (100)	6/30(0.20)	5.00 (2.44 to 10.23)	0.06
Insertion of a peripheral intravenous catheter	3/5 (60)	5/27 (19)	3.24 (1.11 to 9.42)	0.09
Chest tube insertion or removal	0 (0)	0 (0)		
Insertion of a central venous catheter	2/6 (33)	6/26 (23)	1.44 (0.38 to 5.47)	0.62
Bathing or patient transfer	7/26 (27)	1/6 (17)	1.62 (0.24 to 10.78)	1.00
Manipulation of BiPAP mask	3/6 (50)	5/26 (19)	2.60 (0.8 to 7.99)	0.15
Administration of medication	5/23 (22)	3/ 9 (33)	0.65 (0.20 to 2.18)	0.65
Performing an electrocardiogram	4/12 (33)	4/20 (20)	1.67 (0.51 to 5.46)	0.43
Venipuncture	6/17 (35)	2/ 15 (13)	2.65 (0.63 to 11.19)	0.23
Manipulation of commodes or bedpans	3/5 (60)	5/ 27 (19)	3.24 (1.11 to 9.42)	0.09
Feeding	2/10 (20)	6/22 (27)	0.73 (0.18 to 3.02)	1.00
Debrillation	0/2 (0)	8/ 30 (0.27)		1.00
Cardiopulmonary resuscitation	0/3 (0)	8/29 (28)		0.55
Chest physiotherapy	2/7 (29)	6/25 (0.24)	1.19 (0.30 to 4.65)	1.00
Assessment of patient	6/ 23 (26)	2/ 9 (22)	1.17 (0.29 to 4.77)	1.00
Insertion of peripheral intravenous line	1/1 (100)	7/31 (23)	4.43 (2.31 to 8.50)	0.25
Endotracheal aspirate	3/12 (25)	5/ 20 (25)	1.00 (0.29 to 3.45)	1.00
Bronchoscopy	1/2 (50)	7/ 30 (23)	2.14 (0.46 to 9.90)	0.44
Radiology procedures	4/15(26)	4/17 (24)	1.13 (0.34 to 3.76)	1.00
Dressing change	1/6 (17)	7/26 (27)	0.62 (0.09 to 4.13)	1.00
Urine specimen collected	1/2 (50)	7/30 (23)	2.14 (0.46 to 9.90)	0.44
Fecal specimen collected	0/1 (0)	8/31(26)		1.00
Rectal swab obtained	0/1 (0)	8/31 (26)		1.00
Nasopharyngeal swab obtained	0/2 (0)	8/30 (27)		1.00
Other	2/5 (40)	6/27 (22)	1.80 (0.50 to 6.50)	0.58

^aSARS, severe acute respiratory syndrome; CI, confidence interval.

wear a mask (RR 0.23, 95% CI 0.07 to 0.78, $p = 0.02$). The RR for infection was 0.22 (95%CI 0.05 to 0.93, $p = 0.06$) when nurses who always wore an N95 mask (2 SARS-infected and 14 noninfected nurses) were compared with nurses who did not wear any mask (N95 or surgical mask) consistently (5 SARS-infected and 4 noninfected nurses). The RR for infection was 0.45 (95%CI 0.07 to 2.71, $p = 0.56$) when nurses who always wore a surgical mask (one SARS-infected and three noninfected nurses) were compared with nurses who did not wear any mask (N95 or surgical mask) consistently (five SARS-infected and four for non-SARS nurses). The difference for SARS infection for nurses who consistently wore N95 masks and those who consistently wore surgical masks was not significant (RR 0.5, 95% CI 0.06 to 4.23, $p = 0.5$).

Time to Event

A Kaplan-Meier curve of the 32 nurses in the cohort who entered a SARS patient's room is shown in Figure. The figure demonstrates onset of symptoms by number of

shifts worked. It shows that if all nurses had worked eight shifts, 53% of them would become infected with SARS. The probability of SARS infection was 6% (8/143) per shift worked.

Discussion

We found that critical care nurses who assisted with suctioning before intubation and intubation of SARS patients were four times more likely to become infected than nurses who did not. Manipulation of a SARS patient's oxygen mask was also a high-risk factor. Our findings support reports that exposure to respiratory secretions or activities that generate aerosols can result in SARS transmission to healthcare workers (13).

The 11 nurses in our study who did not enter a SARS patient's room did not become infected. This finding, along with the finding that respiratory care activities pose high risk, implicates either droplet or limited aerosol generation as a means of transmission to healthcare workers. The finding is compatible with the relative high risk (6%

EMERGENCE OF SARS

Table 2. Summary of exposure, personal protective equipment, and participation in high-risk activities of the nurses in whom SARS developed^a

Nurse	No. of shifts	Location of shift	Total duration of exposure to index patient ^b (min)	Personal protection used when inside SARS patient's room	Participation in high risk activities ^c
1	3	ICU	60	Gown Gloves Surgical mask	
2	3	ICU	385	Gown Gloves N95 Goggles ^d	Intubation, suctioning before intubation
3	3	ICU ^e	190	Gown ^d Gloves ^d N95 ^d	Suctioning before intubation
4	5	ICU	935	Gloves Gown ^d Goggles ^d N95 ^d	Intubation, suctioning before intubation
5	3	ICU	555	Gloves Gown N95 Goggles ^d	Intubation
6	2	CCU	510	None	
7	2	CCU	40	None	
8	2	CCU	510	Gloves ^d	

^aSARS, severe acute respiratory syndrome; ICU, intensive care unit; CCU, coronary care unit.

^bDuration of exposure is defined as time spent in a SARS patient's room.

^cIntubation, suctioning before intubation.

^dIndicates that use of this precaution was inconsistent (was not used on one or more occasions).

^eNurse 3 worked one shift in coronary care unit.

per shift worked) of critical care nurses. Our results did not implicate environmental transmission (i.e., contact through gowns) as a major risk factor. These data are in keeping with the report by Scales and colleagues, in which activities associated with droplet or limited aerosol spread were implicated as important sources of transmission (14).

We found a near 80% reduction in risk for infection for nurses who consistently wore masks (either surgical or N95). This finding is similar to that of Seto and colleagues, who found that both surgical masks and N95 masks were protective against SARS among healthcare workers in Hong Kong hospitals (9). When we compared use of N95 to use of surgical masks, the relative SARS risk associated with the N95 mask was half that for the surgical mask; however, because of the small sample size, the result was not statistically significant. Our data suggest that the N95 mask offers more protection than a surgical mask.

This study focused on critical care nurses working at the first SARS hospital outbreak in Toronto. Since use of personal protective equipment was not standardized during the study period, it was possible to assess the effect of personal protective equipment. The use of personal protective equipment was highly variable because the nurses were often unaware that their patients had SARS. Our results highlight the importance of using personal protective equipment when caring for SARS patients. We estimate that if the entire cohort had used masks consistently, SARS risk would have been reduced from 6% to 1.4% per shift.

A limitation of this study is that it is retrospective. Recall bias on the part of the critical care nurses is a possibility. We believe that by verifying the information provided (e.g., patient care activities) using medical records, and using the medical records to cue the interviewed nurses, we minimized recall bias. Any prospective evaluation (e.g., using an observer in ICU) after the initial outbreak

Table 3. Nurses' risk of acquiring SARS based on use of personal protective equipment^a

Type of personal protective equipment	Attack rate (%) according to personal protective equipment used		Relative risk (95% CI)	2-Tailed Fisher exact p value
	Consistent	Inconsistent		
Gown	3/20 (15)	5/12 (42)	0.36 (0.10 to 1.24)	0.12
Gloves	4/22 (18)	4/10 (40)	0.45 (0.14 to 1.46)	0.22
N95 or surgical mask	3/23 (13)	5/9 (56)	0.23 (0.07 to 0.78)	0.02
N95 ^a	2/16 (13)	5/9 (56)	0.22 (0.05 to 0.93)	0.06
Surgical mask ^b	1/4 (25)	5/9 (56)	0.45 (0.07 to 2.71)	0.56
N95 versus surgical mask ^c	2/16 (13)	1/4 (25)	0.50 (0.06 to 4.23)	0.51

^aSARS, severe acute respiratory syndrome; CI, confidence interval.

^bThe comparator is use of no mask. The denominator n (total=32) changes for these comparisons as the nurses who consistently used the indicated personal protective equipment were compared to nurses who wore no masks.

^cConsistent use of the N95 mask versus consistent use of a surgical mask. The denominator n (total=32) changes for these comparisons as the nurses who consistently used the indicated personal protective equipment were compared to the indicated unique group, rather than to the rest of the nurses.

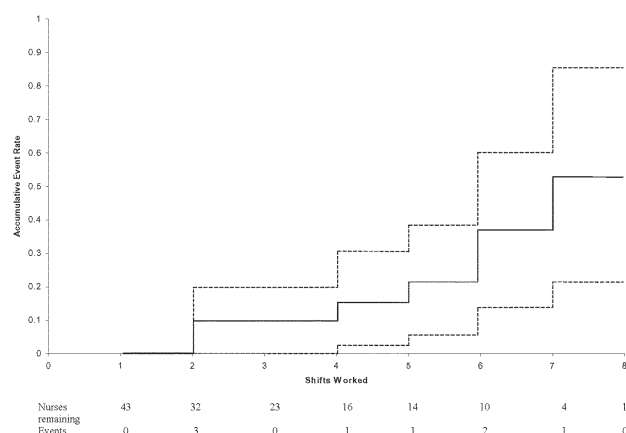


Figure. Onset of symptoms for severe acute respiratory syndrome by number of shifts worked (dashed lines represent 95% confidence limits).

would have been limited by uniformity in use of personal protective equipment (i.e., use of N95 masks, gowns, gloves, goggles). We acknowledge that the study cohort was small, and this limits inferences that can be made. Nevertheless, these data support current recommendations for use of N95 masks and for special precautions when performing intubations on SARS patients.

Acknowledgments

We thank the critical care nurses who participated in this study and acknowledge their dedication and courage in caring for SARS patients.

This study was funded by the Canadian Institutes of Health Research and the Ontario Ministry of Health and Long-term Care. M. Loeb is supported by a career award from the Canadian Institutes for Health Research.

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References:

1. Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K, et al. Identification of severe acute respiratory syndrome in Canada. *N Engl J Med* 2003;348:1995–2005.
2. Ksiazek TG, Erdman D, Goldsmith C, Zaki SR, Peret T, Emery S, et al. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1953–66.
3. Drosten C, Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1967–76.
4. World Health Organization. Cumulative number of probable reported cases of SARS. www.who.int/csr/sars/country/2003_06_30/en/
5. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet* 2003;361:1761–6.
6. Varia M, Wilson S, Sarwal S, McGeer A, Gournis E, Galanis E. Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *CMAJ* 2003;169:285–92.
7. Infection control guidance for healthcare workers in healthcare facilities and other institutional settings. Health Canada Fact Sheet. www.hc-sc.gc.ca/pphb-dgsp/sars-sras/pdf/sarsfactsheetinstitutions06-03-03_e.pdf
8. Updated interim domestic infection control guidance in the health-care and community setting for patients with suspected SARS. CDC recommendations www.cdc.gov/ncidod/sars/infectioncontrol.htm
9. Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, Ho M, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003;361:1519–20.
10. Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA* 2003;289:2801–9.
11. Health Canada. Severe acute respiratory syndrome case definition. http://www.hc-sc.gc.ca/pphb-dgsp/sars-sras/sarscasedef_e.html#case-definition
12. World Health Organization. Case definitions for surveillance of severe acute respiratory syndrome (SARS) (revised May 21, 2003). <http://www.cdc.gov/ncidod/sars/casedefinition.htm>
13. Centers for Disease Control and Prevention. Cluster of severe acute respiratory syndrome cases among protected health-care workers—Toronto, Canada, April 2003. *MMWR* 2003;52:433–6.
14. Scales DC, Green K, Chan AK, Poutanen SM, Foster D, Nowak K, et al. Illness in intensive-care staff after brief exposure to severe acute respiratory syndrome. *Emerg Infect Dis* 2003;9:1205–1210.

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N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel

A Randomized Clinical Trial

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IMPORTANCE Clinical studies have been inconclusive about the effectiveness of N95 respirators and medical masks in preventing health care personnel (HCP) from acquiring workplace viral respiratory infections.

OBJECTIVE To compare the effect of N95 respirators vs medical masks for prevention of influenza and other viral respiratory infections among HCP.

DESIGN, SETTING, AND PARTICIPANTS A cluster randomized pragmatic effectiveness study conducted at 137 outpatient study sites at 7 US medical centers between September 2011 and May 2015, with final follow-up in June 2016. Each year for 4 years, during the 12-week period of peak viral respiratory illness, pairs of outpatient sites (clusters) within each center were matched and randomly assigned to the N95 respirator or medical mask groups.

INTERVENTIONS Overall, 1993 participants in 189 clusters were randomly assigned to wear N95 respirators (2512 HCP-seasons of observation) and 2058 in 191 clusters were randomly assigned to wear medical masks (2668 HCP-seasons) when near patients with respiratory illness.

MAIN OUTCOMES AND MEASURES The primary outcome was the incidence of laboratory-confirmed influenza. Secondary outcomes included incidence of acute respiratory illness, laboratory-detected respiratory infections, laboratory-confirmed respiratory illness, and influenzalike illness. Adherence to interventions was assessed.

RESULTS Among 2862 randomized participants (mean [SD] age, 43 [11.5] years; 2369 [82.8%] women), 2371 completed the study and accounted for 5180 HCP-seasons. There were 207 laboratory-confirmed influenza infection events (8.2% of HCP-seasons) in the N95 respirator group and 193 (7.2% of HCP-seasons) in the medical mask group (difference, 1.0%, [95% CI, -0.5% to 2.5%]; $P = .18$) (adjusted odds ratio [OR], 1.18 [95% CI, 0.95-1.45]). There were 1556 acute respiratory illness events in the respirator group vs 1711 in the mask group (difference, -21.9 per 1000 HCP-seasons [95% CI, -48.2 to 4.4]; $P = .10$); 679 laboratory-detected respiratory infections in the respirator group vs 745 in the mask group (difference, -8.9 per 1000 HCP-seasons, [95% CI, -33.3 to 15.4]; $P = .47$); 371 laboratory-confirmed respiratory illness events in the respirator group vs 417 in the mask group (difference, -8.6 per 1000 HCP-seasons [95% CI, -28.2 to 10.9]; $P = .39$); and 128 influenzalike illness events in the respirator group vs 166 in the mask group (difference, -11.3 per 1000 HCP-seasons [95% CI, -23.8 to 1.3]; $P = .08$). In the respirator group, 89.4% of participants reported "always" or "sometimes" wearing their assigned devices vs 90.2% in the mask group.

CONCLUSIONS AND RELEVANCE Among outpatient health care personnel, N95 respirators vs medical masks as worn by participants in this trial resulted in no significant difference in the incidence of laboratory-confirmed influenza.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: [NCT01249625](https://clinicaltrials.gov/ct2/show/study/NCT01249625)

JAMA. 2019;322(9):824-833. doi:10.1001/jama.2019.11645

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Health care personnel (HCP) who are routinely exposed to viral respiratory infections in the workplace¹ may transmit infection to others. It is widely recognized that HCP, as a group, incompletely adhere to infection prevention recommendations and practice standards. Inpatient respiratory protection studies suggest adherence rates vary from 10% to 84%.²⁻⁴ While laboratory studies designed to achieve 100% intervention adherence have shown that N95 filtering facepiece respirators are more efficacious than medical masks at reducing exposure to aerosols,⁵ comparative clinical effectiveness studies have been inconclusive.^{3,4,6} Some experts argue that N95 respirators and medical masks are equivalent in clinical settings.^{2,7} Pragmatic effectiveness trials are increasingly recognized as an essential component of medical evidence, in part because efficacy studies may overestimate effectiveness and true adherence.⁸

Disposable N95 respirators and medical masks are both worn by HCP for self-protection; however, these masks have different intended uses. N95 respirators are designed to prevent the wearer from inhaling small airborne particles,⁹ must meet filtration requirements,¹⁰ and fit tightly to the wearer's face, limiting facial seal leakage. Medical masks, frequently called surgical masks, are intended to prevent microorganism transmission from the wearer to the patient. Medical masks fit the face loosely and do not reliably prevent inhalation of small airborne particles. However, medical masks prevent hand-to-face contact and facial contact with large droplets and sprays.¹¹

Clinical evidence is inconclusive regarding whether N95 respirators are more effective than medical masks for preventing viral respiratory infection among HCP, including influenza,^{3,4,6,12} accounting for differing practices² and positions held by clinical,⁷ public health,^{13,14} and regulatory organizations.¹⁵ The objective of this study was to compare¹³ the effectiveness of N95 respirators vs medical masks worn by HCP in clinical practice for prevention of workplace-acquired influenza and other viral respiratory infections in geographically diverse, high-exposure, outpatient settings.

Methods

Study Sites and Institutional Review Boards

The Respiratory Protection Effectiveness Clinical Trial (ResPECT) was approved by the human subjects research board at the National Institute for Occupational Safety and Health (protocol #10-NPPTL-O5XP) and the institutional review boards (IRBs) at the 7 participating health systems, as previously described,¹⁶ and approved or exempted by IRBs at the analysis and sample storage sites. All participants were permitted to participate for 1 or more years and gave written consent for each year of participation. Study intervention sites included outpatient settings at the Children's Hospital Colorado (Aurora), Denver Health Medical Center (Denver, Colorado), Johns Hopkins Health System (Baltimore, Maryland), Michael E. DeBakey Veterans Affairs (VA) Medical Center (Houston, Texas), VA Eastern Colorado Healthcare System (Denver), Washington DC VA Medical Center, and

Key Points

Question Is the use of N95 respirators or medical masks more effective in preventing influenza infection among outpatient health care personnel in close contact with patients with suspected respiratory illness?

Findings In this pragmatic, cluster randomized clinical trial involving 2862 health care personnel, there was no significant difference in the incidence of laboratory-confirmed influenza among health care personnel with the use of N95 respirators (8.2%) vs medical masks (7.2%).

Meaning As worn by health care personnel in this trial, use of N95 respirators, compared with medical masks, in the outpatient setting resulted in no significant difference in the rates of laboratory-confirmed influenza.

VA New York Harbor Healthcare System (New York). Sample storage and data analysis sites were the VA St Louis Healthcare System and St Louis University (St Louis, Missouri), University of Florida (Gainesville), University of Massachusetts (Amherst), and University of Texas Southwestern Medical Center (Dallas).

Design and Oversight

This cluster randomized, multicenter, pragmatic effectiveness trial¹⁶ conducted between September 2011 and May 2015, with final follow-up on June 28, 2016, compared the effect of N95 respirators, used as recommended during the 2009 H1N1 pandemic,¹³ and medical masks, used as recommended to prevent seasonal influenza^{17,18} and other viral respiratory infections and illnesses, among HCP.¹⁷ The investigators were blinded to the randomization until completion of the study and analysis. An independent data and safety monitoring board assessed the data. Additional details are included in [Supplement 1](#), including the statistical analysis plan and the full protocol that was previously published in an abridged format.¹⁶

Participants and Setting

This trial was conducted in diverse outpatient settings serving adult and pediatric patients with a high prevalence of acute respiratory illness, including primary care facilities, dental clinics, adult and pediatric clinics, dialysis units, urgent care facilities and emergency departments, and emergency transport services.

All participants in a cluster worked in the same outpatient clinic or outpatient setting. A cluster randomized design was used to improve adherence and increase indirect effects associated with participants in a cluster using the same intervention. Participants were aged at least 18 years, employed at one of the 7 participating health systems, and self-identified as routinely positioned within 6 feet (1.83 m) of patients. Participants were full-time employees (defined as direct patient care for approximately ≥24 hours weekly) and worked primarily at the study site (defined as ≥75% of working hours). Exclusion criteria were medical conditions precluding safe participation or anatomic features that

Box 1. Criteria for Acute Respiratory Illness^a**Signs**

Coryza

Fever (temperature >37.8 °C)

Lymphadenopathy

Tachypnea (respiratory rate >25/min)

Symptoms

Arthralgias/myalgias/body aches

Chills

Cough

Diarrhea

Dyspnea

Fatigue

Headache

Malaise

Other gastrointestinal systems

Sore throat

Sputum production

Sweats

Vomiting/nausea

^a An acute respiratory illness was defined as the presence of at least 1 sign or 2 symptoms listed, representing a change from baseline.

could interfere with respirator fit, such as facial hair or third-trimester pregnancy. Participants self-identified race and sex using fixed categories; these variables were collected because facial anthropometrics related to race and sex may influence N95 respirator fit.

Participants kept diaries that included signs and symptoms of respiratory illness, annual influenza vaccination status, and exposure to household and community members with respiratory illness. Participants also recorded their participation in aerosol-generating procedures and exposure to patients, coworkers, or both with respiratory illness daily. Participants were categorized for exposure risk by occupational roles.

Procedures, Interventions, and Group Allocation

Each year, participating sites were cluster randomized to have participants wear N95 respirators¹³ or medical masks,^{17,18} as previously described.¹⁶ N95 respirator models studied were the 3M Corporation 1860, 1860S, and 1870 (St Paul, Minnesota) and the Kimberly Clark Technol Fluidshield PFR95-270, PFR95-274 (Dallas, Texas); medical mask models were the Precept 15320 (Arden, North Carolina) and Kimberly Clark Technol Fluidshield 47107 (Dallas, Texas).

Within each medical center, for each study year, pairs of clusters (clinics and other settings) were matched by the number of participants, health services delivered, patient population served, and additional personal protective equipment. One cluster was randomly assigned to the medical mask group and one to the N95 respirator group. Random allocation of clusters required using constrained

randomization, a process that maintains random assignment and balance between groups.¹⁹ Computer-generated random sequences of group assignments were generated by an individual not involved in the study implementation and data analyses. Random sequences of assignment assured that every participant in each season had an equal probability of being assigned to the N95 respirator and medical mask groups and allowed participants to switch groups between seasons. Occupational Safety and Health Administration-accepted fit testing¹⁵ of N95 respirators was conducted annually for all study participants.

Participants were instructed to wear their assigned protective devices (ie, N95 respirators or medical masks) during the 12-week period (the intervention period) during which the incidence of viral respiratory illness and infections was expected to be highest that year, as predicted by the ALERT algorithm²⁰ developed for this trial. Participants were instructed to put on a new device whenever they were positioned within 6 feet (1.83 m) of patients with suspected or confirmed respiratory illness. Hand hygiene was recommended to all participants in accordance with Centers for Disease Control and Prevention guidelines.^{13,17,18} Infection prevention policies were followed at each study site. Participants volunteered to participate for up to 12 weeks each intervention period, for a total of 48 weeks of intervention spanning 4 consecutive viral respiratory seasons.

Surveillance, Outcomes, and Measures of Effectiveness

Study personnel obtained swabs of the anterior nares and oropharynx²¹ (FLOQSwabs UTM, Diagnostic Hybrids) from participants who self-reported symptoms of respiratory illness (Box 1). Symptomatic swabs were collected within 24 hours of self-report, and again if signs or symptoms persisted beyond 7 days. If symptomatic participants were not at work, samples were self-obtained using a structured process and shipped to the study laboratory. During each 12-week intervention period, 2 random swabs were obtained from all participants, typically while asymptomatic. Additionally, each year, paired serum samples obtained from all participants were assayed for influenza hemagglutinin levels before and after peak viral respiratory season.

The prespecified primary outcome was the incidence of laboratory-confirmed influenza, defined as detection of influenza A or B virus by reverse-transcription polymerase chain reaction²² in an upper respiratory specimen collected within 7 days of symptom onset; detection of influenza from a randomly obtained swab from an asymptomatic participant; or influenza seroconversion (symptomatic or asymptomatic), defined as at least a 4-fold rise in hemagglutination inhibition antibody titers to influenza A or B virus between pre-season and post-season serological samples deemed not attributable to vaccination. Individuals experiencing seroconversion were not required to have a detected symptomatic illness to meet the defined outcome. Influenza reagents used in the hemagglutination inhibition antibody assays were obtained from the International Reagent Resource Program, established by the Centers for Disease Control and Prevention.

Secondary outcome measures were the incidence of 4 measures of viral respiratory illness and infection: (1) acute respiratory illness (Box 1) with or without laboratory confirmation; (2) laboratory-detected respiratory infection, defined as detection of a respiratory pathogen by polymerase chain reaction or serological evidence of infection with a respiratory pathogen during the study surveillance period(s), which was added to the protocol prior to data analysis; (3) laboratory-confirmed respiratory illness, identified as previously described,²³ defined as self-reported acute respiratory illness plus the presence of at least 1 polymerase chain reaction-confirmed viral pathogen (Box 2) in a specimen collected from the upper respiratory tract within 7 days of the reported symptoms and/or at least a 4-fold rise from preintervention to post-intervention serum antibody titers to influenza A or B virus; and (4) influenzalike illness, defined as temperature of at least 100°F (37.8°C) plus cough and/or a sore throat, with or without laboratory confirmation.

Adherence to Group Assignment and Infection Prevention and Control Practices

Participants were reminded to adhere to protective device and hand hygiene instructions by signage posted at study sites, email, and by study personnel in person. Adherence to assigned devices were reported daily by participants as “always,” “sometimes,” “never,” or “did not recall.” In addition, study personnel observed participants’ device-wearing behaviors as they entered and exited patient care rooms by conducting unannounced, inconspicuous visits to randomly selected study sites throughout the intervention period. However, to preserve patient confidentiality, monitors were not permitted to enter patient care rooms.

Statistical Analyses

Although we identified no standard definition of a “clinically significant difference,” this study¹⁶ was designed to detect a 25% relative reduction in the incidence of laboratory-confirmed influenza or respiratory illness, based on expert opinion, rather than an absolute reduction, which has been described in a previous study.⁶ The total sample size required to provide 80% power to show a 25% reduction in the incidence of laboratory-confirmed influenza in the N95 respirator group compared with the medical mask group, with a type I error rate of .05, was 10 024 participant-sessions, and the sample size needed to provide 80% power to show a 25% reduction in the incidence of laboratory-confirmed respiratory illness was 5104 participant-seasons.

Comparative effects of the interventions were estimated for the primary and secondary outcomes by calculating odds ratios (ORs; for binary outcomes) and incidence rate ratios (IRRs; for count outcomes) between participant clusters randomly assigned to wear N95 respirators or medical masks. Laboratory-confirmed influenza was modeled using logistic regression and viral respiratory infection and illness outcomes were modeled using Poisson regression. Unadjusted and adjusted analyses (both prespecified) were conducted according to the statistical analysis plan (Supplement 2). The primary outcome was an adjusted analysis, as

Box 2. Respiratory Pathogens Assayed by Polymerase Chain Reaction

Adenoviruses

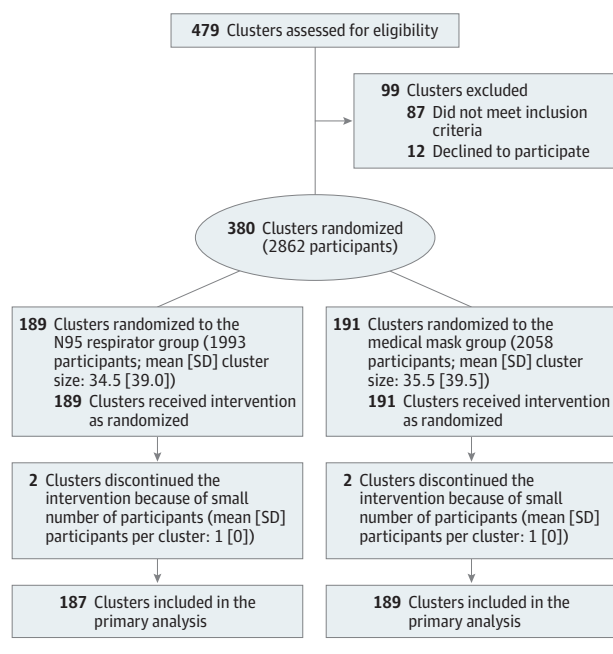
Coxsackie/echoviruses
Coronavirus HKU1
Coronavirus NL63
Coronavirus OC43
Coronavirus 229E
Human metapneumovirus
Human rhinovirus
Influenza A
Influenza B
Parainfluenza virus type 1
Parainfluenza virus type 2
Parainfluenza virus type 3
Parainfluenza virus type 4a
Parainfluenza virus type 4b
Respiratory syncytial virus type A
Respiratory syncytial virus type B

specified in the statistical analysis plan. Prespecified covariates used in adjusted analyses included age, sex, race, number of household members younger than 5 years, occupation risk level (defined as low, medium, or high), binary season-specific influenza vaccination status, the proportion of daily exposures to others with respiratory illness, categorical self-reported adherence to hand hygiene, and intervention group assignment. Prespecified adherence rates were calculated as the proportion of reports of adherence in each group reporting “always,” “sometimes,” “never,” or “did not recall.” Comparison of proportions between groups were done using χ^2 statistics and comparisons of binomial proportions. Analyses included random effects to account for correlation of outcomes at site-level and individual-level random effects to account for correlation of outcomes at the individual level for participants who participated for multiple seasons.

The primary analysis used available data on all randomized participants for the primary comparison of the intervention. A per-protocol analysis, conducted at the same time as the primary analysis, included only individuals who completed at least 8 weeks of study participation.

A sensitivity analysis was conducted using imputation to assign outcomes to participants who did not complete the study. Missing outcomes were imputed using standard multiple imputation techniques, creating multiple imputed data sets with no missing values for each analysis.²³ Details of this analysis are described in Supplement 2. Intervention group withdrawal rates and time to withdrawal were compared to assess for potential bias. In an additional sensitivity analysis, observed and self-reported exposures and adherence were compared using Pearson χ^2 tests. Mean workplace and household rates of exposure to respiratory illness were compared using mixed-effects logistic regression. For

Figure 1. Study Site Enrollment, Randomization, Follow-up, and Analysis in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza Among Health Care Personnel



all calculations, a 2-sided type I error probability of .05 was used. Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory. All statistical analyses were performed in R version 3.3.3 (R Foundation).

Results

Participants

The study sites were randomized to provide 380 cluster-seasons of observation over 4 consecutive intervention periods. Of the 2862 participants, 1416 participated for more than 1 year or intervention period. Among 2862 unique randomized participants (mean [SD] age, 43 [11.5] years; 2369 [82.8%] women), 2371 completed the ResPECT protocol over the course of 48 weeks of intervention spanning 4 years. Among these individuals, 1446 participated in one 12-week intervention period, 723 participated in two 12-week intervention periods, and 693 participated in 3 or more 12-week intervention periods, accounting for 5180 HCP-seasons enrolled and randomized from 137 medical centers. Following randomization, 491 participants withdrew or were excluded because the cluster size was below a preestablished threshold of 2. Overall, 4689 HCP-seasons were included in the per-protocol analysis (2243 in the N95 respirator group and 2446 in the medical mask group; **Figure 1**). Some members of the primary analytic cohort did not complete all weeks of the study and were missing serological outcomes. Data were missing because of early withdrawal in 189 of 2512 participants (7.5%) in the N95 respira-

tor group and 145 of 2668 (5.4%) in the medical mask group. In the per-protocol analysis, data were missing from 16 of 2243 participants (0.7%) in the N95 respirator group and 28 of 2446 (1.1%) in the medical mask group.

Baseline characteristics of the participants in the N95 respirator and medical mask groups were similar (**Table 1**). Daily workplace exposure to respiratory illness was reported 22.5% of the time in the N95 group and 21.6% of the time in the medical mask group, while weekly household exposure to respiratory illness was reported 3.6% of the time in the N95 respirator group and 3.4% of the time in the medical mask group (**Table 1**).

Illness Surveillance and Effectiveness

In the primary analysis, the incidence of laboratory-confirmed influenza infection events occurred in 207 of 2512 HCP-seasons (8.2%) in the N95 respirator group and 193 of 2668 HCP-seasons (7.2%) in the medical mask group, (difference, 1.0% [95% CI, -0.5% to 2.5%]; $P = .18$) (adjusted OR, 1.18 [95% CI, 0.95-1.45]).

Regarding secondary outcomes, there were 1556 acute respiratory illness events in the N95 respirator group (incidence rate [IR], 619.4 per 1000 HCP-seasons) vs 1711 in the medical mask group (IR, 641.3 per 1000 HCP-seasons) (difference, -21.9 per 1000 HCP-seasons [95% CI, -48.2 to 4.4]; $P = .10$; adjusted IRR, 0.99 [95% CI, 0.92-1.06]). There were 679 laboratory-detected respiratory infection events in the N95 respirator group (IR, 270.3 per 1000 HCP-seasons) vs 745 in the medical mask group (IR, 279.2 per 1000 HCP-seasons) (difference, -8.9 per 1000 HCP-seasons [95% CI, -33.3 to 15.4]; $P = .47$; adjusted IRR, 0.99 [95% CI, 0.89-1.09]) (**Table 2** and **Figure 2**). Overall, 371 laboratory-confirmed respiratory illness events occurred in the N95 respirator group (IR, 147.7 per 1000 HCP-seasons) vs 417 in the medical mask group (IR, 156.3 per 1000 HCP-seasons) (difference, -8.6 per 1000 HCP-seasons [95% CI, -28.2 to 10.9]; $P = .39$; adjusted IRR, 0.96 [95% CI, 0.83-1.11]). There were 128 influenzalike illness events in the N95 respirator group (IR, 51.0 per 1000 HCP-seasons) vs 166 in the medical mask group (IR, 62.2 per 1000 HCP-seasons) (difference, -11.3 per 1000 HCP-seasons [95% CI, -23.8 to 1.3]; $P = .08$; adjusted IRR, 0.86 [95% CI, 0.68-1.10]). Results were similar in the adjusted primary analysis and per-protocol analyses (**Figure 2**).

Intervention, Adherence, and Adverse Events

Adherence was reported on daily surveys 22 330 times in the N95 respirator group and 23 315 times in the medical mask group. "Always" was reported 14 566 (65.2%) times in the N95 respirator group and 15 186 (65.1%) times in the medical mask group; "sometimes," 5407 (24.2%) times in the N95 respirator group and 5853 (25.1%) times in the medical mask group; "never," 2272 (10.2%) times in the N95 respirator group and 2207 (9.5%) times in the medical mask group; and "did not recall," 85 (0.4%) times in the N95 respirator group and 69 (0.3%) times in the medical mask group. Participant-reported adherence could not be assessed in 784 participants (31.2%) in the N95 respirator group and 822 (30.8%) in the medical mask group ($P = .84$).

Table 1. Health Care Personnel (HCP) Demographic Characteristics, Risk Factors, and Site Enrollment in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza

Characteristic	No. (%) N95 Respirator (n = 2512 HCP-Seasons) ^a	Medical Mask (n = 2668 HCP-Seasons) ^a
Age, mean (SD), y	43 (11.5)	43 (11.6)
Sex		
Men	378 (15.0)	420 (15.7)
Women	2134 (85.0)	2248 (84.3)
Ethnicity		
Hispanic or Latino	397 (15.8)	427 (16)
Race	(n = 2447)	(n = 2600)
White	1282 (52.4)	1334 (51.3)
Black	720 (29.4)	782 (30.1)
Other	232 (9.5)	252 (9.7)
Asian	195 (8.0)	210 (8.1)
American Indian or Alaska Native	14 (0.6)	13 (0.5)
Native Hawaiian or other Pacific Islander	4 (0.2)	9 (0.3)
Occupation		
Nurse/nursing trainee	1049 (41.8)	1085 (40.7)
Clinical care support staff ^b	574 (22.9)	627 (23.5)
Administrative/clerical	332 (13.2)	337 (12.6)
Other occupation	213 (8.5)	224 (8.4)
Physician/advanced practitioner/physician trainee	207 (8.2)	240 (9.0)
Registration/clerical reception	94 (3.7)	106 (4.0)
Social worker/pastoral care	35 (1.4)	29 (1.1)
Environmental services/housekeeping	8 (0.3)	19 (0.7)
Occupational risk ^c		
High	1492 (59.4)	1594 (59.7)
Medium	295 (11.7)	318 (11.9)
Low	724 (28.8)	755 (28.3)
Patient population		
Adult	1409 (56.1)	1486 (55.7)
Pediatric	573 (22.8)	557 (20.9)
Adult and pediatric	530 (21.1)	625 (23.4)
Clinic type		
Primary care	1734 (69.0)	1881 (70.5)
Emergent/urgent care	665 (26.5)	700 (26.2)
Emergency transport	42 (1.7)	33 (1.2)
Specialty care	40 (1.6)	29 (1.1)
Dental/dialysis	31 (1.2)	25 (0.9)
Site		
Johns Hopkins Health System	882 (35.1)	859 (32.2)
Denver Health	534 (21.3)	521 (19.5)
VA New York Harbor Healthcare System	375 (14.9)	433 (16.2)
The Michael E. DeBakey VA Medical Center	233 (9.3)	287 (10.8)
Washington DC VA Medical Center	183 (7.3)	204 (7.6)
VA Eastern Colorado Healthcare System	177 (7.0)	211 (7.9)
Children's Hospital Colorado	128 (5.1)	153 (5.7)

(continued)

Table 1. Health Care Personnel (HCP) Demographic Characteristics, Risk Factors, and Site Enrollment in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza (continued)

Characteristic	No. (%) N95 Respirator (n = 2512 HCP-Seasons) ^a	Medical Mask (n = 2668 HCP-Seasons) ^a
Comorbid conditions		
Asthma	255 (10.2)	284 (10.6)
Other systemic disease	104 (4.1)	118 (4.4)
Other respiratory disease	49 (2.0)	37 (1.4)
Cardiac disease	41 (1.6)	34 (1.3)
Chronic obstructive pulmonary disease	6 (0.2)	6 (0.2)
Influenza vaccination status	(n = 2444)	(n = 2598)
Vaccinated	1993 (79.3)	2048 (76.8)
Not vaccinated	451 (18.0)	550 (20.6)
Other risk factors		
Eyeglasses wearer	960 (38.2)	999 (37.4)
Household members aged <5 y	606 (24.1)	630 (23.6)
Contact lens wearer	371 (14.8)	349 (13.1)
Tobacco smoker	210 (8.4)	234 (8.8)
Exposure to respiratory illness, %		
Daily workplace	22.5	21.6
Weekly household	3.6	3.4

Abbreviation: VA, veterans affairs.

^a Unless otherwise specified.^b Staff who have direct patient contact, such as clinical medical assistants and clinical technicians.^c Occupational risk based on direct patient contact, such as physical examination and/or performance of high-risk procedures (intubation, airway suctioning, nebulizer treatments, nasopharyngeal aspiration) for high risk, direct patient contact for medium risk, and no or minimal direct patient contact for low risk.

because of lack of response to surveys or lack of adherence opportunities (ie, participants did not encounter an individual with respiratory signs or symptoms).

Analyzed post hoc, participant adherence was reported as always or sometimes 89.4% of the time in the N95 respirator group and 90.2% of the time in the medical mask group. Additional details about adherence are included in [Supplement 1](#). No serious study-related adverse events were reported. Nineteen participants reported skin irritation or worsening acne during years 3 and 4 at one study site in the N95 respirator group.

Per-Protocol Analysis and Sensitivity Analysis

Results of the per-protocol analysis can be seen in Figure 2. A sensitivity analysis assessed whether there was evidence for bias in self-reported outcomes based on group assignment. In a prespecified multiple-imputation analysis, the rates of laboratory-confirmed influenza infection events were 204 of 2243 HCP seasons (9.1%) in the N95 respirator group and 190 of 2446 HCP-seasons (7.8%) in the medical mask group. Quantitative data are available in [Supplement 3](#).

Table 2. Primary and Secondary Outcomes in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza Among Health Care Personnel

Primary and Secondary Outcome Events	No.									
	2011-2012		2012-2013		2013-2014		2014-2015		Totals	
	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask
Influenza (primary outcome)										
Polymerase chain reaction-detected										
Influenza A	2	3	19	19	8	12	37	28	66	62
Influenza B	0	3	8	11	2	1	1	4	11	19
Hemagglutination inhibition assay-detected										
Influenza A	5	9	30	23	38	38	55	47	128	117
Influenza B	0	2	10	11	12	13	14	10	36	36
All events ^a										
Influenza A	6	10	43	37	46	42	85	65	180	154
Influenza B	0	5	15	18	12	14	15	13	42	50
All influenza	6	15	58	55	58	56	100	78	222	204
Laboratory-confirmed influenza	6	13	52	52	55	51	94	77	207	193
Secondary Outcomes										
Acute respiratory illness	235	234	354	446	398	519	569	512	1556	1711
Laboratory-detected respiratory infection ^b	47	71	165	201	217	260	250	213	679	745
Laboratory-confirmed respiratory illness ^b	26	31	91	116	111	150	143	120	371	417
Influenza-like illness	13	10	30	45	22	50	63	61	128	166

^a Influenza events were defined as the number of influenza infections attributed to the combination of polymerase chain reaction detection and hemagglutination

inhibition assay serologies. Instances in which polymerase chain reaction and hemagglutination inhibition assay were both positive counted as 1 event.

^b All respiratory viruses assayed, including influenza.

Discussion

In this pragmatic, cluster randomized trial that involved multiple outpatient sites at 7 health care delivery systems across a wide geographic area over 4 seasons of peak viral respiratory illness, there was no significant difference between the effectiveness of N95 respirators and medical masks in preventing laboratory-confirmed influenza among participants routinely exposed to respiratory illnesses in the workplace. In addition, there were no significant differences between N95 respirators and medical masks in the rates of acute respiratory illness, laboratory-detected respiratory infections, laboratory-confirmed respiratory illness, and influenza-like illness among participants. A sensitivity analysis suggested that the primary analysis reported was fairly robust to the missing outcome data with quantitative outcomes varying by less than 5%. This supports the finding that neither N95 respirators nor medical masks were more effective in preventing laboratory-confirmed influenza or other viral respiratory infection or illness among participants when worn in a fashion consistent with current US clinical practice.

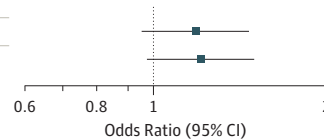
Respiratory viruses are primarily transmitted by large droplets. Because a fraction of respiratory viruses may be transmitted by aerosol, N95 respirators have been presumed to provide better protection than medical masks against viral

respiratory infections in health care settings.² However, definitive evidence of greater clinical effectiveness of N95 respirators is lacking. A well-designed trial⁶ found the effectiveness of medical masks to be noninferior to N95 respirators, but the trial was stopped prematurely and was limited by small sample size. Two additional studies^{3,4} (and a pooled analysis¹²) concluded that N95 respirators may be more effective than medical masks; however, these studies were limited by uncertain clinical significance of end points.²⁴ The current study was undertaken because of remaining uncertainty based on previous studies, which made it challenging for infection control clinicians to effectively implement respiratory protection programs in health care settings.^{2,7,13,18,24,25}

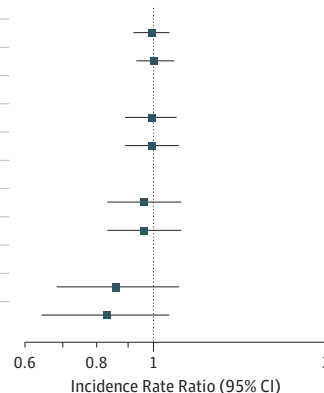
This trial was designed to assess clinical effectiveness, taking into account many challenges of working in outpatient health care settings. This study had several strengths, including the pragmatic design; wide US geographic and climatic distribution; varied adult and pediatric outpatient settings, including emergency departments; and enrollment spanning 4 seasons of peak viral respiratory illness. Respiratory samples were obtained from symptomatic and asymptomatic participants to determine the incidence of viral respiratory infection, including individuals that were subclinical but still potentially transmissible. Influenza vaccination status information was collected. This trial was cluster randomized to avoid mixing of interventions in each clinic and clinical setting and to minimize cross-contamination from

Figure 2. Primary and Secondary Outcomes of Influenza and Respiratory Illnesses and Adjusted Risk Estimates Among Health Care Personnel in the N95 Respirator Group vs the Medical Mask Group**A** Primary outcome

	N95 Respirator Events/Seasons	Medical Mask Events/Seasons	Incidence Rate Ratio (95% CI)
Laboratory-confirmed influenza			
ITT cohort	207/2512	193/2668	1.18 (0.95-1.45)
PP cohort	204/2243	190/2446	1.20 (0.97-1.48)

**B** All secondary outcomes

	N95 Respirator Events/Seasons	Medical Mask Events/Seasons	Incidence Rate Ratio (95% CI)
Acute respiratory illness			
ITT cohort	1556/2512	1711/2668	0.99 (0.92-1.06)
PP cohort	1512/2243	1656/2446	1.00 (0.93-1.08)
Laboratory-detected respiratory infection			
ITT cohort	679/2512	745/2668	0.99 (0.89-1.09)
PP cohort	664/2243	733/2446	0.99 (0.89-1.10)
Laboratory-confirmed respiratory illness			
ITT cohort	371/2512	417/2668	0.96 (0.83-1.11)
PP cohort	361/2243	406/2446	0.96 (0.83-1.11)
Influenza-like illness			
ITT cohort	128/2512	166/2668	0.86 (0.68-1.10)
PP cohort	121/2243	161/2446	0.83 (0.64-1.06)



The adjusted relative risks for the N95 respirator and medical mask groups for both the intention-to-treat (ITT) and per-protocol (PP) groups for the primary outcome and the other predetermined secondary outcomes. Values above 1 indicate higher relative odds or risk in the N95 respirator group compared with the medical mask group.

different HCP behaviors, conducted at 7 medical centers among frontline HCP in varied clinical settings with high exposure risk, and sufficiently powered to detect the predefined difference in laboratory-confirmed respiratory illness. Previous effectiveness studies^{3,4,6,12,26-28} have met some, but not all, of these characteristics and have been inconclusive, contributing to the uncertainty and controversy among experts determining public health guidance, regulatory requirements, and health care delivery practices.^{2,7,14,17,29} In the current study, findings were consistent across all laboratory-based outcomes and clinical syndromes. Results for the primary and secondary outcomes were in opposite directions (ie, one IRR was associated with increased risk and the other with decreased risk), although the differences were nonsignificant, further supporting a finding of no significant difference in the effectiveness of N95 respirators vs medical masks for prevention of influenza or other respiratory illness.

Limitations

This study has several limitations. First, the criteria for viral polymerase chain reaction testing may have missed participants who were infected but asymptomatic. Unrecognized infections may have increased the probability of finding no difference between interventions, even if a difference existed. Second, self-reporting of symptoms in daily diaries likely underestimated illness among HCP who often work while ill.³⁰ Third, despite being intentionally conducted as a pragmatic effectiveness trial,⁸ incomplete participant adherence to as-

signed protective devices could have contributed to more unprotected exposures, increasing the probability of finding no difference between interventions even if a difference existed. However, participant-reported data indicates this did not differ by study group. Fourth, participants were not instructed to wear protective devices outside the workplace, which may have biased the results toward finding no difference between groups, although the rates of adherence did not differ by study group and household exposure was reported as much lower than workplace exposure. Fifth, only 2 N95 respirator and medical mask models were studied, limiting the ability to generalize about the protectiveness of other models. Sixth, the sample size required to definitively determine whether N95 respirators or medical masks are more effective for protection from laboratory-confirmed influenza in the health care setting required approximately 10 000 participant-seasons, which was not feasible with the available funding or resources. However, the morbidity and mortality associated with a wide range of viral respiratory infections, including novel and emerging pathogens, renders a secondary outcome in this study, laboratory-confirmed respiratory illness, important.

Conclusions

Among outpatient HCP, N95 respirators vs medical masks as worn by participants in this trial resulted in no significant difference in the incidence of laboratory-confirmed influenza.

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Accepted for Publication: July 25, 2019.

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Conflict of Interest Disclosures: Dr Bessesen reported receiving grants from the Department of Veterans Affairs during the conduct of the study. Dr Brown reported receiving grants from the US Department of Veterans Affairs during the conduct of the study. Dr Cummings reported receiving grants from the Centers for Disease Control and Prevention, the National Institutes of Health, and

MedImmune outside the submitted work and the Biomedical Advanced Research and Development Authority during the conduct of the study. Ms Los reported receiving grants from Centers for Disease Control and Prevention, the Veterans Health Administration, and the Biodefense Advanced Research and Development Agency during the conduct of the study. Dr Gibert reported receiving financial support for the conduct of the study, including research personnel, from the Veterans Health Administration during the conduct of the study. Dr Gorse reported receiving grants from the US Department of Veterans Affairs during the conduct of the study. Dr Nyquist reported receiving grants from the Centers for Disease Control and Prevention/Division of Healthcare Quality Promotion, the National Institute for Occupational Safety and Health, and the Veterans Health Administration during the conduct of the study; personal fees and nonfinancial support from Sequirus outside the submitted work; and serving on a policy making committee regarding infectious disease for the American Academy of Pediatrics Committee on Infectious Diseases. Dr Reich reported receiving grants from Veterans Health Administration during the conduct of the study. Dr Rodriguez-Barradas reported receiving grants from Veterans Affairs Central Office during the conduct of the study. Dr Perl reported receiving grants from the Centers for Disease Control and Prevention and Biomedical Advanced Research and Development Authority during the conduct of the study and grants from MedImmune outside the submitted work. No other disclosures were reported.

Funding/Support: This trial was funded by the US Centers for Disease Control and Prevention, Veterans Health Administration, and the Biodefense Advanced Research and Development Agency.

Role of the Funder/Sponsor: The sponsors were not involved in data collection, analysis, or interpretation; writing of the manuscript; or the decision to submit the manuscript. The sponsors reviewed and made technical comments about the study protocol prior to enrollment and the final manuscript prior to submission for publication.

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Disclaimer: The findings and conclusions in this article are the authors' own and do not necessarily represent the views of the National Institute for Occupational Safety and Health, the Centers for Disease Control and Prevention, the Department of Veterans Affairs, or other affiliates. Mention of product names does not imply endorsement. All information and materials in this article are original.

Data Sharing Statement: See Supplement 4.

Additional Contributions: We thank the members of the data and safety monitoring board, Daniel Morgan, MD (University of Maryland, Baltimore), Elizabeth Colantuoni, PhD (Johns Hopkins Bloomberg School of Public Health, Baltimore), and Tia Powell, MD (Albert Einstein College of Medicine, Bronx). We also thank David Weissman, MD (National Institute for Occupational Safety and Health) and Michael Hodgson, MD (Occupational Safety and Health Administration). None of our consults were financially compensated for their expertise, support, and guidance throughout the study. We are immensely grateful to the study personnel and coordinators, the supporting clinical staff, and, most importantly, the participants.

REFERENCES

- Goins WP, Talbot HK, Talbot TR. Health care-acquired viral respiratory diseases. *Infect Dis Clin North Am*. 2011;25(1):227-244. doi:10.1016/j.idc.2010.11.010
- Institute of Medicine. *Preparing for an Influenza Pandemic: Personal Protective Equipment for Healthcare Workers*. Washington, DC: National Academies Press; 2008.
- MacIntyre CR, Wang Q, Cauchemez S, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other*

Respir Viruses. 2011;5(3):170-179. doi:10.1111/j.1750-2659.2011.00198.x

4. MacIntyre CR, Wang Q, Seale H, et al. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am J Respir Crit Care Med*. 2013;187(9):960-966. doi:10.1164/rccm.201207-1164OC
5. Noti JD, Lindsley WG, Blachere FM, et al. Detection of infectious influenza virus in cough aerosols generated in a simulated patient examination room. *Clin Infect Dis*. 2012;54(11):1569-1577. doi:10.1093/cid/cis237
6. Loeb M, Dafoe N, Mahony J, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA*. 2009;302(17):1865-1871. doi:10.1001/jama.2009.1466
7. Rupp ME, Whitley R, Nutty C. *Letter on Federal PPE Guidance*. Washington, DC: Infectious Diseases Society of America/Society for Healthcare Epidemiology of America/Association of Professionals in Infection Control and Epidemiology. https://www.idsociety.org/globalassets/idsa/policy--advocacy/current_topics_and_issues/infection-prevention--control/comments/1100509-shea-idsa-apic-letter-re-ppe-guidance.pdf. Published November 5, 2009. Accessed March 28, 2019.
8. Ford I, Norrie J. Pragmatic trials. *N Engl J Med*. 2016;375(5):454-463. doi:10.1056/NEJMr1510059
9. Janssen L, Ettinger H, Graham S, Shaffer R, Zhuang Z. The use of respirators to reduce inhalation of airborne biological agents. *J Occup Environ Hyg*. 2013;10(8):D97-D103. doi:10.1080/15459624.2013.799964
10. Determination of particulate filter efficiency level of N95 series filters against solid particulates for non-powered, air-purifying respirators standard testing procedure. Pittsburgh, PA: National Institute for Occupational Safety and Health; 2016. <https://www.cdc.gov/niosh/npptl/stps/pdfs/TEB-APR-STP-0059-508.pdf>.
11. Lipp A, Edwards P. Disposable surgical face masks for preventing surgical wound infection in clean surgery. The Cochrane Library website. <http://www.cochranelibrary.com/>. Published April 26, 2016. Accessed March 28, 2019.
12. MacIntyre CR, Chughtai AA, Rahman B, et al. The efficacy of medical masks and respirators against respiratory infection in healthcare workers.

Influenza Other Respir Viruses. 2017;11(6):511-517. doi:10.1111/irv.12474

13. Interim recommendations for facemask and respirator use to reduce 2009 influenza A (H1N1) virus transmission. Centers for Disease Control and Prevention website. <https://www.cdc.gov/h1n1flu/masks.htm>. Published September 24, 2009. Accessed December 6, 2016.
14. Infection control webinar. World Health Organization website. http://www.who.int/gpsc/5may/news/webinars/infection_control_webinar_20100413.ppt. Published April 10, 2010. Accessed March 28, 2019.
15. US Department of Labor. 1910.134 -Respiratory protection standard. Washington, DC: Occupational Safety and Health Administration. https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=12716. Accessed March 28, 2019.
16. Radonovich LJ Jr, Bessesen MT, Cummings DA, et al. The respiratory protection effectiveness clinical trial (ResPECT): a cluster-randomized comparison of respirator and medical mask effectiveness against respiratory infections in healthcare personnel. *BMC Infect Dis*. 2016;16:243. doi:10.1186/s12879-016-1494-2
17. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Health Care Infection Control Practices Advisory Committee. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control*. 2007;35(10)(suppl 2):S65-S164. doi:10.1016/j.ajic.2007.10.007
18. Centers for Disease Control and Prevention. Updated guidance: prevention strategies for seasonal influenza in healthcare setting. Government Publishing Office website. <https://www.gpo.gov/fdsys/pkg/FR-2010-06-22/html/2010-15015.htm>. Published June 22, 2010. Accessed March 28, 2019.
19. Moulton LH. Covariate-based constrained randomization of group-randomized trials. *Clin Trials*. 2004;1(3):297-305. doi:10.1191/1740774504cn0240a
20. Reich NG, Cummings DA, Lauer SA, et al. Triggering interventions for influenza: the ALERT algorithm. *Clin Infect Dis*. 2015;60(4):499-504. doi:10.1093/cid/ciu749
21. de la Tabla VO, Masiá M, Antequera P, et al. Comparison of combined nose-throat swabs with nasopharyngeal aspirates for detection of

pandemic influenza A/H1N1 2009 virus by real-time reverse transcriptase PCR. *J Clin Microbiol*. 2010; 48(10):3492-3495. doi:10.1128/JCM.01105-10

22. Tang YW, Lowery KS, Valsamakis A, et al. Clinical accuracy of a PLEX-ID flu device for simultaneous detection and identification of influenza viruses A and B. *J Clin Microbiol*. 2013;51(1):40-45. doi:10.1128/JCM.01978-12
23. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res*. 2011;20(1):40-49. doi:10.1002/mpr.329
24. Bessesen MT, Savor-Price C, Simberloff M, Reich NG, Pavia AT, Radonovich LJ. N95 respirators or surgical masks to protect healthcare workers against respiratory infections: are we there yet? *Am J Respir Crit Care Med*. 2013;187(9):904-905. doi:10.1164/rccm.201303-0581ED
25. Sartor C, Zandotti C, Romain F, et al. Disruption of services in an internal medicine unit due to a nosocomial influenza outbreak. *Infect Control Hosp Epidemiol*. 2002;23(10):615-619. doi:10.1086/501981
26. Jacobs JL, Ohde S, Takahashi O, Tokuda Y, Omata F, Fukui T. Use of surgical face masks to reduce the incidence of the common cold among health care workers in Japan: a randomized controlled trial. *Am J Infect Control*. 2009;37(5):417-419. doi:10.1016/j.ajic.2008.11.002
27. Offeddu V, Yung CF, Low MSF, Tam CC. Effectiveness of masks and respirators against respiratory infections in healthcare workers: a systematic review and meta-analysis. *Clin Infect Dis*. 2017;65(11):1934-1942. doi:10.1093/cid/cix681
28. Smith JD, MacDougall CC, Johnstone J, Copes RA, Schwartz B, Garber GE. Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. *CMAJ*. 2016;188(8):567-574. doi:10.1503/cmaj.150835
29. Peterson K, Novak D, Stradtman L, Wilson D, Couzens L. Hospital respiratory protection practices in 6 U.S. states: a public health evaluation study. *Am J Infect Control*. 2015;43(1):63-71. doi:10.1016/j.ajic.2014.10.008
30. Chiu S, Black CL, Yue X, et al. Working with influenza-like illness: presenteeism among US health care personnel during the 2014-2015 influenza season. *Am J Infect Control*. 2017;45(11):1254-1258. doi:10.1016/j.ajic.2017.04.008

EDITORIAL

Respiratory Protection of Health Care Personnel to Prevent Respiratory Viral Transmission

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Influenza and other respiratory viruses continue to cause patient morbidity and mortality, including health care utilization for outpatient visits and inpatient and intensive care unit care. Occupational health and infection-prevention



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programs partner to prevent these infections among health care personnel (HCP) and their patients through a multifaceted approach that includes comprehensive strategies to achieve high rates of influenza vaccination, rational sick leave and attendance policies that do not reward coming to work while ill (presenteeism), early identification and isolation of possibly infected patients, and appropriate use of personal protective equipment (PPE). While influenza still gets the most attention, these efforts also protect HCP from other respiratory infections.

Questions have been raised about the best PPE to limit HCP exposure to respiratory viral pathogens, leading to a debate between those who suggest use of medical masks and those who suggest use of particulate respirators. While official recommendations for most encounters still support the use of medical masks,¹ some concerns remain about the risk posed by the potential for small particle aerosol transmission of respiratory viruses, particularly influenza.² This risk has been demonstrated primarily in laboratory simulation settings^{3,4} or inferred from transmission events occurring on airplanes⁵ or despite PPE use.⁶ As a result, particulate respirators, or even powered air-purifying respirators, have been suggested for improved protection.⁷ Respirators provide filtration of smaller particles than medical masks, and the correct use of a fit-tested respirator also prevents particles of any size getting around the mask to the user's nose or mouth. However, it remains unclear if respirators provide benefits beyond medical masks in clinical settings. Prior studies attempting to address this important question have reached differing conclusions,⁸⁻¹¹ but have also used different study designs.

For many years, medical masks have been used to protect HCP from respiratory viral infections. In 2009, facing the first influenza pandemic in decades, "an abundance of caution" led to a recommendation for respirator use when caring for any patient infected with the emerging H1N1 pandemic influenza strain¹² until it was clear whether usual transmission routes had been altered in the new strain. The recommendation also recognized that a vaccine against the pandemic strain was not yet available and, therefore, HCP were more susceptible to infection in the event of exposure. Later, when it appeared that the transmission of pandemic H1N1 was not dif-

ferent from seasonal influenza, the recommendation for medical masks in most settings was reinstated. However, based on the same abundance of caution, respirators were (and are still) recommended for HCP when performing potentially aerosol-generating procedures (such as bronchoscopy), and the question of whether respirators would provide better protection during all encounters with patients infected with influenza and other respiratory virus infections has persisted.

To help address this question, in this issue of *JAMA*, Radonovich et al report the results of the ResPECT study,¹³ a pragmatic, cluster randomized trial of medical masks vs respirators (fit-tested N95 masks) worn by HCP while within 6 feet (1.83 m) of a symptomatic patient. The study included HCP who worked in multiple outpatient settings, including adult and pediatric ambulatory clinics, dental practices, urgent care centers, hemodialysis units, emergency departments, and emergency medical services, over 4 seasons of peak respiratory viral illness. Participants self-reported symptoms of acute respiratory illness, which prompted polymerase chain reaction testing for a wide range of respiratory viruses. In addition, nares and oropharynx swabs were performed twice per participant per season, when participants were asymptomatic, and influenza hemagglutination inhibition titers were measured at the beginning and end of each season. Randomization to wear medical masks or N95 respirators was at the level of the cluster or clinical site and occurred anew each year so that no one site or participant used the same type of PPE for all 4 seasons. Analyses of pre-specified clinically relevant outcomes occurred at the level of the participant-season, and were adjusted for age, race, sex, vaccination status, occupational exposure risk, self-reported hand hygiene adherence, and the number of children younger than 5 years at home.

The primary outcome was laboratory-confirmed influenza by either polymerase chain reaction or serology, for which the study was underpowered. The authors note that it would have required more than 10 000 HCP-seasons to have sufficient power for that outcome to detect the 25% relative reduction selected as the target, even though they did amass an impressive near 5000 HCP-seasons. Secondary outcomes included 4 other measures of respiratory illness among the participants: symptomatic acute respiratory illness with or without laboratory pathogen detection; influenzalike illness with or without influenza detection; acute respiratory illness with pathogen detection (laboratory-confirmed respiratory illness); and detection of a pathogen with or without reported symptoms (laboratory-detected respiratory infection).

The study included 1993 participants in 189 clusters who were randomized to wear N95 respirators (accounting for 2512 HCP-seasons of observation) and 2058 participants in 191 clusters who were randomized to wear medical masks (2668 HCP-seasons of observation). For all outcomes, illness with or without laboratory detection of a pathogen and pathogen detection with or without reported symptoms, there were no statistically significant differences between participants wearing N95 respirators and those wearing medical masks. For the primary outcome of laboratory-confirmed influenza, 207 laboratory-confirmed influenza infection events (8.2% of 2512 HCP-seasons) occurred in the N95 respirator group and 193 (7.2% of 2668 HCP-seasons) occurred in the medical mask group (difference, 1.0%, [95% CI, -0.5% to 2.5%]; $P = .18$).

In many ways, the ResPECT study was specifically designed to address limitations of earlier studies. The cohorts that were randomized to use medical masks and N95 respirators were similar, with no significant between-group differences in job title, vaccination status, patient population served, smoking status, use of glasses or contact lenses, and presence of children at home, minimizing the risk of bias through differential exposure risk. The design included serologic testing for influenza hemagglutination inhibition titers and random polymerase chain reaction testing of asymptomatic participants to minimize the chances of missing asymptomatic or clinically mild infections. The symptoms used as criteria for an acute respiratory illness were broad and fairly nonspecific to avoid excluding participants with atypical presentations. The process developed for participants to self-collect samples decreased the risk of laboratory testing being missed because of timing or study staff access. The study included testing for other viruses in addition to influenza because influenza is not the only respiratory virus from which HCP need protection.

The study also had several limitations. One limitation was that the study was underpowered for its prespecified primary outcome. Laboratory-confirmed infections can be missed because of under-reporting of symptoms, limitations in specimen collection technique (self-collection), and delayed specimen collection (allowed up to 7 days after symptom onset). Inclusion of influenza hemagglutination inhibition testing mitigates the risk of missed infections somewhat, although only for influenza. Symptom-based outcomes are also problematic because most symptoms are not specific to the respiratory viral infections, potentially diluting the effectiveness of the intervention. To address these issues, the authors chose to include multiple outcomes, both symptom-based and laboratory-based. The finding of no difference across all of the reported outcomes is reassuring that medical masks provide comparable protection for HCP against respiratory viruses.

The ResPECT study did not directly address inpatient settings and particularly the appropriate protection for potentially aerosol-generating procedures. Although it seems unlikely that most basic principles of viral transmission differ between outpatient and inpatient settings, some differences may potentially affect transmission in inpatient settings, including higher viral burden among more symptomatic patient populations, a higher proportion of immunocompromised patients, and longer and closer interactions between HCP and patients while providing care (eg, bathing patients). It is unclear whether the effect of those possible differences would be affected by the use of respirators. For example, a 2008 study found that in usual use conditions (ie, wearing a mask while caring for possibly infected patients) there was no difference in outcomes between participants wearing medical masks vs N95 respirators in inpatient settings.⁸ Additional pragmatic studies of HCP outcomes based on PPE use would still be helpful in these settings; however, such a study among inpatient HCP would require extensive funding support and likely would be quite expensive. Other studies defining changes in particle sizes and risk for pathogen transmission during patient procedures may also provide some guidance for those situations.¹⁴

Occasionally, the desire for an abundance of caution gets ahead of the available data and leads to changing recommended levels of protection just to be safe. These changes, which can be politically challenging to reverse, may not lead to better protection, but instead only create additional burdens on busy HCP and health care systems. The ResPECT trial provides useful data on appropriate protection against respiratory viral infections for HCP in outpatient settings. In addition to the findings reported in the current manuscript, the authors have previously noted through the ResPECT cohort the association between mandatory HCP influenza vaccination policies on vaccination rates and subsequent reductions in HCP symptomatic absenteeism.¹⁵

The pragmatic design of the ResPECT study reflects the conditions that many hospital epidemiologists are accustomed to: HCP may or may not wear the PPE they are supposed to, may or may not wear it correctly if they do wear it, and may self-report higher levels of adherence to hand hygiene and PPE use than noted by independent observers. Even though some may consider these elements of the study as weaknesses, these aspects increase the generalizability of the findings outside of a research study and provide reassurance to those making programmatic and policy decisions that, in outpatient settings under usual use conditions, there are no significant differences between medical masks and respirators for protection of HCP against respiratory viruses.

ARTICLE INFORMATION

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Conflict of Interest Disclosures: None reported.

REFERENCES

1. Prevention strategies for seasonal influenza in healthcare settings: guidelines and

recommendations. Centers for Disease Control and Prevention website. <https://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm#fundamental>. Accessed July 18, 2019.

2. Shiu EYC, Leung NHL, Cowling BJ. Controversy around airborne versus droplet transmission of respiratory viruses: implication for infection prevention. *Curr Opin Infect Dis*. 2019;32(4):372-379.

3. Zhou J, Wei J, Choy K. Defining the sizes of airborne particles that mediate influenza transmission in ferrets. *Proc Natl Acad Sci USA*. 2018;115(10):E2386-E2392. doi:10.1073/pnas.1716771115
4. Yan J, Grantham M, Pantelic J, et al; EMIT Consortium. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc Natl Acad Sci USA*. 2018;115(5):1081-1086. doi:10.1073/pnas.1716561115
5. Leitmeyer K, Adlhoch C. Review article: influenza transmission on aircraft: a systematic literature review. *Epidemiology*. 2016;27(5):743-751. doi:10.1097/EDE.0000000000000438
6. Christian MD, Loutfy M, McDonald LC, et al; SARS Investigation Team. Possible SARS coronavirus transmission during cardiopulmonary resuscitation. *Emerg Infect Dis*. 2004;10(2):287-293. doi:10.3201/eid1002.030700
7. Bischoff WE, Turner J, Russell G, Blevins M, Missaile E, Stehle J. How well do N95 respirators protect healthcare providers against aerosolized influenza virus? *Infect Control Hosp Epidemiol*. 2018;40(2):1-3. doi:10.1017/ice.2018.326
8. Loeb M, Dafoe N, Mahony J, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA*. 2009;302(17):1865-1871. doi:10.1001/jama.2009.1466
9. MacIntyre CR, Wang Q, Seale H, et al. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am J Respir Crit Care Med*. 2013;187(9):960-966. doi:10.1164/rccm.201207-1164OC
10. MacIntyre CR, Wang Q, Cauchemez S, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other Respir Viruses*. 2011;5(3):170-179. doi:10.1111/j.1750-2659.2011.00198.x
11. Smith JD, MacDougall CC, Johnstone J, Copes RA, Schwartz B, Garber GE. Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. *CMAJ*. 2016;188(8):567-574. doi:10.1503/cmaj.150835
12. Interim guidance on infection control measures for 2009 H1N1 influenza in healthcare settings, including protection of healthcare personnel. Centers for Disease Control and Prevention website. https://www.cdc.gov/h1n1flu/guidelines_infection_control.htm. Published July 15, 2010. Accessed July 18, 2019.
13. Radonovich L Jr, Simberloff M, Bessesen M, et al. N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial [published September 3, 2019]. *JAMA*. doi:10.1001/jama.2019.11645
14. O'Neil CA, Li J, Leavey A, et al; Centers for Disease Control and Prevention Epicenters Program. Characterization of aerosols generated during patient care activities. *Clin Infect Dis*. 2017;65(8):1335-1341.
15. Frederick J, Brown AC, Cummings DA, et al. Protecting healthcare personnel in outpatient settings: the influence of mandatory versus nonmandatory influenza vaccination policies on workplace absenteeism during multiple respiratory virus seasons. *Infect Control Hosp Epidemiol*. 2018;39(4):452-461. doi:10.1017/ice.2018.9

Evolving Priorities for Imaging Utilization Research From Outputs to Outcomes

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In this issue of JAMA, Smith-Bindman et al¹ report findings from a study of advanced imaging utilization in 3 US integrated health care programs, in 4 US mixed-model insurance plans, and in individuals living in Ontario, Canada. Using electronic health record data from 2000 to 2016, the authors respectively characterized

more than 135 million medical imaging examinations for 16 million to 21 million individuals annually, including segmenting utilization by both imaging mode and body region.

Smith-Bindman et al found that among all adults, imaging rates increased significantly from 2000 to 2016 for all imaging tests other than nuclear medicine. For example, among older adults (aged ≥65 years) in US health care systems, rates of imaging with computed tomography (CT) in 2000 and 2016 were 204 per 1000 person-years compared with 428 per 1000 person-years, and in Ontario, were 161 per 1000 person-years compared with 409 per 1000 person-years. For magnetic resonance imaging (MRI), the US rates were 62 per 1000 person-years in 2000 and 139 per 1000 person-years in 2016, and the rates in Ontario were 13 per 1000 person-years in 2000 and 89 per 1000 person-years in 2016. For ultrasound, the rates in 2000 and 2016, respectively, were 324 per 1000 person-years and 495 per 1000 person-years in the United States and 332 per 1000 person-years vs 580 per 1000 person-years in Ontario. The notable exceptions to increased utilization were for nuclear medicine, which declined over time among older

adults (from 94 per 1000 person-years in 2000 to 64 per 1000 person-years in 2016 in the United States and from 87 per 1000 person-years in 2000 to 74 per 1000 person-years in 2016 in Ontario) and for CT in children, which declined after 2009 in the United States and after 2006 in Ontario. Additional analyses also found a general slowing in the increase in imaging in the 3 to 5 years up to 2016.

The study findings are both interesting and provocative, but without information about discrete episodes of care, they are not immediately actionable. Without knowing who ordered this imaging (eg, physicians vs an expanding pool of non-physician practitioners), for what indications (eg, new diagnoses or follow-up of incidental findings), and in what settings (eg, expanding emergency departments vs contracting outpatient imaging centers), more work will be necessary to translate this information into improved patient outcomes. In addition, with passage and implementation in the United States of the Affordable Care Act during the study interval, the contributing role of broader national policy on health care service utilization overall is unclear (for instance, it is not possible to determine whether the addition of a large previously underserved population to health systems may, at least in part, have contributed to these findings).

Nonetheless, utilization research remains important in guiding meaningful health policy, and imaging is associated with both substantial cost and some risk. Such work informs ongoing research and guidelines to optimize imaging



Related article [page 843](#)

A Quantitative Assessment of the Efficacy of Surgical and N95 Masks to Filter Influenza Virus in Patients with Acute Influenza Infection

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We assessed the in vivo efficacy of surgical and N95 (respirator) masks to filter reverse transcription-polymerase chain reaction (RT-PCR)-detectable virus when worn correctly by patients with laboratory-confirmed acute influenza. Of 26 patients with a clinical diagnosis of influenza, 19 had the diagnosis confirmed by RT-PCR, and 9 went on to complete the study. Surgical and N95 masks were equally effective in preventing the spread of PCR-detectable influenza.

Influenza virus is a well-recognized nosocomial pathogen spread from person to person through transmission via large droplets (droplet transmission), small particle aerosols (airborne transmission), or direct and indirect contact (contact transmission). The primary mode of influenza transmission is uncertain, although droplet transmission appears to be the dominant form [1, 2].

Recommendations for mask use vary according to whether use is to prevent disease transmission or acquisition. To prevent disease transmission from patients with acute influenza to other patients and staff, the Centers for Disease Control and Prevention, the American Occupational Safety and Health Administration, and the World Health Organization each rec-

ommend that either a routine surgical or procedure mask be worn by the infected patient [3–5]. In contrast, to prevent influenza acquisition by health care workers (HCWs) from infected patients, these bodies vary in their recommendations with respect to the type of mask used (surgical or N95) and whether the influenza outbreak is seasonal or pandemic [3–5].

Surgical masks are designed to trap respiratory secretions (including bacteria and viruses) expelled by the wearer and prevent disease transmission to others [4]. Surgical masks are not designed to prevent inhalation of airborne particles, and their ability to protect HCWs from disease acquisition varies. In contrast, N95 masks (termed *respirators* in the United States) are designed to reduce an individual's exposure to airborne contaminants, including infectious viral or bacterial particles. Although N95 masks are designed to primarily protect the wearer from infection, they presumably also prevent transmission if fitted correctly on a patient at high risk of transmitting a virus [4]. However, some HCWs find the more expensive N95 masks difficult to tolerate [2, 6].

Data assessing the ability of masks to filter influenza virus are limited [7]. Most research has been in vitro in design [8], using nonbiological particles [9] rather than assessing their efficacy in preventing influenza transmission. Thus, we assessed the efficacy of both standard surgical masks and N95 masks to adequately filter influenza virus among patients with laboratory-proven acute influenza A and B to determine which was more appropriate to prevent spread.

Methods. Study participants (age, >18 years) with a clinical diagnosis of influenza were recruited from our hospital emergency department during the 2007 winter influenza season. Clinical influenza was defined as previously by the presence of cough and fever during an influenza outbreak [10]. Informed written consent was obtained for all participants, and the study was approved by the Research Ethics Committee at Austin Health.

All referred patients who fulfilled the clinical entry criteria had 2 nasal swabs performed for assessment by a rapid point-of-care test (Binax-Now Influenza A and B; Binax) and for a respiratory reverse transcription-polymerase chain reaction (RT-PCR) that detected influenza A and B, parainfluenza virus, picornavirus, respiratory syncytial virus, and adenovirus [11]. The point-of-care test is reported to have a sensitivity of 62%–82% for influenza A, a sensitivity of 58%–71% for influenza B, and a specificity of 92%–100% for influenza A and B [12]. Only patients who had cases that met the clinical criteria of influenza and who had a positive point-of-care test result were

Received 17 December 2008; accepted 1 March 2009; electronically published 12 June 2009.

Presented in part: 48th Interscience Conference on Antimicrobial Agents and Chemotherapy/46th Infectious Diseases Society of America Annual Meeting, Washington, DC, 25–28 October 2008 (abstract K-4206).

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Clinical Infectious Diseases 2009;49:275–7

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1058-4838/2009/4902-0018\$15.00

DOI: 10.1096/600041

Table 1. Efficacy of surgical and N95 masks to filter influenza in point-of-care assay-positive patients.

Patient or variable	Influenza type	Cycle number					Duration of illness, days per week
		Nasal swab	No mask, before control (step 1)	N95 mask (step 2)	Surgical mask (step 3)	No mask, after control (step 4)	
Patient							
1	A	31	38	Negative	Negative	39	3
2	A	26	40	Negative	Negative	Negative	1
3	A	22	Negative	Negative	Negative	40	3
4	A	26	34	Negative	Negative	35	1
5	A	23	32	Negative	Negative	33	2
6	A	25	27	Negative	Negative	25	1
7	B	22	38	Negative	Negative	27	2
8	A	29	34	Negative	Negative	Negative	3
9	B	27	Negative	Negative	Negative	39	3
Mean cycle time for patients with detected influenza A	...	26 ^a	34.17 ^a	0	0	34.4 ^a	2 ^b
Estimated viral load for detected influenza A, copies/mL	...	5 million ^a	50,000 ^a	0	0	50,000 ^a	...

NOTE. Cycle number indicates real-time reverse transcription-polymerase chain reaction cycle number. The cycle number value is inversely proportional to the titer of virus present.

^a Mean value calculated from patients with detectable influenza A.

^b Mean duration.

included in the assessment of the mask efficacy, because their influenza status was confirmed in real time.

Routine disposable surgical masks (TECNOL classical surgical mask; Kimberly Clark) were compared with standard N95 respirator masks (Proshield N95 Medium; BSN Medical). Neither mask was formally fit tested, but all were carefully placed on the patients by the study clinician who was trained and accredited in fit testing N95 masks. The presence of influenza was assessed using a technique whereby participants coughed 5 times onto a 90-mm diameter (14-mm deep) Petri dish (Sarsted) containing 1 mL of viral transport media (influenza sample plate [ISP]; Victorian Infectious Diseases Reference Laboratory). The ISP was held 20 cm directly in front of the participant's mouth. After coughing, viral transport media from each of the ISPs were assessed by quantitative real-time RT-PCR for influenza A and B, with the quantity of virus detected expressed as a cycle number and an estimate of viral copy number calculated as previously described [13]. The lower limit of sensitivity of the RT-PCR was ~250 copies/mL.

A 4-stage schedule was used to assess the presence of detectable influenza virus during coughing and the efficacy of each mask. This required the participant to cough 5 times onto a unique ISP during each of the 4 steps of the study; performed in the following sequence: (1) coughing without a mask (before control), (2) coughing while wearing a fitted N95 mask, (3) coughing while wearing a routine surgical mask, and (4) coughing without a mask (after control). Thus, each participant coughed a total of 20 times (5 × 4) for the study. The order

of coughing with a surgical and N95 mask (steps 2 and 3) was randomized between patients.

Results. Twenty-six patients with a clinical diagnosis of influenza were enrolled during the 8 weeks from 9 August 2007 through 8 October 2007; 19 were confirmed to have influenza by RT-PCR of a nasal swab. Ten (52%) of these 19 participants had influenza also confirmed by the point-of-care assay and participated in the mask efficacy protocol. Of these 10 participants, 1 participant (influenza A) was unable to complete the protocol because of respiratory distress; thus, 9 (7 with influenza A and 2 with influenza B) completed the mask efficacy. Results are given in table 1. All 9 patients had influenza detected by RT-PCR during stage 1 (before control) and/or stage 4 (after control). The estimated mean viral titer from coughing 5 times was ~2 log₁₀ less than that detected by direct nasal swab (table 1). Surgical and N95 masks appeared to be equally effective in filtering influenza, given that no influenza could be detected by RT-PCR of the ISP viral transport medium in any of the 9 participants for either mask (table 1).

Discussion. To our knowledge, this is the first human study to assess the comparative efficacy of surgical versus N95 masks in patients with laboratory-confirmed acute influenza and suggests that, within our study design, both masks are equally effective when used for short periods to prevent the spread of infection. Our findings support current guidelines recommending surgical or procedural masks be worn by patients with suspected influenza to limit viral dissemination to others. The findings also support the guidelines that N95 respirators (de-

signed to prevent disease acquisition) may not be necessary, because they appear to offer no additional benefit over surgical masks [3–5]. Thus, the choice of masks may be reasonably influenced by other factors, such as cost, fit testing, availability, and tolerability [2, 6]—all factors that favor routine surgical masks. Of course, our data may be less relevant to HCWs (or patients) who are wearing a mask to prevent disease acquisition. In such circumstances, the greater filtration capacity of N95 masks may have some benefits as long as they can be worn appropriately and tolerated. However, our study did not assess this latter form of mask use.

Although our study is small, we believe it is unique because most previous research has been conducted in vitro using predominantly nonbiological particles [8, 9]. Previous epidemiological studies have focused on prevention of disease acquisition rather than on spread. They include a study that suggested that both N95 and surgical masks were protective during the severe acute respiratory syndrome outbreak in 2003 [14]. Similarly, 2 recent presentations suggested that the use of masks reduced the incidence of seasonal influenza-like illness (not laboratory confirmed) in both the community and health care situations [15, 16].

Our study has some limitations. First, only participants with a positive point-of-care assay result participated in the mask assessment protocol. Thus, we cannot be sure that other patients who have negative point-of-care assay results but positive PCR results would necessarily generate the same results; however, this would seem likely. Second, because of our strict study entry criteria, we were able to only recruit a relatively small number of participants. Third, we did not formally demonstrate that the virus detected in the study participants was infectious and could be transmitted to other individuals. However, given the clinical presentation of the patients, it is likely that the virus quantitated by real-time PCR was infectious. Fourth, our method for detecting influenza during coughing may have been too insensitive to detect small differences in mask filtration efficacy or influenza expelled from around the edge of the mask. Finally, because our protocol required the mask to be worn for only 3–5 minutes, we cannot be sure that longer periods of mask use, such as may occur in some clinical situations, would be associated with the same efficacy. Thus, our data provide important preliminary information to allow appropriate planning for larger future study cohorts that focus on prevention of influenza dissemination and protection from acquisition of influenza.

On the basis of these preliminary findings, both surgical and N95 masks appear equally effective in preventing influenza dissemination from patients with confirmed influenza. These findings support current guidelines regarding mask use by patients with acute influenza.

Acknowledgments

Binax Now kits were provided gratis by Inverness Medical Innovations. **Potential conflicts of interest.** All authors: no conflicts.

References

1. World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, international measures. *Emerg Infect Dis* **2006**; 12:81–7.
2. Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. *Lancet Infect Dis* **2007**; 7: 257–65.
3. Centers for Disease Control and Prevention. Infection control guidance for the prevention and control of influenza in acute care facilities. 15 November **2007**. Available at: <http://www.cdc.gov/flu/professionals/infectioncontrol/healthcarefacilities.htm>. Accessed 28 July 2008.
4. Occupational Safety and Health Administration. Occupational Safety and Health Administration (OSHA) pandemic influenza preparedness and response guidance for healthcare workers and healthcare employers. **2007**. Available at: http://www.osha.gov/Publications/OSHA_pandemic_health.pdf. Accessed 28 July 2008.
5. World Health Organization. Avian influenza, including influenza A (H5N1), in humans: WHO interim infection control guideline for health care facilities. May **2007**. Available at: http://www.wpro.who.int/NR/rdonlyres/EA6D9DF3-688D-4316-91DF-5553E7B1DBCD/0/AI_Inf_Control_Guide_10May2007.pdfv. Accessed 28 July 2008.
6. Lim EC, Seet RC, Lee KH, Wilder-Smith EP, Chuah BY, Ong BK. Headaches and the N95 face-mask amongst healthcare providers. *Acta Neurol Scand* **2006**; 113:199–202.
7. Bell DM. Non-pharmaceutical interventions for pandemic influenza, international measures. *Emerg Infect Dis* **2006**; 12:81–7.
8. Balazy A, Toivola M, Adhikari A, Sivasubramani SK, Reponen T, Grinshpun SA. Do N95 respirators provide 95% protection level against airborne viruses, and how adequate are surgical masks? *Am J Infect Control* **2006**; 34:51–7.
9. Martin SB Jr, Moyer ES. Electrostatic respirator filter media: filter efficiency and most penetrating particle size effects. *Appl Occup Environ Hyg* **2000**; 15:609–17.
10. Treanor JJ. Influenza virus. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Bennett, & Dolin: principles and practice of infectious diseases*. 6th ed. Philadelphia: Elsevier Churchill Livingstone, **2005**:2072.
11. Druce J, Tran T, Kelly H, et al. Laboratory diagnosis and surveillance of human respiratory viruses by PCR in Victoria, Australia, 2002–2003. *J Med Virol* **2005**; 75:122–9.
12. Charles PG, Grayson ML. Point-of-care tests for lower respiratory tract infections. *Med J Aust* **2007**; 187:36–9.
13. Grayson ML, Melvani S, Druce J, et al. Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers. *Clin Infect Dis* **2009**; 48:285–91.
14. Seto WH, Tsang D, Yung RW, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* **2003**; 361:1519–20.
15. Aiello AE, Murray G, Coulborn R, Noone A, Monto AS. Mask use reduces seasonal influenza-like illness in the community setting [abstract V-924]. In: Program and abstracts of the 48th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)/46th Infectious Diseases Society of America (IDSA) Annual Meeting (Washington, DC). Alexandria, VA: IDSA, **2008**.
16. Ng K, Lee N, Hui D, Lai R, Ip M. A survey on ILI among healthcare workers during a peak “flu” season: what are the risk factors [abstract K4202]. In: Program and abstracts of the 48th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)/46th Infectious Diseases Society of America (IDSA) Annual Meeting (Washington, DC). Alexandria, VA: IDSA, **2008**.

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Received 17 December 2008; accepted 1 March 2009; electronically published 12 June 2009.

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Clinical Infectious Diseases 2009;49:275–7

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1058-4838/2009/4902-0018\$15.00

DOI: 10.1096/600041

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6	A	25	27	Negative	Negative	25	1
7	B	22	38	Negative	Negative	27	2
8	A	29	34	Negative	Negative	Negative	3
9	B	27	Negative	Negative	Negative	39	3
Mean cycle time for patients with detected influenza A	...	26 ^a	34.17 ^a	0	0	34.4 ^a	2 ^b
Estimated viral load for detected influenza A, copies/mL	...	5 million ^a	50,000 ^a	0	0	50,000 ^a	...

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^b Mean duration.

included in the assessment of the mask efficacy, because their influenza status was confirmed in real time.

Routine disposable surgical masks (TECNOL classical surgical mask; Kimberly Clark) were compared with standard N95 respirator masks (Proshield N95 Medium; BSN Medical). Neither mask was formally fit tested, but all were carefully placed on the patients by the study clinician who was trained and accredited in fit testing N95 masks. The presence of influenza was assessed using a technique whereby participants coughed 5 times onto a 90-mm diameter (14-mm deep) Petri dish (Sarsted) containing 1 mL of viral transport media (influenza sample plate [ISP]; Victorian Infectious Diseases Reference Laboratory). The ISP was held 20 cm directly in front of the participant's mouth. After coughing, viral transport media from each of the ISPs were assessed by quantitative real-time RT-PCR for influenza A and B, with the quantity of virus detected expressed as a cycle number and an estimate of viral copy number calculated as previously described [13]. The lower limit of sensitivity of the RT-PCR was ~250 copies/mL.

A 4-stage schedule was used to assess the presence of detectable influenza virus during coughing and the efficacy of each mask. This required the participant to cough 5 times onto a unique ISP during each of the 4 steps of the study; performed in the following sequence: (1) coughing without a mask (before control), (2) coughing while wearing a fitted N95 mask, (3) coughing while wearing a routine surgical mask, and (4) coughing without a mask (after control). Thus, each participant coughed a total of 20 times (5 × 4) for the study. The order

of coughing with a surgical and N95 mask (steps 2 and 3) was randomized between patients.

Results. Twenty-six patients with a clinical diagnosis of influenza were enrolled during the 8 weeks from 9 August 2007 through 8 October 2007; 19 were confirmed to have influenza by RT-PCR of a nasal swab. Ten (52%) of these 19 participants had influenza also confirmed by the point-of-care assay and participated in the mask efficacy protocol. Of these 10 participants, 1 participant (influenza A) was unable to complete the protocol because of respiratory distress; thus, 9 (7 with influenza A and 2 with influenza B) completed the mask efficacy. Results are given in table 1. All 9 patients had influenza detected by RT-PCR during stage 1 (before control) and/or stage 4 (after control). The estimated mean viral titer from coughing 5 times was ~2 log₁₀ less than that detected by direct nasal swab (table 1). Surgical and N95 masks appeared to be equally effective in filtering influenza, given that no influenza could be detected by RT-PCR of the ISP viral transport medium in any of the 9 participants for either mask (table 1).

Discussion. To our knowledge, this is the first human study to assess the comparative efficacy of surgical versus N95 masks in patients with laboratory-confirmed acute influenza and suggests that, within our study design, both masks are equally effective when used for short periods to prevent the spread of infection. Our findings support current guidelines recommending surgical or procedural masks be worn by patients with suspected influenza to limit viral dissemination to others. The findings also support the guidelines that N95 respirators (de-

signed to prevent disease acquisition) may not be necessary, because they appear to offer no additional benefit over surgical masks [3–5]. Thus, the choice of masks may be reasonably influenced by other factors, such as cost, fit testing, availability, and tolerability [2, 6]—all factors that favor routine surgical masks. Of course, our data may be less relevant to HCWs (or patients) who are wearing a mask to prevent disease acquisition. In such circumstances, the greater filtration capacity of N95 masks may have some benefits as long as they can be worn appropriately and tolerated. However, our study did not assess this latter form of mask use.

Although our study is small, we believe it is unique because most previous research has been conducted in vitro using predominantly nonbiological particles [8, 9]. Previous epidemiological studies have focused on prevention of disease acquisition rather than on spread. They include a study that suggested that both N95 and surgical masks were protective during the severe acute respiratory syndrome outbreak in 2003 [14]. Similarly, 2 recent presentations suggested that the use of masks reduced the incidence of seasonal influenza-like illness (not laboratory confirmed) in both the community and health care situations [15, 16].

Our study has some limitations. First, only participants with a positive point-of-care assay result participated in the mask assessment protocol. Thus, we cannot be sure that other patients who have negative point-of-care assay results but positive PCR results would necessarily generate the same results; however, this would seem likely. Second, because of our strict study entry criteria, we were able to only recruit a relatively small number of participants. Third, we did not formally demonstrate that the virus detected in the study participants was infectious and could be transmitted to other individuals. However, given the clinical presentation of the patients, it is likely that the virus quantitated by real-time PCR was infectious. Fourth, our method for detecting influenza during coughing may have been too insensitive to detect small differences in mask filtration efficacy or influenza expelled from around the edge of the mask. Finally, because our protocol required the mask to be worn for only 3–5 minutes, we cannot be sure that longer periods of mask use, such as may occur in some clinical situations, would be associated with the same efficacy. Thus, our data provide important preliminary information to allow appropriate planning for larger future study cohorts that focus on prevention of influenza dissemination and protection from acquisition of influenza.

On the basis of these preliminary findings, both surgical and N95 masks appear equally effective in preventing influenza dissemination from patients with confirmed influenza. These findings support current guidelines regarding mask use by patients with acute influenza.

Acknowledgments

Binax Now kits were provided gratis by Inverness Medical Innovations. **Potential conflicts of interest.** All authors: no conflicts.

References

1. World Health Organization Writing Group. Non-pharmaceutical interventions for pandemic influenza, international measures. *Emerg Infect Dis* **2006**; 12:81–7.
2. Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. *Lancet Infect Dis* **2007**; 7: 257–65.
3. Centers for Disease Control and Prevention. Infection control guidance for the prevention and control of influenza in acute care facilities. 15 November **2007**. Available at: <http://www.cdc.gov/flu/professionals/infectioncontrol/healthcarefacilities.htm>. Accessed 28 July 2008.
4. Occupational Safety and Health Administration. Occupational Safety and Health Administration (OSHA) pandemic influenza preparedness and response guidance for healthcare workers and healthcare employers. **2007**. Available at: http://www.osha.gov/Publications/OSHA_pandemic_health.pdf. Accessed 28 July 2008.
5. World Health Organization. Avian influenza, including influenza A (H5N1), in humans: WHO interim infection control guideline for health care facilities. May **2007**. Available at: http://www.wpro.who.int/NR/rdonlyres/EA6D9DF3-688D-4316-91DF-5553E7B1DBCD/0/AI_Inf_Control_Guide_10May2007.pdfv. Accessed 28 July 2008.
6. Lim EC, Seet RC, Lee KH, Wilder-Smith EP, Chuah BY, Ong BK. Headaches and the N95 face-mask amongst healthcare providers. *Acta Neurol Scand* **2006**; 113:199–202.
7. Bell DM. Non-pharmaceutical interventions for pandemic influenza, international measures. *Emerg Infect Dis* **2006**; 12:81–7.
8. Balazy A, Toivola M, Adhikari A, Sivasubramani SK, Reponen T, Grinshpun SA. Do N95 respirators provide 95% protection level against airborne viruses, and how adequate are surgical masks? *Am J Infect Control* **2006**; 34:51–7.
9. Martin SB Jr, Moyer ES. Electrostatic respirator filter media: filter efficiency and most penetrating particle size effects. *Appl Occup Environ Hyg* **2000**; 15:609–17.
10. Treanor JJ. Influenza virus. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Bennett, & Dolin: principles and practice of infectious diseases*. 6th ed. Philadelphia: Elsevier Churchill Livingstone, **2005**:2072.
11. Druce J, Tran T, Kelly H, et al. Laboratory diagnosis and surveillance of human respiratory viruses by PCR in Victoria, Australia, 2002–2003. *J Med Virol* **2005**; 75:122–9.
12. Charles PG, Grayson ML. Point-of-care tests for lower respiratory tract infections. *Med J Aust* **2007**; 187:36–9.
13. Grayson ML, Melvani S, Druce J, et al. Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers. *Clin Infect Dis* **2009**; 48:285–91.
14. Seto WH, Tsang D, Yung RW, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* **2003**; 361:1519–20.
15. Aiello AE, Murray G, Coulborn R, Noone A, Monto AS. Mask use reduces seasonal influenza-like illness in the community setting [abstract V-924]. In: Program and abstracts of the 48th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)/46th Infectious Diseases Society of America (IDSA) Annual Meeting (Washington, DC). Alexandria, VA: IDSA, **2008**.
16. Ng K, Lee N, Hui D, Lai R, Ip M. A survey on ILI among healthcare workers during a peak “flu” season: what are the risk factors [abstract K4202]. In: Program and abstracts of the 48th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)/46th Infectious Diseases Society of America (IDSA) Annual Meeting (Washington, DC). Alexandria, VA: IDSA, **2008**.



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Physical interventions to interrupt or reduce the spread of respiratory viruses.

Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD006207.

DOI: 10.1002/14651858.CD006207.pub4.

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Physical interventions to interrupt or reduce the spread of respiratory viruses (Review)
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Physical interventions to interrupt or reduce the spread of respiratory viruses

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Editorial group: Cochrane Acute Respiratory Infections Group.

Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 7, 2011.

Citation: Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, van Driel ML, Nair S, Jones MA, Thorning S, Conly JM. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD006207. DOI: 10.1002/14651858.CD006207.pub4.

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ABSTRACT

Background

Viral epidemics or pandemics of acute respiratory infections like influenza or severe acute respiratory syndrome pose a global threat. Antiviral drugs and vaccinations may be insufficient to prevent their spread.

Objectives

To review the effectiveness of physical interventions to interrupt or reduce the spread of respiratory viruses.

Search methods

We searched *The Cochrane Library*, the Cochrane Central Register of Controlled Trials (CENTRAL 2010, Issue 3), which includes the Acute Respiratory Infections Group's Specialised Register, MEDLINE (1966 to October 2010), OLDMEDLINE (1950 to 1965), EMBASE (1990 to October 2010), CINAHL (1982 to October 2010), LILACS (2008 to October 2010), Indian MEDLARS (2008 to October 2010) and IMSEAR (2008 to October 2010).

Selection criteria

In this update, two review authors independently applied the inclusion criteria to all identified and retrieved articles and extracted data. We scanned 3775 titles, excluded 3560 and retrieved full papers of 215 studies, to include 66 papers of 67 studies. We included physical interventions (screening at entry ports, isolation, quarantine, social distancing, barriers, personal protection, hand hygiene) to prevent respiratory virus transmission. We included randomised controlled trials (RCTs), cohorts, case-controls, before-after and time series studies.

Data collection and analysis

We used a standardised form to assess trial eligibility. We assessed RCTs by randomisation method, allocation generation, concealment, blinding and follow up. We assessed non-RCTs for potential confounders and classified them as low, medium and high risk of bias.

Main results

We included 67 studies including randomised controlled trials and observational studies with a mixed risk of bias. A total number of participants is not included as the total would be made up of a heterogeneous set of observations (participant people, observations on participants and countries (object of some studies)). The risk of bias for five RCTs and most cluster-RCTs was high. Observational studies were of mixed quality. Only case-control data were sufficiently homogeneous to allow meta-analysis. The highest quality cluster-RCTs suggest respiratory virus spread can be prevented by hygienic measures, such as handwashing, especially around younger children. Benefit from reduced transmission from children to household members is broadly supported also in other study designs where the potential for confounding is greater. Nine case-control studies suggested implementing transmission barriers, isolation and hygienic measures are effective at containing respiratory virus epidemics. Surgical masks or N95 respirators were the most consistent and comprehensive supportive measures. N95 respirators were non-inferior to simple surgical masks but more expensive, uncomfortable and irritating to skin. Adding virucidals or antiseptics to normal handwashing to decrease respiratory disease transmission remains uncertain. Global measures, such as screening at entry ports, led to a non-significant marginal delay in spread. There was limited evidence that social distancing was effective, especially if related to the risk of exposure.

Authors' conclusions

Simple and low-cost interventions would be useful for reducing transmission of epidemic respiratory viruses. Routine long-term implementation of some measures assessed might be difficult without the threat of an epidemic.

PLAIN LANGUAGE SUMMARY

Physical interventions to interrupt or reduce the spread of respiratory viruses

Although respiratory viruses usually only cause minor disease, they can cause epidemics. Approximately 10% to 15% of people worldwide contract influenza annually, with attack rates as high as 50% during major epidemics. Global pandemic viral infections have been devastating. In 2003 the severe acute respiratory syndrome (SARS) epidemic affected around 8000 people, killed 780 and caused an enormous social and economic crisis. In 2006 a new avian H5N1, and in 2009 a new H1N1 'swine' influenza pandemic threat, caused global anxiety. Single and potentially expensive measures (particularly the use of vaccines or antiviral drugs) may be insufficient to interrupt the spread. Therefore, we searched for evidence for the effectiveness of simple physical barriers (such as handwashing or wearing masks) in reducing the spread of respiratory viruses, including influenza viruses.

We included 67 studies including randomised controlled trials and observational studies with a mixed risk of bias. A total number of participants is not included as the total would be made up of a varied set of observations: participant people and observations on participants and countries (the object of some studies). Any total figure would therefore be misleading. Respiratory virus spread can be reduced by hygienic measures (such as handwashing), especially around younger children. Frequent handwashing can also reduce transmission from children to other household members. Implementing barriers to transmission, such as isolation, and hygienic measures (wearing masks, gloves and gowns) can be effective in containing respiratory virus epidemics or in hospital wards. We found no evidence that the more expensive, irritating and uncomfortable N95 respirators were superior to simple surgical masks. It is unclear if adding virucidals or antiseptics to normal handwashing with soap is more effective. There is insufficient evidence to support screening at entry ports and social distancing (spatial separation of at least one metre between those infected and those non-infected) as a method to reduce spread during epidemics.

BACKGROUND

Description of the condition

Pandemic viral infections pose a serious threat to all nations. There have been several recently, including pandemic influenza (one of which has just occurred) (Jefferson 2009; WHO 2009) and a novel coronavirus causing severe acute respiratory syndrome (SARS) (Shute 2003).

Even non-epidemic acute respiratory infections (ARIs) place a serious burden on the health of nations. In total these cause much of the 7% of total deaths in the world that are attributed to lower respiratory tract infections (representing four million deaths worldwide, mostly occurring in low-income countries). In addition there is a huge burden from ARIs on morbidity and nations' healthcare systems (www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html).

High viral load and infectiousness probably increase the spread of acute respiratory infection outbreaks (Jefferson 2006a). Stopping the spread of virus from person to person may be effective at preventing these outbreaks. This can be achieved in a number of ways. However, single interventions (such as vaccination or antiviral drugs) may be inadequate (Jefferson 2005a; Jefferson 2005b; Jefferson 2005c; Jefferson 2006a).

Description of the intervention

There is increasing evidence (Jefferson 2005a; Jefferson 2005b; Jefferson 2005c; Jefferson 2006a; Thomas 2010) that single measures (such as the use of vaccines or antivirals) may be insufficient to interrupt the spread of influenza. However, a recent trial showed that handwashing may be effective in diminishing mortality due to respiratory disease (Luby 2005). The possible effectiveness of public health measures during the 'Spanish Flu' pandemic of 1918 to 1919 (Bootsma 2007) in US cities led us to wonder what evidence exists on the effectiveness of combined public health measures such as isolation, distancing and barriers. We also considered the major social implications for any community adopting them (CDC 2005a; CDC 2005b; WHO 2006). Given the potential global importance of interrupting viral transmission, up-to-date, concise estimates of effectiveness are necessary to inform planning and decision-making. We could find no previous systematic review of such evidence.

How the intervention might work

Epidemics and pandemics are more likely during antigenic shift in the virus (especially influenza), when the viral genes sufficiently alter to create a new subtype against which there is little circulating natural immunity (Smith 2006). This may happen when viruses cross from animal species such as ducks or pigs to infect humans

(Bonn 1997). Minor changes in viral antigenic configurations, known as 'drift', cause local or more circumscribed epidemics (Smith 2006).

High viral load and high viral infectiousness are likely to be the drivers of such epidemics and pandemics (Jefferson 2006a).

Physical means might prevent the spread of virus by **aerosols or large droplets** from infected to susceptible people (such as by using masks and distancing measures) and by **contact** (such as by using handwashing, gloves and protective gowns). Such public health measures were widely adopted during the 'Spanish Flu' pandemic of 1918 to 1919 (Bootsma 2007).

Why it is important to do this review

Although the benefits of physical methods seem self-evident, they require establishing and quantifying. Physical methods have several possible advantages over other methods of suppressing acute respiratory infection outbreaks: they can be instituted rapidly and may be independent of any specific type of infective agent including novel viruses.

OBJECTIVES

To systematically review the evidence of effectiveness of physical interventions to interrupt or reduce the spread of acute respiratory viruses.

METHODS

Criteria for considering studies for this review

Types of studies

We considered trials (individual-level or cluster-randomised, or quasi-randomised), observational studies (cohort and case-control designs) and any other comparative design, provided some attempt had been made to control for confounding, carried out in people of all ages.

Types of participants

People of all ages.

Types of interventions

We included any intervention to prevent viral animal-to-human or human-to-human transmission of respiratory viruses (screening at entry ports, isolation, quarantine, social distancing, barriers, personal protection and hand hygiene) compared with doing nothing or with another intervention. We excluded vaccines and antivirals.

Types of outcome measures

1. Deaths.
2. Numbers of cases of viral illness.
3. Severity of viral illness in the compared populations. In children and healthy adults we measured burden by consequences of influenza, for example, losses in productivity due to absenteeism by parents. For the elderly in the community, we measured the burden by repeated primary healthcare contacts, hospital admissions and the risk of complications.
4. Any proxies for these (for example, clinical symptoms as a proxy for viral illness and confirmed viral polymerase chain reaction (PCR) testing or viral serological tests).

Search methods for identification of studies

Electronic searches

In this 2010 update we searched, as we have done previously, the Cochrane Central Register of Controlled Trials (CENTRAL) 2010, Issue 3, which includes the Acute Respiratory Infections Group's Specialised Register, MEDLINE (April 2009 to October week 2, 2010), EMBASE (April 2009 to October 2010) and CINAHL (January 2009 to October 2010). Details of previous searches are in [Appendix 1](#). In addition, to include more of the literature of low-income countries in this update, we ran searches in LILACS (2008 to October 2010), Indian MEDLARS (2008 to October 2010) and IMSEAR (2008 to October 2010).

We used the following search strategy (updated to include new and emerging respiratory viruses) to search MEDLINE and CENTRAL. We combined the MEDLINE search strategy with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) (Ovid format) ([Lefebvre 2009](#)). We also included an additional search strategy based on the work of Fraser, Murray and Burr ([Fraser 2006](#)) to identify observational studies. The search strategies were adapted for Embase.com ([Appendix 2](#)), CINAHL ([Appendix 3](#)), LILACS ([Appendix 4](#)), Indian MEDLARS ([Appendix 5](#)) and IMSEAR ([Appendix 6](#)).

MEDLINE (Ovid)

1 Influenza, Human/

2 exp Influenzavirus A/
3 exp Influenzavirus B/
4 Influenzavirus C/
5 (influenza* or flu).tw.
6 Common Cold/
7 common cold*.tw.
8 Rhinovirus/
9 rhinovir*.tw.
10 adenoviridae/ or mastadenovirus/ or adenoviruses, human/
11 adenoviridae infections/ or adenovirus infections, human/
12 adenovir*.tw.
13 coronavirus/ or coronavirus 229e, human/ or coronavirus oc43, human/ or infectious bronchitis virus/ or sars virus/
14 coronavir*.tw.
15 coronavirus infections/ or severe acute respiratory syndrome/
16 (severe acute respiratory syndrome* or sars).tw.
17 respiratory syncytial viruses/ or respiratory syncytial virus, human/
18 Respiratory Syncytial Virus Infections/
19 (respiratory syncytial virus* or rsv).tw.
20 Pneumovirus Infections/
21 parainfluenza virus 1, human/ or parainfluenza virus 3, human/
22 parainfluenza virus 2, human/ or parainfluenza virus 4, human/
23 (parainfluenza* or para-influenza* or para influenza).tw.
24 enterovirus a, human/ or exp enterovirus b, human/ or enterovirus c, human/ or enterovirus d, human/
25 Enterovirus Infections/
26 enterovir*.tw.
27 Human bocavirus/
28 bocavirus*.tw.
29 Metapneumovirus/
30 metapneumovir*.tw.
31 Parvovirus B19, Human/
32 parvoviridae infections/ or erythema infectiosum/
33 parvovirus*.tw.
34 Parechovirus/
35 parechovirus*.tw.
36 acute respiratory tract infection*.tw.
37 acute respiratory infection*.tw.
38 or/1-37
39 Handwashing/
40 (handwashing or hand washing or hand-washing).tw.
41 hand hygiene.tw.
42 (sanitiser* or sanitizer*).tw.
43 (cleanser* or disinfectant*).tw.
44 gloves, protective/ or gloves, surgical/
45 glov*.tw.
46 masks/ or respiratory protective devices/
47 (mask or masks or respirator or respirators).tw.
48 Protective Clothing/
49 Protective Devices/
50 Patient Isolators/

51 Patient Isolation/
 52 patient isolat*.tw.
 53 (barrier* or curtain* or partition*).tw.
 54 negative pressure room*.tw.
 55 ((reverse barrier or reverse-barrier) adj3 (nurs* or unit or isolation)).tw.
 56 Cross Infection/pc [Prevention & Control]
 57 (cross infection* adj2 prevent*).tw.
 58 Communicable Disease Control/
 59 Infection Control/
 60 (school* adj3 (clos* or dismissal*)).tw.
 61 temporary closur*.tw.
 62 mass gathering*.tw.
 63 (public adj2 (gathering* or event*)).tw.
 64 (bans or banning or banned or ban).tw.
 65 (outbreak adj3 control*).tw.
 66 distancing*.tw.
 67 Quarantine/
 68 quarantine*.tw.
 69 (protective adj2 (cloth* or garment* or device* or equipment)).tw.
 70 ((protective or preventive) adj2 (procedure* or behaviour* or behavior*)).tw.
 71 personal protect*.tw.
 72 (isolation room* or isolation strateg*).tw.
 73 (distance adj2 patient*).tw.
 74 ((spatial or patient) adj separation).tw.
 75 cohorting.tw.
 76 or/39-75
 77 38 and 76
 78 (animals not (animals and humans)).sh.
 79 77 not 78

Searching other resources

There were no language restrictions. Study design filters designed to retrieve RCTs, cohort case-control and cross-over studies, and before-after and time series trials were used in the original searches but we applied no filters to the searches carried out for this update. We scanned the references of all included studies to identify other potentially relevant studies. We also accessed the archives of the former MRC Common Cold Unit (Jefferson 2005d) as a possible source for interruption of transmission evidence.

Data collection and analysis

Selection of studies

We scanned the titles and abstracts after conducting the searches. We obtained full-text articles if a study appeared to meet our eligibility criteria (or when there was insufficient information to ex-

clude it). We then used a standardised form to assess the eligibility of each study, based on the full article.

Data extraction and management

For this 2010 update, two review authors (TOJ, JMC) independently applied inclusion criteria to all identified and retrieved articles and extracted data. CDM checked the procedure and arbitrated. MJ carried out data analysis.

Assessment of risk of bias in included studies

For the 2009 update (Jefferson 2009) we contacted one trial author (Dr Michael Broderick) to better understand the risk of bias in his study (Broderick 2008). For this 2010 update Drs Aiello and Larson were contacted and provided additional information. A common problem in these studies was a lack of reporting of viral circulation in the reference population, making interpretation and generalisability of their conclusions questionable.

Randomised studies

Three RCTs were poorly reported with no description of randomisation sequence, concealment or allocation in three studies (Gwaltney 1980; Turner 2004a; Turner 2004b). Satomura 2005 reported the generation of randomisation but the very nature of the intervention (gargling with water with or without povidone iodine versus standard gargling with no attempt at masking the taste of iodine) made blinding impossible. The design of two trials was so artificial that their results cannot be generalised to everyday situations (Turner 2004a; Turner 2004b). One trial (Satomura 2005) is linked to a subsequent brief report which provides contradictory information which is difficult to reconcile (Kitamura 2007).

The quality of the cluster-randomised trials varied. Only the best reported cluster coefficients and conducted analysis of data by unit of (cluster) allocation instead of by individuals (Luby 2005; Roberts 2000; Sandora 2005). Analysing cluster-randomised trials at the individual level leads to spuriously narrow confidence intervals around the estimates of effect (Grimshaw 2004). Other frequent problems were a lack of description of randomisation procedure, partial reporting of outcomes, unclear numerators or denominators and unexplained attrition (Carabin 1999; Kotch 1994; Morton 2004; White 2001), and either complete failure of double-blinding (Farr 1988a; Farr 1988b) or inappropriate choice of placebo (Longini 1988). Three cluster-randomised trials involving the use of face masks (Cowling 2008; Cowling 2009; MacIntyre 2009) by influenza-like illness (ILI) contacts had poor compliance. This shows the difficulty of conducting clinical trials using bulky equipment in the absence of the perception of a real threat. One trial (Cowling 2008) was also conducted in a period of low viral circulation and randomisation was carried out on the basis of two different sequences. The other study (MacIntyre 2009)

was underpowered to detect differences in effect between different types of masks.

The cluster-randomised trial by Sandora and colleagues (Sandora 2008) is at low risk of bias with careful evaluation of compliance in the intervention arm (hand sanitiser wipes and disinfection of surfaces).

Of the four RCTs in the 2010 update, one was classified at low risk of bias (Loeb 2009), one at medium risk of bias (Aiello 2010a) and two (Jacobs 2009; Larson 2010) at high risk of bias.

Non-randomised studies

These were assessed for the presence of potential confounders using the appropriate Newcastle-Ottawa Scales (NOS) (Wells 2005) for case-control and cohort studies and a three-point checklist for controlled before and after and ecological studies (Khan 2000).

Case-control studies

We classified five of the nine case-control studies as having medium risk of bias (Lau 2004a; Seto 2003; Wu 2004; Yin 2004; Yu 2007) and two as at low risk of bias (Nishiura 2005; Teleman 2004), mostly because of inconsistencies in the text and lack of adequate description of controls. Two were at high risk of bias (Chen 2009; Liu 2009).

Prospective cohort studies

Six of the 16 prospective cohort studies were classified as at low risk of bias (Agah 1987; Dick 1986; Falsey 1999; Leung 2004; Madge 1992; Somogyi 2004), six as of medium risk (Broderick 2008; Dyer 2000; Kimel 1996; Murphy 1981; White 2003; Yen 2006), and four as of high risk of bias (Makris 2000; Master 1997; Niffenegger 1997; Wang 2007). One was a very brief report of a small study with insufficient details to allow assessment (Derrick 2005).

Retrospective cohort studies

All six retrospective cohort studies had high risk of bias (Cowling 2010; Doherty 1998; Foo 2006; Isaacs 1991; Ou 2003; Yen 2006). In general, retrospective designs are prone to recall bias.

Time series studies

Six of the 13 controlled before-after studies were at low risk of bias (Hall 1981a; Leclair 1987; Macartney 2000; Pang 2003; Ryan 2001; Simon 2006), two of medium risk (Krasinski 1990; Pelke 1994) and five at high risk (Gala 1986; Hall 1981b; Heymann 2004; Krilov 1996; Snyderman 1988).

Measures of treatment effect

When possible, we performed a quantitative analysis and summarised effectiveness as odds ratio (OR) using 95% confidence intervals (CI). We expressed absolute intervention effectiveness as a percentage using the formula $\text{intervention effectiveness} = 1 - \text{OR}$, whenever significant. In studies which could not be pooled, we used the effect measures reported by the trial authors (such as risk ratio (RR) or incidence rate ratio (IRR) with 95% CI or, when these were not available, relevant P values).

Unit of analysis issues

Outcome measures varied from incidence of experimentally-induced rhinovirus infections, to the incidence of naturally occurring undifferentiated acute respiratory infections (ARIs). This was measured in a variety of ways, including numbers of ARIs per time period, or number of ARIs per household per time period. In some studies the ARIs were replaced by influenza-like illness (ILI). Other included studies focused on SARS specifically, or respiratory syncytial virus (RSV).

Proxy measures of illness included absenteeism.

Dealing with missing data

Whenever details of studies were unclear or studies were only known to us by abstracts or communications at meetings we corresponded with first or corresponding authors.

Assessment of heterogeneity

Aggregation of data was dependent on study design, types of comparisons, sensitivity and homogeneity of definitions of exposure, populations and outcomes used. We calculated the I^2 statistic for each pooled estimate to assess the presence of statistical heterogeneity (Higgins 2002; Higgins 2003).

Assessment of reporting biases

Given the limited nature of our quantitative synthesis and the widely disparate nature of our evidence base, we limited our assessment of possible reporting biases to funnel plot visual inspection.

Data synthesis

We systematically described and reviewed included studies separately by study design. In other words randomised studies were described and reviewed separately from case-control studies which were described and reviewed separately from prospective cohort studies, and so on. If possible and appropriate, we combined studies within a particular study design in a meta-analysis. We used fixed-effect meta-analysis providing there was no evidence of heterogeneity, otherwise we used random-effects meta-analysis.

Subgroup analysis and investigation of heterogeneity

An a priori subgroup analysis was planned for:

1. pandemic influenza outbreaks;
2. seasonal influenza; and
3. other epidemics (for example, SARS).

We had sufficient data to carry out only the last.

Sensitivity analysis

We aimed to perform a sensitivity analysis on the results of our meta-analysis. We assessed the robustness of the conclusions from the evidence of the effects of each intervention by comparing the results across the original multivariable analysis, looking for consistency of findings.

RESULTS

Description of studies

Results of the search

We scanned 3775 titles, excluded 3560 and retrieved full papers of 215 studies, to include 66 papers of 67 studies.

Included studies

See [Summary of main results](#) section for a summary table of interventions and types of evidence.

In 2010 we included seven new studies and listed three trials as awaiting assessment. The seven newly included studies are four RCTs ([Aiello 2010a](#); [Jacobs 2009](#); [Larson 2010](#); [Loeb 2009](#)), one retrospective cohort ([Cowling 2010](#)) and two case-control studies ([Chen 2009](#); [Liu 2009](#)).

Excluded studies

We excluded 36 additional studies. The most frequent reasons for exclusion were no reporting of original data/non-comparative design, confounding by use of antivirals or other medication and in vitro studies (carried out without live patients).

Risk of bias in included studies

Three RCTs were poorly reported with no description of randomisation sequence, concealment or allocation ([Gwaltney 1980](#); [Turner 2004a](#); [Turner 2004b](#)). The design of two trials by one author means their results may not be generalised to everyday situations. This is due to the artefactual delivery of the interventions tested (see [Quality of the evidence](#) in the [Discussion](#) section) ([Turner 2004a](#); [Turner 2004b](#)).

The quality of the cluster-randomised trials varied. Only the highest quality trials ([Cowling 2009](#); [Luby 2005](#); [Roberts 2000](#); [Sandora 2005](#)) reported cluster coefficients and conducted analysis of data by unit of (cluster) allocation instead of by individuals. Analysing cluster-randomised trials at the individual level leads to spuriously narrow CIs around the estimates of effect ([Grimshaw 2004](#)). Other common problems were a lack of description of randomisation procedure, partial reporting of outcomes, unclear numerators or denominators and unexplained attrition ([Carabin 1999](#); [Kotch 1994](#); [Morton 2004](#); [White 2001](#)) and either complete failure of double-blinding ([Farr 1988a](#); [Farr 1988b](#)) or inappropriate choice of placebo ([Longini 1988](#)). [Jacobs 2009](#) is an underpowered individual randomised trial carried out in Japan. Its open design means that due to lack of accounting for drop outs and definitions of outcomes the trial is at high risk of bias. In addition, no guidance as to the generalisability of its results to other settings and countries is provided to readers.

[Aiello 2010a](#) is at medium risk of bias. Despite logistical and design problems the trial appears to show an effectiveness gradient of mask-wearing and hand sanitation combined versus instruction on hand sanitation and mask-wearing in student halls. The last cluster-randomised trial ([Larson 2010](#)) compared the effects of education alone versus education plus the use of an alcohol-based hand sanitiser versus education plus the use of an alcohol-based hand sanitiser plus the use of medical face masks on the interruption of self-reported upper respiratory tract infection (URTI), ILI and laboratory-confirmed influenza or other viral pathogen by culture or polymerase chain reaction (PCR) in US immigrant Latino households. Due to design issues, difficulty interpreting whether there was an intention-to-treat (ITT) analysis and lack of sufficient details of dropouts and other reporting problems, we classified it at high risk of bias.

[Loeb 2009](#) is a low risk of bias non-inferiority trial directly comparing the effects of surgical mask wearing versus N95 fit-tested respirators in nurses in acute units in Ontario Canada. The outcomes measured range from symptomatic and asymptomatic influenza to physician visits and ILI caused by non-influenza agents. This is possibly the most reliable piece of evidence available for this 2010 update.

We classified five of the nine case-control studies as having medium risk of bias ([Lau 2004a](#); [Seto 2003](#); [Wu 2004](#); [Yin 2004](#); [Yu 2007](#)) and two as at low risk of bias ([Nishiura 2005](#); [Teleman 2004](#)), mostly because of inconsistencies in the text and lack of adequate description of controls. Two case-control studies ([Chen 2009](#); [Liu 2009](#)) were at high risk of bias. Their interpretation is not straightforward. Both studies assess the effects of multiple factors as risk and protective measures for SARS during the epidemic in China. They appeared to be searching for associations and lacked precision with respect to conducting true matched blinded assessments. Only live cases were considered when we know that between 10% to 20% of infected healthcare workers died in the first weeks of the epidemic ([Liu 2009](#) mentions the high mortality rate in the

Introduction). However, the studies did ascertain the cases and controls of SARS by performing confirmatory laboratory testing rather than relying on a clinical diagnosis.

Six of the 16 prospective cohort studies were classified as at low risk of bias (Agah 1987; Dick 1986; Falsey 1999; Leung 2004; Madge 1992; Somogyi 2004), four as of medium risk (Dyer 2000; Kimel 1996; Murphy 1981; White 2003) and three as of high risk of bias (Makris 2000; Master 1997; Niffenegger 1997). One was a very brief report of a small study (Derrick 2005) and two recent studies (Broderick 2008; Wang 2007) report insufficient details to allow assessment.

Four retrospective cohort studies exploring the effect of barrier interventions (Doherty 1998; Isaacs 1991; Ou 2003; Yen 2006) and one study reporting on adverse effects of barrier interventions (Foo 2006) had a high risk of bias. The other high risk of bias retrospective cohort study is Cowling 2010, mainly due to the nature of its design, heavily dependent on web availability of information.

Six of the 13 controlled before-after studies were at low risk of bias (Hall 1981a; Leclair 1987; Macartney 2000; Pang 2003; Ryan 2001; Simon 2006), two of medium risk (Krasinski 1990; Pelke 1994) and five at high risk (Gala 1986; Hall 1981b; Heymann 2004; Krilov 1996; Snyderman 1988).

The most common problem in all of these studies was a lack of reporting of viral circulation in the reference population, making interpretation and generalisability of their conclusions questionable.

The results of a GRADE evaluation (the GRADE Working Group available from <http://www.gradeworkinggroup.org/index.htm>) of the case-control studies categorised them as providing low to very low quality evidence and categorised the updated RCTs as very low quality with the exception of two studies which were considered of moderate quality (Appendix 7).

The overall risk of bias is presented graphically in Figure 1 and summarised in Figure 2.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included RCTs.

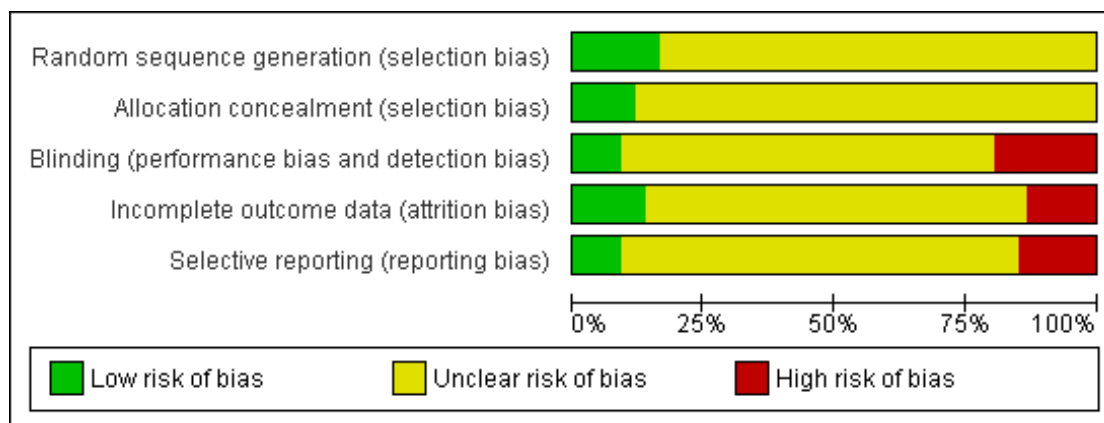
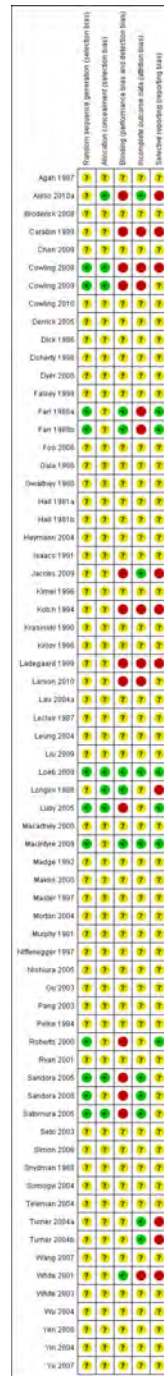


Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included RCT.



Effects of interventions

We scanned 3775 titles, excluded 3560 and retrieved the full papers of 215 studies, to include 66 papers of 67 studies. Four trials were listed in the [Studies awaiting classification](#) section. For one trial currently being submitted for publication we had insufficient information for assessment ([Aiello 2010b](#)). Two studies ([Hubner 2009](#); [Savolainen-Kopra 2010](#)) assessed the effects of handwashing practices which were of less interest at this time than the use of the physical interventions featured in this update. Another study was identified after our searches had been conducted ([Raboud 2010](#)).

Reported results from randomised studies

Three studies tested the effects of hand-cleaning on inactivating the virus and preventing experimental rhinovirus colds. These resulted in either a reduction in the incidence of rhinovirus infection among volunteers treated using different combinations of the acids used for cleaning ($P = 0.025$) ([Turner 2004a](#)) or did not reach statistical significance (13% versus 30% with combined denominator of only 60) ([Turner 2004b](#)). Using iodine treatment of fingers, one out of 10 volunteers were infected compared to six out of 10 in the placebo preparation arm ($P = 0.06$ with Fisher's exact test) ([Gwaltney 1980](#)). One study found that gargling with water or povidone-iodine solution in addition to handwashing is effective in preventing URTIs, but not influenza-like illnesses ([Satomura 2005](#)).

Three cluster-randomised studies tested the effects of virucidal cleaning disposable handkerchief wipes on the incidence and spread of ARI. One reported a reduced incidence of ARI in the household over 26 weeks, from 14% to 5% ([Farr 1988a](#)). A similar study reported a small non-significant (5%) drop across families ([Farr 1988b](#)). However, since the drop in incidence was confined to primary illness, unaffected by tissue use, we might assume they were ineffective. A community trial also reported a non-significant reduction in ARI secondary attack rates (18.7% versus 11.8%) during a time of high circulation of influenza H3N2 and rhinoviruses in the community ([Longini 1988](#)). This result is likely to be an underestimate because of any barrier effect of the inert tissue wipes used in controls.

Eight cluster-randomised studies tested educational programmes to promote handwashing, with or without the adjunct of antiseptic agents, on the incidence of ARI either in schools or in households. Because of different definitions, comparisons, lack of reporting of cluster coefficients and (in two cases) missing participant data ([Carabin 1999](#); [Kotch 1994](#)), we judged it improper to meta-analyse the data. Two of these trials reported a lack of effect: RR for the prevention of acute respiratory illness of 0.94 (95% CI -2.43 to 0.66) ([Kotch 1994](#)); and 0.97 (95% CI 0.72 to 1.30) ([Sandora 2005](#)). Nevertheless, the highest quality trials reported a significant decrease in respiratory illness in children up to 24

months (RR 0.90, 95% CI 0.83 to 0.97), although the decrease was not significant in older children (RR 0.95, 95% CI 0.89 to 1.01) ([Roberts 2000](#)); and a 50% (95% CI -65% to -34%) lower incidence of pneumonia in children aged less than five years of age in a low-income country ([Luby 2005](#)). Another study reported a decrease of 30% to 38% in respiratory infections with additional hand-rubbing (RR for illness absence incidence 0.69, RR for absence duration 0.71) ([White 2001](#)). One study reported decreased school absenteeism of 43% with the additional use of alcohol gel as well as handwashing ([Morton 2004](#)). Two trials reported that repeated handwashing significantly reduced the incidence of colds by as much as 20% ([Carabin 1999](#); [Ladegaard 1999](#)). One study found that in households in which interventions (handwashing with or without wearing a facemask) were implemented within 36 hours of symptom onset in the index patient, transmission of reverse transcription polymerase chain reaction (RT-PCR)-confirmed infection was reduced, an effect attributable to reductions in infection among participants using face masks plus hand hygiene (adjusted OR 0.33 (95% CI 0.13 to 0.87)) ([Cowling 2009](#)). The findings of the cluster-randomised trial by Aiello et al ([Aiello 2010a](#)) suggest that face masks and hand hygiene may reduce respiratory illnesses in shared living settings and mitigate the impact of the influenza A (H1N1) pandemic compared to no intervention or hand sanitiser and education. This conclusion is based on a significantly lower level of ILI incidence in the mask and hand sanitiser arm compared to the other two arms after adjustment for covariates (30% to 50% less in arm one compared to controls in the last two weeks of the study). However, influenza virus circulation was very low during the study period.

The authors of [Jacobs 2009](#) were unable to detect a difference in incidence of ILI of surgical mask wearing compared to no mask in healthcare workers in a Japanese hospital, possibly because of the study's lack of power.

The cluster-randomised trial by Larson et al ([Larson 2010](#)) tested the addition of mask and hand sanitiser use to hand sanitiser use alone to nothing other than education which was common to all three arms. Given the many biases in the design and reporting the results are difficult to interpret: the hand sanitiser group was significantly more likely to report that no household member had symptoms ($P = 0.01$) but there were no significant differences in rates of infection by intervention group in multivariate analyses. Knowledge improved significantly more in the hand sanitiser group ($P = 0.0001$).

The credible results of the individual trial by Loeb et al ([Loeb 2009](#)) report that the use of surgical masks was not inferior to the use of N95 respirators against influenza.

Reported results from case-control studies

Nine case-control studies assessed the impact of public health measures to curb the spread of the SARS epidemic during February to June 2003 in China, Singapore and Vietnam. Homogeneity of case definition, agent, settings and outcomes allowed meta-analysis. We pooled binary data; one of the comparisons showed significant heterogeneity (handwashing), however we used a fixed-effect model. A random-effects model made no appreciable difference to the handwashing comparison. Although continuous data were often available, the variables were different and measured in different units with standard deviations usually missing, which prevented their meta-analysis.

Studies reported that disinfection of living quarters was highly effective in preventing the spread of SARS (OR 0.30, 95% CI 0.23 to 0.39) (Lau 2004a); handwashing for a minimum of 11 times daily prevented many cases (OR 0.54, 95% CI 0.44 to 0.67) (Analysis 1.2), based on seven studies (Chen 2009; Lau 2004a; Nishiura 2005; Seto 2003; Teleman 2004; Wu 2004; Yin 2004); simple mask-wearing was highly effective (OR 0.32, 95% CI 0.26 to 0.39) (Analysis 1.3), based on seven studies (Chen 2009; Lau 2004a; Liu 2009; Nishiura 2005; Seto 2003; Wu 2004; Yin 2004); three studies found N95 respirator-wearing even more effective (OR 0.17, 95% CI 0.07 to 0.43) (Analysis 1.4), (Seto 2003; Teleman 2004; Liu 2009); glove-wearing was effective (OR 0.32, 95% CI 0.23 to 0.45) (Analysis 1.5) (Chen 2009; Liu 2009; Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); gown-wearing was also effective (OR 0.33, 95% CI 0.24 to 0.45) (Analysis 1.6) (Chen 2009; Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); all means combined (handwashing, masks, gloves and gowns) achieved very high effectiveness (OR 0.09, 95% CI 0.02 to 0.35) (Analysis 1.7) (Nishiura 2005; Seto 2003); use of eye protection such as goggles or masks with goggles is protective (OR 0.10, 95% CI 0.05 to 0.17) (Analysis 1.8) (Chen 2009; Liu 2009; Yin 2004) and nose-washing was also protective (OR 0.30, 95% CI 0.16 to 0.57) (Analysis 1.9) (Chen 2009; Liu 2009). As the data are all based on univariable analyses, they may be subject to confounding. We have separately tested how many of these measures were statistically significant in multivariable analyses (Table 1).

These data suggest that wearing a surgical mask or a N95 mask is the measure with the most consistent and comprehensive supportive evidence. Seven out of eight studies included masks as a measure in their study and six out of seven of these studies found masks to be statistically significant in multivariable analysis. Handwashing was also included in seven of the studies with four studies showing handwashing to be statistically significant in multivariable analysis. All other measures were shown to be statistically significant in multivariable analysis on only one or two occasions.

Another case-control study from Hong Kong and Guangzhou hospital wards reported that a minimum distance between beds of less than one metre was a risk factor for transmission (Yu 2007). Disaggregated data were not reported and therefore we did not pool this study in the meta-analysis. All studies selected cases from hospitals, except for one (Lau 2004a) in which cases were peo-

ple with probable SARS reported to the Department of Health in Hong Kong.

The detailed results of Chen 2009 report that avoiding face-to-face contact while caring for SARS patient (OR 0.30, 95% CI 0.15 to 0.60) and wearing gloves coupled with methods of ventilation are highly protective practices (various ORs for the various combinations intensity of wearing and ventilation methods, all significant). Liu 2009 reports that personal protective measures against droplet spread, such as wearing multiple layers of mask, are effective against the nosocomial spread of SARS.

Reported results from prospective cohort studies

Using an alcohol rub in students' communal residences resulted in significantly fewer symptoms (reductions of 14.8% to 39.9 %) and lower absenteeism (40% reduction) (White 2003). In a much-cited small experimental study, virucidal paper handkerchiefs containing citric acid interrupted the transmission of rhinovirus colds transmitted through playing cards: 42% of re-usable cotton handkerchief users developed colds compared with none using disposable virucidal tissues (Dick 1986).

Few identified studies reported interventions in the daycare setting, either in staff or patients. One staff educational programme on handwashing in a daycare centre for adults was effective over a four-year period in reducing rates of respiratory infection in daycare patients from 14.5 to 10.4 per 100 person-months to 5.7 ($P < 0.001$), with an accompanying decline in viral isolates. This seems to be more effective than the use of additional portable virucidal hand foam as an adjunct to handwashing (Falsey 1999). This confirmed an earlier report of the effectiveness of a handwashing programme in reducing absenteeism for ILI in a primary school (Kimmel 1996).

Two high risk of bias studies reported that education, a handwashing routine and encouragement for kindergarten children, parents and staff in correct sneezing and coughing procedure were effective, although there were considerable fluctuations in incidence of infections in the control and test centres (Niffenegger 1997); but the intervention was not effective in reducing absenteeism caused by ARIs (RR 0.79, $P = 0.756$) (Master 1997).

Dyer and colleagues reported a prospective, cluster, open-label, cross-over cohort study. The study assessed the effectiveness of a hand sanitiser in conjunction with at will soap-and-water handwashing in a private elementary school in California. Use of the sanitiser reduced illness absenteeism by 41.9% (reduction in respiratory illnesses of 49.7% over the 10-week period of the study) (Dyer 2000).

Curiously, an infection-control education programme reinforcing handwashing and other hygienic measures in a nosocomial setting reported reducing the number of organisms present on hands and surfaces, and ARIs, although the data tabled suggested the opposite (an incidence rate of 4.15/1000 patient-days in the test homes versus 3.15/1000 in the control homes) (Makris 2000).

A study found wearing a goggle-mask apparatus in healthcare workers visiting and caring for children aged up to five with respiratory syncytial virus (RSV) and symptoms of respiratory disease was effective (5% illness rate in goggle wearers against 61% in no-goggle controls) (Agah 1987).

Rapid laboratory diagnosis, cohort nursing and the wearing of gowns and gloves for all contacts with RSV-infected children significantly reduced the risk of nosocomial RSV infection (OR 0.013 to 0.76) (Madge 1992), although another similar study reported no effect of adding the use of both gown and mask to the usual handwashing routine on the development of illness in personnel caring for infants with respiratory disease (4 out of 30 in the handwashing group alone compared to 5 out of 28 in the handwashing, gown and masking group, $P > 0.20$); although the authors described poor compliance with the barrier protocol (Murphy 1981). Strict procedures of triage and infection control to stop transmission of SARS from infected children to carers and visitors of a large hospital at the height of the epidemic in 2003 in Hong Kong was reported effective at interrupting the transmission of SARS, as no healthcare worker became ill, in contrast to experiences in other institutions (Leung 2004).

A tiny study comparing the N95 respirator with paper surgical masks in volunteers found that surgical masks, even when worn in multiple layers (up to five), filtered ambient particles poorly (Derrick 2005); this principle was confirmed in another small study of air filtration to prevent droplet spread (Somogyi 2004).

Reported results from retrospective cohort studies

Two studies investigated isolating together children less than three years of age with suspected RSV. In one, transmission was diminished by “up to 60%” (Isaacs 1991), while the statement that nosocomial transmission “was minimised” was not supported by data in the other study (Doherty 1998).

Isolation of cases during the 2003 epidemic of SARS in China was reported to limit transmission only to those contacts who actually had home or hospital contact with a symptomatic SARS patient (attack rate 31.1%, 95% CI 20.2 to 44.4 for carers; 8.9%, 95% CI 2.9 to 22.1 for visitors; 4.6%, 95% CI 2.3 to 8.9 for those living with a SARS case) but not to contacts living in the same building, working with cases, or without contact with SARS cases during the incubation period. This suggests extending quarantine only for contacts of symptomatic SARS cases (Ou 2003).

Another brief report carried out in 2003 during the SARS epidemic, in a military hospital in Taiwan, China and 86 control hospitals, compared an integrated infection-control policy to protect healthcare workers against infection; only two from the military hospital were infected with SARS compared to 43 suspected and 50 probable cases in the control hospitals (Yen 2006).

Cowling 2010 reports a marginal (one to two weeks) non-significant benefit in delaying spread of novel A/H1N1 autochthonous pandemic influenza by various means of entry screening. The high

risk of bias is mainly due to the nature of its design, heavily dependent on web availability of information. However, it is difficult to see how else a similar study could have been conducted.

Reported results from controlled before and after studies

Two small studies by the same first author assessed means of nosocomial transmission of RSV in small children and the effects of introducing distancing and barriers: one with low risk of bias reported effective physical distancing and room separation (0 infected out of 14 who sat away from RSV-infected infants compared with five out of seven who cuddled and four out of 10 who touched infected infants) (Hall 1981a). The second with high risk of bias reported no incremental benefits of gowns and masks (32% infection versus 41%) (Hall 1981b). Adding disposable plastic eye-nose goggles to other respiratory infection-control procedures (isolating infected from uninfected people, handwashing) also reduced transmission of RSV (6% versus 42% of controls) (Gala 1986). Screening and subsequent isolation of infected from uninfected people (‘cohorting’) also reduced nosocomial RSV transmission in older children (from 5.33 infections per 1000/patient days of care to 1.23 infections per 1000/patient days after introduction of screening) (Krasinski 1990). A similar study reported that increased compliance with a policy of glove and gown isolation precautions reduced the high rate of nosocomial RSV transmission on an infant and toddler ward (RR for pre- and post-intervention periods infection rates 2.9, 95% CI 1.5 to 5.7) (Leclair 1987).

A study of protective gowning did not protect neonatal intensive care unit infants from RSV or any other type of infection, or affect mortality (1.21 per 100 patient-days of gowning compared to 1.38 of none), although selection bias was likely with 17% of participating children lost to follow up (Pelke 1994).

A German study conducted over three seasons reported a decrease of nosocomial RSV infections, from 1.67/1000 patient-days in the first season to 0.18/1000 patient-days in the last season, after instituting enhanced surveillance and feedback, rapid diagnosis, barriers and isolation, and disinfection of surfaces (Simon 2006). A similar study but with high risk of bias reported a decrease from eight confirmed RSV cases per 1000 patient-days to none (Snydman 1988). A better conducted study over eight years implemented a combination of education with high index of suspicion for case-finding (contact precautions), with barriers (but no goggles or masks) and handwashing for patients and staff reduced RSV infections in a hospital in Philadelphia, USA: RR 0.61, 95% CI 0.53 to 0.69 (Macartney 2000).

One small study with serious potential biases assessed training and a sanitary programme (handwashing, disinfection of school buses, appliances and toys) in a special-needs daycare facility for children with Downs Syndrome, a pupil to staff ratio of five or six to one, and reported reductions in: respiratory illnesses from a mean of 0.67 to 0.42 per child per month ($P < 0.07$); physician visits from 0.50 to 0.33 ($P < 0.05$); mean courses of antibiotics prescribed

from 0.33 to 0.28 ($P < 0.05$); and days of school missed because of respiratory infections from 0.75 to 0.40 ($P < 0.05$) (Krillov 1996). A very large study of military recruits reported that a structured top-down programme of handwashing at least five times daily nearly halved the incidence of ARIs. Recruits who handwashed less frequently reported more episodes of ARIs (OR 1.5, 95% CI 1.2 to 1.8), which represents a difference of 4.7 versus 3.2 mean infections per recruit per year, and more hospitalisations (OR 10.9, 95% CI 2.7 to 46.2). However, implementation was difficult (Ryan 2001).

An ecological study analysed the effects of quarantine and port of entry screening on the SARS epidemic in early 2003 in Beijing, China, from data collected centrally. Hospitals were the initial sources of transmission of the SARS virus. The shape of the epidemic suggests these measures may have reduced SARS transmission although only 12 cases identified out of over 13 million people screened puts in doubt the direct effectiveness of entry port checks at airports and railway stations, and screening was probably more important (Pang 2003).

An Israeli study of 186,094 children aged six to 12 years reported that school closure was temporally associated with a 42% decreased morbidity from respiratory tract infections, a consequent 28% decrease in visits to physicians and to emergency departments, and a 35% reduction in purchase of medications (Heymann 2004).

DISCUSSION

Quality issues

Several features need consideration before drawing generalisations from these studies.

The settings of the studies, conducted over four decades, were heterogeneous and ranged from suburban schools (Carabin 1999; Dyer 2000; Heymann 2004; Niffenegger 1997) to military barracks (Ryan 2001), emergency departments, intensive care units and paediatric wards (Gala 1986; Leclair 1987; Loeb 2009) in high-income countries; slums in low-income countries (Luby 2005); an upper Manhattan immigrant Latino neighbourhood (Larson 2010) and special-needs daycare centres with a very high teacher to pupil ratio (Krillov 1996). Few attempts were made to obtain socio-economic diversity by (for example) involving more schools in the evaluations of the same programme (Dyer 2000). We were able to identify few studies from low-income countries where the vast majority of the burden lies, and where cheap interventions are so critical. Even in high-income countries, such as Israel, the dramatic fall in ARIs subsequent to school closure may have been related to that country's high child population (34%). Additionally, limited availability of over-the-counter medications and national universal comprehensive health insurance provided

with consequent physician prescription of symptomatic treatment may further limit generalisability of findings (Heymann 2004). The variable quality of the methods of these studies is striking. Hasty design of interventions for public health crises, particularly the SARS case-control studies, is understandable but less so when no randomisation - not even of clusters - was carried out in several unhurried cohort and before and after studies. Randomisation could often have involved minimal disruption to service delivery. Inadequate reporting especially made interpretation difficult of before-after studies. Incomplete or no reporting of randomisation (Turner 2004a), blinding (Farr 1988a; Farr 1988b), numerators and denominators (Carabin 1999; Korch 1994), interventions, outcomes (White 2003), participant attrition (Makris 2000), confidence intervals (CIs) (Madge 1992) and cluster coefficients in the relevant trials (Carabin 1999) led to a considerable loss of information. Potential biases (such as cash incentives given to participants (White 2003)) were not discussed. Some trial authors even confused cohort with before-after designs to elaborate conclusions unsupported by their data (Makris 2000). Methodological quality was sometimes eroded by the need to deliver behavioural interventions in the midst of service delivery (Niffenegger 1997). Nonetheless, even when suboptimal designs were selected, trial authors rarely attempted to articulate potential confounders. A commonly ignored confounder, specific to this area, is the huge variability in viral incidence (Heymann 2004; Isaacs 1991). Sometimes this was addressed in the study design (Falsey 1999), even in controlled before and after studies (one attempted correlation between respiratory syncytial virus (RSV) admissions and RSV circulating in the community) (Krasinski 1990). Another attempted linking exposure (measured as nasal excretion) and infection rate in the pre- and post-intervention periods (Leclair 1987).

Inappropriate placebos caused design problems. In some studies the placebo probably carried sufficient intervention effect apparently to dilute the intervention effects (Longini 1988). Two valiant attempts probably failed because placebo handkerchiefs were impregnated with a dummy compound which stung the users' nostrils (Farr 1988a; Farr 1988b).

Some studies used impractical interventions. Volunteers subjected to the intervention hand cleaner (organic acids) were not allowed to use their hands between cleaning and virus challenge, so the effect of normal use of the hands on the intervention remains unknown (Turner 2004a; Turner 2004b). Two per cent aqueous iodine painted on the hands, although a successful antiviral intervention, causes unacceptable cosmetic staining, impractical for all but those at the highest risk of epidemic contagion (Gwaltney 1980).

Compliance with interventions, especially educational programmes, was a problem for several studies despite the importance of many such low-cost interventions. Overall the logistics of carrying out trials in immigrant neighbourhoods or students' halls of residence are demanding and recognition should be given to all those who planned and carried out studies in very difficult

circumstances (as in the middle of an epidemic).

The evidence

The highest quality cluster-randomised trials indicate most effect on preventing respiratory virus spread from hygienic measures in younger children. Perhaps this is because younger children are least capable of hygienic behaviour themselves (Roberts 2000), and have longer-lived infections and greater social contact, thereby acting as portals of infection into the household (Monto 1969). Additional benefit from reduced transmission from them to other members of the household is broadly supported by the results of other study designs where the potential for confounding is greater. The pooled case-control studies, which focused on the SARS coronavirus (SARS CoV), suggest that implementing barriers to transmission, isolation and hygienic measures are effective with the use of relatively cheap interventions to contain respiratory virus epidemics. We found limited evidence of the superior effectiveness of devices such as the N95 respirator over simple surgical masks. This evidence is supported by a high quality hospital-based trial (Loeb 2009) which reports non-inferiority between face barriers. Overall masks were the best performing intervention across populations, settings and threats. More expensive and uncomfortable (especially if worn for long periods) than simple surgical masks, N95 respirators may be useful in very high-risk situations but additional studies are required to define these situations.

It is uncertain whether the incremental effect of adding virucidals or antiseptics to normal handwashing actually decreased the respiratory disease burden outside the confines of the rather atypical studies, upon which we reported. The extra benefit may have been, at least in part, accrued by confounding additional routines.

Studies preventing transmission of RSV and similar viruses appeared to be closer to real life and suggest good effectiveness. However, methodological quality concerns of the controlled before and after studies, mentioned previously, suggest benefits may have been due to population differences, especially virus infection rates. These were poorly reported in most studies.

Routine long-term implementation of some of the measures assessed in this review would be problematic, particularly maintaining strict hygiene and barrier routines for long periods of time. This would probably only be feasible in highly motivated environments, such as hospitals, without a real threat of a looming epidemic. Most of the trial authors commented on the major logistic burden that barrier routines imposed at the community level. However, the threat of a looming epidemic may provide stimulus for their inception.

A disappointing finding was the lack of proper evaluation of global and highly resource-intensive measures such as screening at entry ports and social distancing. The handful of studies (mostly conducted during the SARS epidemic) do not allow us to reach any firm conclusions. It is remarkable that despite a long lead time to the declaration of a pandemic, an international, prospective study

to evaluate entry screening practices was not set up. The study by Cowling et al is a good contribution to our evidence base but no substitute for a well designed and conducted trial (Cowling 2010). Finally, few studies reported harms from the interventions studied. Harms affect compliance, which may decrease even if the intervention is merely cumbersome (such as a mask) and the threat is unclear.

Summary of main results

See Table 2.

Overall completeness and applicability of evidence

See Discussion.

Quality of the evidence

See Discussion.

Potential biases in the review process

Through the World Health Organization (WHO), we made inquiries to identify a list of manufacturers of the interventions assessed in this review. However, no such list appears to exist. The low-tech (i.e. locally manufacturable) nature of some of the interventions, the lack of effective regulation in some settings and the possible endless number of manufacturers make the compilation and updating of such a list in a satisfactory manner very difficult. As a consequence it is impossible to gauge the existence of unpublished data. Low-tech device marketing is poorly regulated and incompletely understood.

Agreements and disagreements with other studies or reviews

We are not aware of systematic reviews of the same evidence.

AUTHORS' CONCLUSIONS

Implications for practice

The following effective interventions should be implemented, preferably in a combined fashion, to reduce transmission of viral respiratory disease:

1. frequent handwashing with or without adjunct antiseptics;

2. barrier measures such as gloves, gowns and masks with filtration apparatus; and
3. suspicion diagnosis with isolation of likely cases.

Special efforts should be focused on implementing the three above interventions in order to reduce transmission from young children, who are generally the most fecund sources of respiratory viruses.

Implications for research

Public health measures can be highly effective, especially when they are part of a structured programme that includes instruction and education and when they are delivered together. There is a clear requirement to carry out further large, pragmatic trials to evaluate the best combinations in the community and in healthcare settings and with other respiratory viruses. RCTs with a pragmatic design, similar to the Luby et al trial, should be carried out whenever possible (Luby 2005). Nevertheless, this systematic review of the available research does provide some important insights. Perhaps the impressive effect of the hygienic measures aimed at younger children derives from the children's poor capability with their own hygiene. The variable quality and small scale of some studies is known from descriptive studies (Aiello 2002; Fung 2006; WHO 2006) and systematic reviews of selected interventions (Meadows 2004). More research is needed to evaluate the most effective strategies to implement successful physical interventions in practice, both on a small scale and at a population level. More attention should be paid to describing and quantifying the harms of the interventions assessed in this review and their relationship with compliance.

ACKNOWLEDGEMENTS

Thanks to the following people for commenting on the draft protocol and review: Anne Lyddiatt, Stephanie Kondos, Tom Sandora, Kathryn Glass, Max Bulsara, Rick Shoemaker and Allen Cheng. Thanks also to the following people for translating non-English language trials for the draft review: Jørgen Lous for translating a Danish paper and extracting data, Ryuki Kassai who translated a Japanese paper, and Taixiang Wu who translated several Chinese papers. We thank the following people for commenting on the 2009, 2010 and 2011 updated reviews, respectively, for 2009: Anne Lyddiatt, Thomas Sandora, Michael Broderick, Sree Nair and Allen Cheng; for 2010: Carmem Pessoa da Silva, Sergey Eremin; and for 2011: Amy Zelmer, Tom Sandora, Sree Nair and Allen Cheng. Drs Aiello and Larson provided additional information on their trials for the 2010 update. Dr V Shukla, Dr J Conly and K Lee prepared the GRADE tables using the GRADE Profiler software. Drs Carmem Pessoa da Silva and Thomas Hausteine provided linguistic assistance for the 2010 update.

We gratefully acknowledge funding for this 2009 update from the UK National Institute for Health Research (NIHR) and the National Health and Research Council (NHMRC) of Australia and from WHO for the 2010 update. We also thank Ruth Foxlee and Alex Rivetti for constructing the search strategies for the previous review versions and Bill Hewak and Adi Prabhala for extracting data in the original review.

REFERENCES

References to studies included in this review

Agah 1987 *{published data only}*

Agah R, Cherry JD, Garakian AJ, Chapin M. Respiratory syncytial virus (RSV) infection rate in personnel caring for children with RSV infections. Routine isolation procedure vs routine procedure supplemented by use of masks and goggles. *American Journal of Diseases of Children* 1987;**141**(6):695–7.

Aiello 2010a *{published data only}*

Aiello AE, Murray GF, Perez V, Coulborn RM, Davis BM, Uddin M, et al. Mask use, hand hygiene, and seasonal influenza-like illness among young adults: a randomized intervention trial. *Journal of Infectious Diseases* 2010;**201**(4):491–8.

Broderick 2008 *{published data only}*

Broderick MP, Hansen CJ, Russell KL. Exploration of the effectiveness of social distancing on respiratory pathogen transmission implicates environmental contributions. *Journal of Infectious Diseases* 2008;**198**(10):1420–6.

Carabin 1999 *{published data only}*

Carabin H, Gyorkos TW, Soto JC, Joseph L, Payment P, Collet JP. Effectiveness of a training program in reducing infections in toddlers attending day care centers. *Epidemiology* 1999;**10**(3):219–27.

Chen 2009 *{published data only}*

Chen WQ, Ling WH, Lu CY, Hao YT, Lin ZN, Ling L, et al. Which preventive measures might protect health care workers from SARS?. *BMC Public Health* 2009;**9**:81.

Cowling 2008 *{published data only}*

Cowling BJ, Fung RO, Cheng CK, Fang VJ, Chan KH, Seto WH, et al. Preliminary findings of a randomized trial of non-pharmaceutical interventions to prevent influenza transmission in households. *PLoS ONE* 2008;**3**(5):e2101.

Cowling 2009 *{published data only}*

Cowling BJ, Chan KH, Fang VJ, Cheng CKY, Fung ROP, Wai W, et al. Facemasks and hand hygiene to prevent influenza transmission in households. A randomized trial. *Annals of Internal Medicine* 2009;**151**(7):437–46.

Cowling 2010 *{published data only}*

Cowling BJ, Lau LLH, Wu P, Wong HWC, Fang VJ, Riley

- S, et al. Entry screening to delay local transmission of 2009 pandemic influenza A (H1N1). *BMC Infectious Diseases* 2010;**10**:82.
- Derrick 2005** *{published data only}*
Derrick JL, Gomersall CD. Protecting healthcare staff from severe acute respiratory syndrome: filtration capacity of multiple surgical masks. *Journal of Hospital Infection* 2005;**59**(4):365–8.
- Dick 1986** *{published data only}*
Dick EC, Hossain SU, Mink KA, Meschievitz CK, Schultz SB, Raynor WJ, et al. Interruption of transmission of rhinovirus colds among human volunteers using virucidal paper handkerchiefs. *Journal of Infectious Diseases* 1986;**153**(2):352–6.
- Doherty 1998** *{published data only}*
Doherty JA, Brookfield DS, Gray J, McEwan RA. Cohorting of infants with respiratory syncytial virus. *Journal of Hospital Infection* 1998;**38**(3):203–6.
- Dyer 2000** *{published data only}*
Dyer DL, Shinder A, Shinder F. Alcohol-free instant hand sanitizer reduces elementary school illness absenteeism. *Family Medicine* 2000;**32**:633–8.
- Falsey 1999** *{published data only}*
Falsey AR, Criddle MM, Kolassa JE, McCann RM, Brower CA, Hall WJ. Evaluation of a handwashing intervention to reduce respiratory illness rates in senior day-care centers. *Infection Control and Hospital Epidemiology* 1999;**20**(3):200–2.
- Farr 1988a** *{published data only}*
Farr BM, Hendley JO, Kaiser DL, Gwaltney JM. Two randomised controlled trials of virucidal nasal tissues in the prevention of natural upper respiratory infections. *American Journal of Epidemiology* 1988;**128**:1162–72.
- Farr 1988b** *{published data only}*
Farr BM, Hendley JO, Kaiser DL, Gwaltney JM. Two randomised controlled trials of virucidal nasal tissues in the prevention of natural upper respiratory infection. *American Journal of Epidemiology* 1988;**128**:1162–72.
- Foo 2006** *{published data only}*
Foo CC, Goon AT, Leow YH, Goh CL. Adverse skin reactions to personal protective equipment against severe acute respiratory syndrome - a descriptive study in Singapore. *Contact Dermatitis* 2006;**55**(5):291–4.
- Gala 1986** *{published data only}*
Gala CL, Hall CB, Schnabel KC, Pincus PH, Blossom P, Hildreth SW, et al. The use of eye-nose goggles to control nosocomial respiratory syncytial virus infection. *JAMA* 1986;**256**(19):2706–8.
- Gwaltney 1980** *{published data only}*
Gwaltney JM Jr, Moskalski PB, Hendley JO. Interruption of experimental rhinovirus transmission. *Journal of Infectious Diseases* 1980;**142**(6):811–5.
- Hall 1981a** *{published data only}*
Hall CB, Douglas RG. Modes of transmission of respiratory syncytial virus. *Journal of Pediatrics* 1981;**99**(1):100–3.
- Hall 1981b** *{published data only}*
Hall CB, Douglas RG Jr. Nosocomial respiratory syncytial viral infections. Should gowns and masks be used?. *American Journal of Diseases of Children* 1981;**135**(6):512–5.
- Heymann 2004** *{published data only}*
* Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. *Pediatric Infectious Disease Journal* 2004;**23**(7):675–7.
Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiology and Infection* 2009;**137**(10):1369–76.
- Isaacs 1991** *{published data only}*
Isaacs D, Dickson H, O'Callaghan C, Sheaves R, Winter A, Moxon ER. Handwashing and cohorting in prevention of hospital acquired infections with respiratory syncytial virus. *Archives of Disease in Childhood* 1991;**66**(2):227–31.
- Jacobs 2009** *{published data only}*
Jacobs JL, Ohde S, Takahashi O, Tokuda Y, Omata F, Fukui T. Use of surgical face masks to reduce the incidence of the common cold among health care workers in Japan: a randomized controlled trial. *American Journal of Infection Control* 2009;**37**(5):417–9.
- Kimel 1996** *{published data only}*
Kimel LS. Handwashing education can decrease illness absenteeism. *Journal of School Nursing* 1996;**12**(2):14–6, 8.
- Kotch 1994** *{published data only}*
Kotch JB, Weigle KA, Weber DJ, Clifford RM, Harms TO, Loda FA, et al. Evaluation of an hygienic intervention in child day-care centers. *Pediatrics* 1994;**94**(6 Pt 2):991–4.
- Krasinski 1990** *{published data only}*
Krasinski K, LaCouture R, Holzman RS, Waithe E, Bonk S, Hanna B. Screening for respiratory syncytial virus and assignment to a cohort at admission to reduce nosocomial transmission. *Journal of Pediatrics* 1990;**116**(6):894–8.
- Krilov 1996** *{published data only}*
Krilov LR, Barone SR, Mandel FS, Cusack TM, Gaber DJ, Rubino JR. Impact of an infection control program in a specialized preschool. *American Journal of Infection Control* 1996;**24**(3):167–73.
- Ladegaard 1999** *{published data only}*
Ladegaard MB, Stage V. Hand hygiene and sickness among small children attending day care centres. An interventional study. *Ukesgrift von Laeger* 1999;**161**:4396–400.
- Larson 2010** *{published data only}*
Larson EL, Ferng Y, Wong-McLoughlin J, Wang S, Haber M, Morse SS. Impact of non-pharmaceutical interventions on URIs and influenza in crowded, urban households. *Public Health Reports* 2010;**125**(2):178–91.
- Lau 2004a** *{published data only}*
Lau JT, Tsui H, Lau M, Yang X. SARS transmission, risk factors, and prevention in Hong Kong. *Emerging Infectious Diseases* 2004;**10**(4):587–92.

Leclair 1987 {published data only}

Leclair JM, Freeman J, Sullivan BF, Crowley CM, Goldmann DA. Prevention of nosocomial respiratory syncytial virus infections through compliance with glove and gown isolation precautions. *New England Journal of Medicine* 1987;**317**(6):329–34.

Leung 2004 {published data only}

Leung TF, Ng PC, Cheng FW, Lyon DJ, So KW, Hon EK, et al. Infection control for SARS in a tertiary paediatric centre in Hong Kong. *Journal of Hospital Infection* 2004;**3**: 215–22.

Liu 2009 {published data only}

Liu W, Tang F, Fang LQ, De Vlas SJ, Ma HJ, Zhou JP, et al. Risk factors for SARS infection among hospital healthcare workers in Beijing: a case control study. *Tropical Medicine and International Health* 2009;**14**(Suppl 1):52–9.

Loeb 2009 {published data only}

Loeb M, Dafoe N, Mahony J, John M, Sarabia A, Glavin V, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA* 2009;**302**(17):1865–71.

Longini 1988 {published data only}

Longini IM Jr, Monto AS. Efficacy of virucidal nasal tissues in interrupting familial transmission of respiratory agents. A field trial in Tecumseh, Michigan. *American Journal of Epidemiology* 1988;**128**(3):639–44.

Luby 2005 {published data only}

Luby SP, Agboatwalla M, Feikin DR, Painter J, Billhimer W, Alataf A, et al. Effect of handwashing on child health: a randomised controlled trial. *Lancet* 2005;**366**(9481): 225–33.

Macartney 2000 {published data only}

Macartney KK, Gorelick MH, Manning ML, Hodinka RL, Bell LM. Nosocomial respiratory syncytial virus infections: the cost-effectiveness and cost-benefit of infection control. *Pediatrics* 2000;**106**(3):520–6.

MacIntyre 2009 {published data only}

MacIntyre CR, Cauchemez S, Dwyer DE, Seale H, Cheung P, Browne G, et al. Face mask use and control of respiratory virus transmission in households. *Emerging Infectious Diseases* 2009;**15**(2):233–41.

Madge 1992 {published data only}

Madge P, Paton JY, McColl JH, Mackie PL. Prospective controlled study of four infection-control procedures to prevent nosocomial infection with respiratory syncytial virus. *Lancet* 1992;**340**(8827):1079–83.

Makris 2000 {published data only}

Makris AT, Morgan L, Gaber DJ. Effect of a comprehensive infection control program on the incidence of infections in long-term care facilities. *American Journal of Infection Control* 2000;**28**(1):3–7.

Master 1997 {published data only}

Master D, Longe SH, Dickson H. Scheduled hand washing in an elementary school population. *Family Medicine* 1997; **29**:336–9.

Morton 2004 {published data only}

Morton JL, Schultz AA. Healthy hands: use of alcohol gel as an adjunct to handwashing in elementary school children. *Journal of School Nursing* 2004;**20**(3):161–7.

Murphy 1981 {published data only}

Murphy D, Todd JK, Chao RK, Orr I, McIntosh K. The use of gowns and masks to control respiratory illness in pediatric hospital personnel. *Journal of Pediatrics* 1981;**99** (5):746–50.

Niffenegger 1997 {published data only}

Niffenegger JP. Proper handwashing promotes wellness in child care. *Journal of Pediatric Health Care* 1997;**11**(1): 26–31.

Nishiura 2005 {published data only}

Nishiura H, Kuratsuji T, Quy T, Phi NC, Van Ban V, Ha LE, et al. Rapid awareness and transmission of severe acute respiratory syndrome in Hanoi French Hospital, Vietnam. *American Journal of Tropical Medicine & Hygiene* 2005;**73** (1):17–25.

Ou 2003 {published data only}

* Centers for Disease Control and Prevention (CDC). Efficiency of quarantine during an epidemic of severe acute respiratory syndrome - Beijing, China, 2003. *Morbidity & Mortality Weekly Report* 2003;**52**(43):1037–40.
Ou JM, Dun Zhe, Li Q, Qin AL, Zeng G. Efficiency of the quarantine system during the epidemic of severe acute respiratory syndrome in Beijing, 2003. *Chung-Hua Liu Hsing Ping Hsueh Tsa Chih [Chinese Journal of Epidemiology]* 2003;**24**(12):1093–5.

Pang 2003 {published data only}

Pang X, Zhu Z, Xu F, Guo J, Gong X, Liu D, et al. Evaluation of control measures implemented in the severe acute respiratory syndrome outbreak in Beijing, 2003. *JAMA* 2003;**290**(24):3215–2.

Pelke 1994 {published data only}

Pelke S, Ching D, Easa D, Melish ME. Gowning does not affect colonization or infection rates in a neonatal intensive care unit. *Archives of Pediatrics & Adolescent Medicine* 1994; **148**(10):1016–20.

Roberts 2000 {published data only}

Roberts L, Smith W, Jorm L, Patel M, Douglas RM, McGilchrist C. Effect of infection control measures on the frequency of upper respiratory infection in child care: a randomised controlled study. *Pediatrics* 2000;**105**:738–42.

Ryan 2001 {published data only}

Ryan MA, Christian RS, Wohlrabe J. Handwashing and respiratory illness among young adults in military training. *American Journal of Preventive Medicine* 2001;**21**(2):79–83.

Sandora 2005 {published data only}

Sandora TJ, Taveras EM, Shih MC, Resnick EA, Lee GM, Ross-Degnan D, et al. A randomized, controlled trial of a multifaceted intervention including alcohol-based hand sanitizer and hand-hygiene education to reduce illness transmission in the home. *Pediatrics* 2005;**116**(3):587–94.

Sandora 2008 {published data only}

Sandora TJ, Shih MC, Goldmann DA. Reducing absenteeism from gastrointestinal and respiratory illness in elementary school students: a randomized, controlled trial of an infection-control intervention. *Pediatrics* 2008;**121**(6):e1555–62.

Satomura 2005 {published data only}

Kitamura T, Satomura K, Kawamura T, Yamada S, Takashima K, Sugauma N, et al. Can we prevent influenza-like illnesses by gargling?. *Internal Medicine* 2007;**46**(18): 1623–4.

* Satomura K, Kitamura T, Kawamura T, Shimbo T, Watanabe M, Kamei M, et al. Prevention of upper respiratory tract infections by gargling: a randomized trial. *American Journal of Preventive Medicine* 2005;**29**(4):302–7.

Seto 2003 {published data only}

Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, Ho M, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003;**361**(9368): 1519–20.

Simon 2006 {published data only}

Simon A, Khurana K, Wilkesmann A, Muller A, Engelhart S, Exner M, et al. Nosocomial respiratory syncytial virus infection: impact of prospective surveillance and targeted infection control. *International Journal of Hygiene and Environmental Health* 2006;**209**(4):317–24.

Snydman 1988 {published data only}

Snydman DR, Greer C, Meissner HC, McIntosh K. Prevention of nosocomial transmission of respiratory syncytial virus in a newborn nursery. *Infection Control and Hospital Epidemiology* 1988;**9**(3):105–8.

Somogyi 2004 {published data only}

Somogyi R, Vesely AE, Azami T, Preiss D, Fisher J, Correia J, et al. Dispersal of respiratory droplets with open vs closed oxygen delivery masks: implications for the transmission of severe acute respiratory syndrome. *Chest* 2004;**125**(3): 1155–7.

Teleman 2004 {published data only}

Teleman MD, Boudville IC, Heng BH, Zhu D, Leo YS. Factors associated with transmission of severe acute respiratory syndrome among health-care workers in Singapore. *Epidemiology and Infection* 2004;**135**(5): 797–803.

Turner 2004a {published data only}

Turner RB, Biedermann KA, Morgan JM, Keswick B, Ertel KD, Barker MF. Efficacy of organic acids in hand cleansers for prevention of rhinovirus infections. *Antimicrobial Agents and Chemotherapy* 2004;**48**(7):2595–8.

Turner 2004b {published data only}

Turner RB, Biedermann KA, Morgan JM, Keswick B, Ertel KD, Barker MF. Efficacy of organic acids in hand cleansers for prevention of rhinovirus infections. *Antimicrobial Agents and Chemotherapy* 2004;**48**(7):2595–8.

Wang 2007 {published data only}

Wang TH, Wei KC, Hsiung CA, Maloney SA, Eidex RB, Posey DL, et al. Optimizing severe acute respiratory syndrome response strategies: lessons learned from quarantine. *American Journal of Public Health* 2007;**97**(Suppl):1541–8.

White 2001 {published data only}

White CG, Shinder FS, Shinder AL, Dyer DL. Reduction of illness absenteeism in elementary schools using and alcohol-free instant hand sanitizer. *Journal of School Nursing* 2001;**17**(5):258–65.

White 2003 {published data only}

White C, Kolble R, Carlson R, Lipson N, Dolan M, Ali Y, et al. The effect of hand hygiene on illness rate among students in university residence halls. *American Journal of Infection Control* 2003;**31**(6):364–70.

Wu 2004 {published data only}

Wu J, Xu F, Zhou W, Feikin DR, Lin CY, He X. Risk factors for SARS among persons without known contact with SARS patients, Beijing, China. *Emerging Infectious Diseases* 2004;**10**(2):210–6.

Yen 2006 {published data only}

Yen MY, Lin YE, Su IJ, Huang FY, Huang FY, Ho MS, et al. Using an integrated infection control strategy during outbreak control to minimize nosocomial infection of severe acute respiratory syndrome among healthcare workers. *Journal of Hospital Infection* 2006;**62**(2):195–9.

Yin 2004 {published data only}

Yin WW, Gao LD, Lin WS, Gao LD, Lin WS, Du L, et al. Effectiveness of personal protective measures in prevention of nosocomial transmission of severe acute respiratory syndrome. *Chung-Hua Liu Hsing Ping Hsueh Tsa Chih (Chinese Journal of Epidemiology)* 2004;**25**(1):18–22.

Yu 2007 {published data only}

Yu IT, Xie ZH, Tsoi KK, Chiu YL, Lok SW, Tang XP, et al. Why did outbreaks of severe acute respiratory syndrome occur in some hospital wards but not in others?. *Clinical Infectious Diseases* 2007;**44**(8):1017–25.

References to studies excluded from this review

Abou El Hassan 2004 {published data only}

Abou El Hassan MA, van der Meulen-Muileman I, Abbas S, Kruijff FA. Conditionally replicating adenoviruses kill tumor cells via a basic apoptotic machinery-independent mechanism that resembles necrosis-like programmed cell death. *Journal of Virology* 2004;**78**(22):12243–51.

Amirav 2005 {published data only}

Amirav I, Oron A, Tal G, Cesar K, Ballin A, Houry S, et al. Aerosol delivery in respiratory syncytial virus bronchiolitis: hood or face mask?. *Journal of Pediatrics* 2005;**147**(5): 627–31.

Anderson 2004 {published data only}

Anderson RM, Fraser C, Ghani AC, Donnelly CA, Riley S, Ferguson NM, et al. Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic.

Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences 2004;**359**(1447):1091–105.

Anonymous 2002 {published data only}

Anonymous. Antiseptic skin cleansers may prevent rhinovirus transmission. *Clinical Infectious Diseases* 2002;**34**(3):ii.

Anonymous 2003 {published data only}

Anonymous. Use of quarantine to prevent transmission of severe acute respiratory syndrome - Taiwan, 2003. *Morbidity & Mortality Weekly Report* 2003;**52**(52):29.

Anonymous 2004 {published data only}

Anonymous. Can antiviral tissues prevent the spread of colds?. *Consumer Reports* 2004;**69**(12):56.

Anonymous 2005a {published data only}

Anonymous. Antiviral Kleenex. *Medical Letter on Drugs & Therapeutic* 2005;**47**(1199):3–4.

Anonymous 2005b {published data only}

Anonymous. Focusing on this year's flu...use healthy handwashing...and when soap and water aren't handy, hand gels work well, too. *Child Health Alert* 2005;**23**:1–2.

Anonymous 2005c {published data only}

Anonymous. How long is a cold contagious? Is there any way to prevent transmitting a cold?. Johns Hopkins Medical Letter, *Health After 50* 2005; Vol. 17, issue 10:8.

Apisarnthanarak 2009 {published data only}

Apisarnthanarak A, Apisarnthanarak P, Cheevakumjorn B, Mundy LM. Intervention with an infection control bundle to reduce transmission of influenza-like illnesses in a Thai preschool. *Infection Control and Hospital Epidemiology* 2009;**30**(9):817–22.

Apisarnthanarak 2010 {published data only}

Apisarnthanarak A, Uyeki TM, Puthavathana P, Kitphati R, Mundy LM. Reduction of seasonal influenza transmission among healthcare workers in an intensive care unit: a 4-year intervention study in Thailand. *Infection Control and Hospital Epidemiology* 2010;**31**(10):996–1003.

Aragon 2005 {published data only}

Aragon D, Sole ML, Brown S. Outcomes of an infection prevention project focusing on hand hygiene and isolation practices. *AACN Clinical Issues* 2005;**16**(2):121–3.

Barros 1999 {published data only}

Barros AJ, Ross DA, Fonseca WV, Williams LA, Moreira-Filho DC. Preventing acute respiratory infections and diarrhoea in child care centres. *Acta Paediatrica* 1999;**88**(10):1113–8.

Bauer 2009 {published data only}

Bauer G, Bossi L, Santoalla M, Rodríguez S, Fariña D, Speranza AM. Impacto de un programa de prevención de infecciones respiratorias en lactantes prematuros de alto riesgo: estudio prospectivo y multicéntrico. *Archivos Argentinos de Pediatría* 2009;**107**(2):111–8.

Bell 2004 {published data only}

Bell DM. World Health Organization Working Group on International and Community Transmission of SARS. *Emerging Infectious Diseases* 2004;**10**(11):1900–6.

Bellissimo-Rodrigues 2009 {published data only}

Bellissimo-Rodrigues F, Bellissimo-Rodrigues WT, Viana JM, Teixeira GCA, Nicolini E, Auxiliadora-Martins M, et al. Effectiveness of oral rinse with chlorhexidine in preventing nosocomial respiratory tract infections among intensive care unit patients. *Infection Control and Hospital Epidemiology* 2009;**30**(10):952–8.

Ben-Abraham 2002 {published data only}

Ben-Abraham R, Keller N, Szold O, Vardi A, Weinberg M, Barzilay Z, et al. Do isolation rooms reduce the rate of nosocomial infections in the pediatric intensive care unit?. *Journal of Critical Care* 2002;**17**(3):176–80.

Black 1981 {published data only}

Black RE, Dykes AC, Anderson KE, Wells JG, Sinclair SP, Gary GW, et al. Handwashing to prevent diarrhea in day-care centers. *American Journal of Epidemiology* 1981;**113**(4):445–51.

Borkow 2010 {published data only}

Borkow G, Zhou SS, Page T, Gabbay J. A novel anti-influenza copper oxide containing respiratory face mask. *PLoS One* 2010;**5**(6):1–8.

Bouadma 2010 {published data only}

Bouadma L, Mourvillier B, Deiler V, Le Corre B, Lolom I, Régnier B, et al. A multifaceted program to prevent ventilator-associated pneumonia: impact on compliance with preventive measures. *Critical Care Medicine* 2010;**38**(3):789–96.

Breugelmans 2004 {published data only}

Breugelmans JG, Zucs P, Porten K, Broll S, Niedrig M, Ammon A, et al. SARS transmission and commercial aircraft. *Emerging Infectious Diseases* 2004;**10**(8):1502–3.

Cai 2009 {published data only}

Cai W, Schweiger B, Buchholz U, Buda S, Littmann M, Heusler J, et al. Protective measures and H5N1-seroprevalence among personnel tasked with bird collection during an outbreak of avian influenza A/H5N1 in wild birds, Ruegen, Germany, 2006. *BMC Infectious Diseases* 2009;**9**:170.

Cantagalli 2010 {published data only}

Cantagalli MR, Alvim VF, Andrade EC, Leite ICG. Associação entre desnutrição energético-proteica e infecção respiratória aguda em crianças na atenção primária à saúde. *Revista de APS* 2010;**13**(1):26–33.

Carbonell-Estrany 2008 {published data only}

Carbonell-Estrany X, Bont L, Doering G, Gouyon JB, Lanari M. Clinical relevance of prevention of respiratory syncytial virus lower respiratory tract infection in preterm infants born between 33 and 35 weeks gestational age. *European Journal of Clinical Microbiology and Infectious Diseases* 2008;**27**(10):891–9.

Carter 2002 {published data only}

Carter JM. Hand washing decreases risk of colds and flu. *Journal of the National Medical Association* 2002;**94**(2):A11.

Castillo-Chavez 2003 {published data only}

Castillo-Chavez C, Castillo-Garsow CW, Yakubu AA. Mathematical models of isolation and quarantine. *JAMA* 2003;**290**(21):2876–7.

Cava 2005a {published data only}

Cava MA, Fay KE, Beanlands HJ, McCay EA, Wignall R. Risk perception and compliance with quarantine during the SARS outbreak. *Journal of Nursing Scholarship* 2005;**37**(4):343–7.

Cava 2005b {published data only}

Cava MA, Fay KE, Beanlands HJ, McCay EA, Wignall R. The experience of quarantine for individuals affected by SARS in Toronto. *Public Health Nursing* 2005;**22**(5):398–406.

CDC 2003 {published data only}

Centers for Disease Control and Prevention (CDC). Cluster of severe acute respiratory syndrome cases among protected health-care workers - Toronto, Canada, April 2003. *MMWR - Morbidity & Mortality Weekly Report* 2003;**52**(19):433–6.

Chai 2005 {published data only}

Chai LY, Ng TM, Habib AG, Singh K, Kumarasinghe G, Tambyah PA. Paradoxical increase in methicillin-resistant *Staphylococcus aureus* acquisition rates despite barrier precautions and increased hand washing compliance during an outbreak of severe acute respiratory syndrome. *Clinical Infectious Diseases* 2005;**40**(4):623–3.

Chaovanich 2004 {published data only}

Chaovanich A, Wongsawat J, Dowell SF, Inthong Y, Sangsajja C, Sanguanwongse N, et al. Early containment of severe acute respiratory syndrome (SARS); experience from Bamrasnaradura Institute, Thailand. *Journal of the Medical Association of Thailand* 2004;**87**(10):1182–7.

Chau 2003 {published data only}

Chau PH, Yip PS. Monitoring the severe acute respiratory syndrome epidemic and assessing effectiveness of interventions in Hong Kong Special Administrative Region. *Journal of Epidemiology and Community Health* 2003;**57**(10):766–9.

Chau 2008 {published data only}

Chau JPC, Thompson DR, Twinn S, Lee DTF, Lopez V, Ho LSY. An evaluation of SARS and droplet infection control practices in acute and rehabilitation hospitals in Hong Kong. *Hong Kong Medical Journal* 2008;**14**(Suppl 4):44–7.

Chen 2007 {published data only}

Chen YC, Chiang LC. Effectiveness of hand-washing teaching programs for families of children in paediatric intensive care units. *Journal of Clinical Nursing* 2007;**16**(6):1173–9.

Cheng 2010 {published data only}

Cheng VCC, Tai JWM, Wong LMW, Chan JFW, Li IWS, To KKW, et al. Prevention of nosocomial transmission of swine-origin pandemic influenza virus A/H1N1 by infection control bundle. *Journal of Hospital Infection* 2010;**74**(3):271–7.

Chia 2005 {published data only}

Chia SE, Koh D, Fones C, Qian F, Ng V, Tan BH, et al. Appropriate use of personal protective equipment among healthcare workers in public sector hospitals and primary healthcare polyclinics during the SARS outbreak in Singapore. *Occupational and Environmental Medicine* 2005;**62**(7):473–7.

Clynes 2010 {published data only}

Clynes N. Surgical masks vs N95 respirators for preventing influenza. *JAMA* 2010;**303**(10):937–9.

Cowling 2007 {published data only}

Cowling BJ, Muller MP, Wong IO, Ho LM, Louie M, McGeer A, et al. Alternative methods of estimating an incubation distribution: examples from severe acute respiratory syndrome. *Epidemiology* 2007;**18**(2):253–9.

Daniels 2010 {published data only}

Daniels TL, Talbot TR. Unmasking the confusion of respiratory protection to prevent influenza-like illness in crowded community settings. *Journal of Infectious Diseases* 2010;**201**(4):483–5.

Daugherty 2008 {published data only}

Daugherty EL. Health care worker protection in mass casualty respiratory failure: infection control, decontamination, and personal protective equipment. *Respiratory Care* 2008;**53**(2):201–12; discussion 212–4.

Davies 1994 {published data only}

Davies KJ, Herbert AM, Westmoreland D, Bagg J. Seroepidemiological study of respiratory virus infections among dental surgeons. *British Dental Journal* 1994;**176**(7):262–5.

Day 1993 {published data only}

Day RA, St Arnaud S, Monsma M. Effectiveness of a handwashing program. *Clinical Nursing Research* 1993;**2**(1):24–40.

Day 2006 {published data only}

Day T, Park A, Madras N, Gumel A, Wu J. When is quarantine a useful control strategy for emerging infectious diseases?. *American Journal of Epidemiology* 2006;**163**(5):479–85.

Dell'Omodarme 2005 {published data only}

Dell'Omodarme M, Prati MC. The probability of failing in detecting an infectious disease at entry points into a country. *Statistics in Medicine* 2005;**24**(17):2669–79.

Desenclos 2004 {published data only}

Desenclos JC, van der Werf S, Bonmarin I, Levy-Bruhl D, Yazdanpanah Y, Hoen B, et al. Introduction of SARS in France, March-April, 2003. *Emerging Infectious Diseases* 2004;**10**(2):195–200.

DiGiovanni 2004 {published data only}

DiGiovanni C, Conley J, Chiu D, Zaborski J. Factors influencing compliance with quarantine in Toronto during the 2003 SARS outbreak. *Biosecurity and Bioterrorism* 2004;**2**(4):265–72.

Doebbeling 1992 {published data only}

Doebbeling BN, Stanley GL, Sheetz CT. Comparative efficacy of alternative hand-washing agents in reducing

- nosocomial infections in intensive care units. *New England Journal of Medicine* 1992;**327**(2):88–92.
- Dwosh 2003** {published data only}
Dwosh HA, Hong HH, Austgarden D, Herman S, Schabas R. Identification and containment of an outbreak of SARS in a community hospital. *Canadian Medical Association Journal* 2003;**168**(11):1415–20.
- Edmonds 2010** {published data only}
Edmonds S, Dzyakanava V, Macinga D. Efficacy of hand hygiene products against pandemic H1N1 influenza. *American Journal of Infection Control* 2010;**38**(5):E132–3.
- Fendler 2002** {published data only}
Fendler EJ, Ali Y, Hammond BS, Lyons MK, Kelley MB, Vowell NA. The impact of alcohol hand sanitizer use on infection rates in an extended care facility. *American Journal of Infection Control* 2002;**30**(4):226–33.
- Flint 2003** {published data only}
Flint J, Burton S, Macey JF, Deeks SL, Tam TW, King A, et al. Assessment of in-flight transmission of SARS - results of contact tracing. *Canadian Communicable Disease Report* 2003;**29**(12):105–10.
- Fung 2004** {published data only}
Fung CP, Hsieh TL, Tan KH, Loh CH, Wu JS, Li CC, et al. Rapid creation of a temporary isolation ward for patients with severe acute respiratory syndrome in Taiwan. *Infection Control and Hospital Epidemiology* 2004;**25**(12):1026–32.
- Garcia 2010** {published data only}
Garcia MC. The protection against influenza provided by surgical masks is not inferior to what the FFP2 (N95) respiratory protector can give. *FMC Formacion Medica Continuada en Atencion Primaria* 2010;**17**(5):365.
- Gaydos 2001** {published data only}
Gaydos JC. Returning to the past: respiratory illness, vaccines, and handwashing. *American Journal of Preventive Medicine* 2001;**21**(2):150–1.
- Gensini 2004** {published data only}
Gensini GF, Yacoub MH, Conti AA. The concept of quarantine in history: from plague to SARS. *Journal of Infection* 2004;**49**(4):257–61.
- Giroud 2002** {published data only}
Giroud E, Loyeay S, Legrand S, et al. Efficacy of handrubbing with alcohol based solution versus standard handwashing with antiseptic soap: randomised clinical trial. *BMJ* 2002;**325**:362–5.
- Glass 2006** {published data only}
Glass K, Becker NG. Evaluation of measures to reduce international spread of SARS. *Epidemiology and Infection* 2006;**134**(5):1092–101.
- Goel 2007** {published data only}
Goel S, Gupta AK, Singh A, Lenka SR. Preparations and limitations for prevention of severe acute respiratory syndrome in a tertiary care centre of India. *Journal of Hospital Infection* 2007;**66**(2):142–7.
- Gomersall 2006** {published data only}
Gomersall CD, Joynt GM, Ho OM, Ip M, Yap F, Derrick JL, et al. Transmission of SARS to healthcare workers. The experience of a Hong Kong ICU. *Intensive Care Medicine* 2006;**32**(4):564–9.
- Gore 2001** {published data only}
Gore J, Lambert JA. Does use of an instant hand sanitizer reduce elementary school illness absenteeism?. *Journal of Family Practice* 2001;**50**(1):64.
- Gostin 2003** {published data only}
Gostin LO, Bayer R, Fairchild AL. Ethical and legal challenges posed by severe acute respiratory syndrome: implications for the control of severe infectious disease threats. *JAMA* 2003;**290**(24):3229–37.
- Gralton 2010** {published data only}
Gralton J, McLaws ML. Protecting healthcare workers from pandemic influenza: N95 or surgical masks?. *Critical Care Medicine* 2010;**38**(2):657–67.
- Guinan 2002** {published data only}
Guinan M, McGukin M, Ali Y. The effect of a comprehensive handwashing program on absenteeism in elementary schools. *American Journal of Infection Control* 2002;**30**(4):217–20.
- Gupta 2005** {published data only}
Gupta AG, Moyer CA, Stern DT. The economic impact of quarantine: SARS in Toronto as a case study. *Journal of Infection* 2005;**50**(5):386–93.
- Gwaltney 1982** {published data only}
Gwaltney JM Jr, Hendley JO. Transmission of experimental rhinovirus infection by contaminated surfaces. *American Journal of Epidemiology* 1982;**116**:828–33.
- Han 2003** {published data only}
Han H, Li X, Qu W, Shen T, Xu F, Gao D, et al. The building and practice of the emergency isolation radiology information system at the department of radiology in polyclinic during the epidemic outbreak stage of SARS. *Beijing Da Xue Xue Bao [Journal of Peking University]* 2003;**35**(Suppl):86–8.
- Hayden 1985** {published data only}
Hayden GF, Hendley JO, Gwaltney JM Jr. The effect of placebo and virucidal paper handkerchiefs on viral contamination of the hand and transmission of experimental rhinoviral infection. *Journal of Infectious Diseases* 1985;**152**(2):403–7.
- Hendley 1988** {published data only}
Hendley JO, Gwaltney JM Jr. Mechanisms of transmission of rhinovirus infections. *Epidemiologic Reviews* 1988;**10**:243–58.
- Hens 2009** {published data only}
Hens N, Ayele GM, Goeyvaerts N, Aerts M, Mossong J, Edmunds JW, et al. Estimating the impact of school closure on social mixing behaviour and the transmission of close contact infections in eight European countries. *BMC Infectious Diseases* 2009;**9**:187.

Heymann 2009 {published data only}

Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. *Epidemiology and Infection* 2009;**137**(10):1369–76.

Hilburn 2003 {published data only}

Hilburn J, Hammond BS, Fendler EJ, Groziak PA. Use of alcohol hand sanitizer as an infection control strategy in an acute care facility. *American Journal of Infection Control* 2003;**31**(2):109–16.

Hilmarsson 2007 {published data only}

Hilmarsson H, Traustason BS, Kristmundsdottir T, Thormar H. Virucidal activities of medium- and long-chain fatty alcohols and lipids against respiratory syncytial virus and parainfluenza virus type 2: comparison at different pH levels. *Archives of Virology* 2007;**152**(1):225–36.

Hirsch 2006 {published data only}

Hirsch HH, Steffen I, Francioli P, Widmer AF. Respiratory syncytial virus infections: measures in immunocompromised patients [Respiratorisches Syncytial-virus (RSV)–Infektion: Massnahmen beim immunsupprimierten Patienten]. *Praxis* 2006;**95**(3):61–6.

Ho 2003 {published data only}

Ho AS, Sung JJ, Chan-Yeung M. An outbreak of severe acute respiratory syndrome among hospital workers in a community hospital in Hong Kong. *Annals of Internal Medicine* 2003;**139**(7):564–7.

Hsieh 2007 {published data only}

Hsieh YH, King CC, Chen CW, Ho MS, Hsu SB, Wu YC. Impact of quarantine on the 2003 SARS outbreak: a retrospective modeling study. *Journal of Theoretical Biology* 2007;**244**(4):729–36.

Hugonnet 2007 {published data only}

Hugonnet S, Legros D, Roth C, Pessoa-Silva CL. Nosocomial transmission of severe acute respiratory syndrome: better quality of evidence is needed. *Clinical Infectious Diseases* 2007;**45**(12):1651.

Jiang 2003 {published data only}

* Jiang S, Huang L, Chen X, Wang J, Wu W, Yin S. Ventilation of wards and nosocomial outbreak of severe acute respiratory syndrome among healthcare workers. *Chinese Medical Journal* 2003;**116**(9):1293–7.
Jiang SP, Huang LW, Wang JF, Wu W, Yin SM, Chen WX. A study of the architectural factors and the infection rates of healthcare workers in isolation units for severe acute respiratory syndrome. *Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih (Chinese Journal of Tuberculosis & Respiratory Diseases)* 2003;**26**(10):594–7.

Johnson 2009 {published data only}

Johnson DF, Druce JD, Birch C, Grayson ML. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. *Clinical Infectious Diseases* 2009;**49**(2):275–7.

Jones 2005 {published data only}

Jones EW. “Co-operation in All Human Endeavour”: quarantine and immigrant disease vectors in the 1918-1919 influenza pandemic in Winnipeg. *Canadian Bulletin of Medical History* 2005;**22**(1):57–82.

Kaydos-Daniels 2004 {published data only}

Kaydos-Daniels SC, Olowokure B, Chang HJ, Barwick RS, Deng JF, Lee ML, et al. Body temperature monitoring and SARS fever hotline, Taiwan. *Emerging Infectious Diseases* 2004;**10**(2):373–6.

Kelso 2009 {published data only}

Kelso JK, Milne GJ, Kelly H. Simulation suggests that rapid activation of social distancing can arrest epidemic development due to a novel strain of influenza. *BMC Public Health* 2009;**9**:117.

Khaw 2008 {published data only}

Khaw KS, Ngan Kee WD, Tam YH, Wong MK, Lee SW. Survey and evaluation of modified oxygen delivery devices used for suspected severe acute respiratory syndrome and other high-risk patients in Hong Kong. *Hong Kong Medical Journal* 2008;**14**(Suppl 5):27–31.

Kilabuko 2007 {published data only}

Kilabuko JH, Nakai S. Effects of cooking fuels on acute respiratory infections in children in Tanzania. *International Journal of Environmental Research and Public Health* 2007;**4**(4):283–8.

Kosugi 2004 {published data only}

Kosugi Y, Ishikawa T, Chimura Y, Annaka M, Shibasaki S, Adachi K, et al. Control of hospital infection of influenza: administration of neuraminidase inhibitor and cohort isolation of influenza patients. *Kansenshogaku Zasshi [Journal of the Japanese Association for Infectious Diseases]* 2004;**78**(12):995–9.

Lam 2004 {published data only}

Lam BC, Lee J, Lau YL. Hand hygiene practices in a neonatal intensive care unit: a multimodal intervention and impact on nosocomial infection. *Pediatrics* 2004;**114**(5):e565–71.

Lange 2004 {published data only}

Lange JH. Use of disposable face masks for public health protection against SARS. *Journal of Epidemiology and Community Health* 2004;**58**(5):434.

Larson 2004 {published data only}

Larson EL, Lin SX, Gomez-Pichardo C, Della-Latta P. Effect of antibacterial home cleaning and handwashing products on infectious disease symptoms: a randomized, double-blind trial. *Annals of Internal Medicine* 2004;**140**(5):321–9.

Larson 2005 {published data only}

Larson EL, Cimiotti J, Haas J, Parides M, Nesin M, Della-Latta P, et al. Effect of antiseptic handwashing vs alcohol sanitizer on health care-associated infections in neonatal intensive care units. *Archives of Pediatrics & Adolescent Medicine* 2005;**159**(4):377–83.

Lau 2004b *{published data only}*

Lau JT, Yang X, Tsui HY, Pang E. SARS related preventive and risk behaviours practised by Hong Kong-mainland China cross border travellers during the outbreak of the SARS epidemic in Hong Kong. *Journal of Epidemiology and Community Health* 2004;**58**(12):988–96.

Lau 2005 *{published data only}*

Lau JT, Leung PC, Wong EL, Fong C, Cheng KF, Zhang SC, et al. The use of an herbal formula by hospital care workers during the severe acute respiratory syndrome epidemic in Hong Kong to prevent severe acute respiratory syndrome transmission, relieve influenza-related symptoms, and improve quality of life: a prospective cohort study. *Alternative & Complementary Medicine* 2005;**11**(1):49–55.

Lee 2005 *{published data only}*

Lee GM, Salomon JA, Friedman JF, Hibberd PL, Ross-Degnan D, Zasloff E, et al. Illness transmission in the home: a possible role for alcohol-based hand gels. *Pediatrics* 2005;**115**(4):852–60.

Lee 2010 *{published data only}*

Lee VJ, Yap J, Cook AR, Chen MI, Tay JK, Barr I, et al. Effectiveness of public health measures in mitigating pandemic influenza spread: a prospective sero-epidemiological cohort study. *Journal of Infectious Diseases* 2010;**202**(9):1319–26.

Lipsitch 2003 *{published data only}*

Lipsitch M, Cohen T, Cooper B, Robins JM, Ma S, James L, et al. Transmission dynamics and control of severe acute respiratory syndrome. *Science* 2003;**300**(5627):1966–70.

Luckingham 1984 *{published data only}*

Luckingham B. To mask or not to mask: a note on the 1918 Spanish influenza epidemic in Tucson. *The Journal of Arizona History* 1984;**25**(2):191–204.

Ma 2004 *{published data only}*

Ma HJ, Wang HW, Fang LQ, Jiang JF, Wei MT, Liu W, et al. A case-control study on the risk factors of severe acute respiratory syndromes among health care workers. *Chung-Hua Liu Hsing Ping Hsueh Tsa Chih [Chinese Journal of Epidemiology]* 2004;**25**(9):741–4.

MacIntyre 2010 *{published data only}*

MacIntyre CR. Cluster randomised controlled trial: hand hygiene and face mask use within 36 hours of index patient symptom onset reduces flu transmission to household contacts. *Evidence-Based Medicine* 2010;**15**(2):48–9.

Malone 2009 *{published data only}*

Malone JD, Brigantic R, Muller GA, Gadgil A, Delp W, McMahon BH, et al. U.S. airport entry screening in response to pandemic influenza: modeling and analysis. *Travel Medicine and Infectious Disease* 2009;**7**(4):181–91.

Marin 1991 *{published data only}*

Marin J, Dragas AZ, Mavsar B. Virus permeability of protective gloves used in medical practice. *Zentralblatt fur Hygiene und Umweltmedizin (International Journal of Hygiene and Environmental Medicine)* 1991;**191**(5-6):516–22.

McSweeney 2007 *{published data only}*

McSweeney K, Colman A, Fancourt N, Parnell M, Stantiall S, Rice G, et al. Was rurality protective in the 1918 influenza pandemic in New Zealand?. *New Zealand Medical Journal* 2007;**120**(1256):2579.

Mielke 2009 *{published data only}*

Mielke M, Nassauer A. Pandemic influenza: nonpharmaceutical protective measures in ambulatory care. *Fortschritte der Medizin* 2009;**151**(40):32–4.

Mikolajczyk 2008 *{published data only}*

Mikolajczyk RT, Akmatov MK, Rastin S, Kretzschmar M. Social contacts of school children and the transmission of respiratory-spread pathogens. *Epidemiology and Infection* 2008;**136**(6):813–22.

Monsma 1992 *{published data only}*

Monsma M, Day R, St Arnaud S. Handwashing. *Journal of School Health* 1992;**62**(3):109–11.

Nishiura 2009 *{published data only}*

Nishiura H, Wilson N, Baker MG. Quarantine for pandemic influenza control at the borders of small island nations. *BMC Infectious Diseases* 2009;**9**:27.

O'Callaghan 1993 *{published data only}*

O'Callaghan CA. Prevention of nosocomial respiratory syncytial virus infection. *Lancet* 1993;**341**(8838):182.

Olsen 2003 *{published data only}*

Olsen SJ, Chang HL, Cheung TY, Tang AF, Fisk TL, Ooi SP. Transmission of the severe acute respiratory syndrome on aircraft. *New England Journal of Medicine* 2003;**349**(25):2416–22.

Ooi 2005 *{published data only}*

Ooi PL, Lim S, Chew SK. Use of quarantine in the control of SARS in Singapore. *American Journal of Infection Control* 2005;**33**(5):252–7.

Orellano 2010 *{published data only}*

Orellano PW, Grassi A, Reynoso JI, Palmieri A, Uez O, Carlino O. Impact of school closings on the influenza A (H1N1) outbreak in Tierra del Fuego, Argentina. *Pan American Journal of Public Health* 2010;**27**(3):226–9.

Panchabhai 2009 *{published data only}*

Panchabhai TS, Dangayach NS, Krishnan A, Kothari VM, Karnad KR. Oropharyngeal cleansing with 0.2% chlorhexidine for prevention of nosocomial pneumonia in critically ill patients: an open-label randomized trial with 0.01% potassium permanganate as control. *Chest* 2009;**135**(5):1150–6.

Pang 2004 *{published data only}*

Pang XH, Liu DL, Gong XH, Xu FJ, Liu ZJ, Zhang Z, et al. Study on the risk factors related to severe acute respiratory syndrome among close contactors in Beijing. *Chung-Hua Liu Hsing Ping Hsueh Tsa Chih Chinese Journal of Epidemiology* 2004;**25**(8):674–6.

Pittet 2000 *{published data only}*

Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene.

- Infection Control Programme (Erratum in: *Lancet* 2000 Dec 23-30;356(9248):2196). *Lancet* 2000;**356**(9238):1307–12.
- Prasad 2004** {published data only}
Prasad GV, Nash MM, Zaltzman JS. Handwashing precautions taken by renal transplant recipients for severe acute respiratory syndrome. *Transplantation* 2004;**77**(12):1917.
- Rabenau 2005** {published data only}
Rabenau HF, Kampf G, Cinatl J, Doerr HW. Efficacy of various disinfectants against SARS coronavirus. *Journal of Hospital Infection* 2005;**61**(2):107–11.
- Reynolds 2008** {published data only}
Reynolds DL, Garay JR, Deamond SL, Moran MK, Gold W, Styra R. Understanding, compliance and psychological impact of the SARS quarantine experience. *Epidemiology and Infection* 2008;**136**(7):997–1007.
- Richardson 2010** {published data only}
Richardson A, Hofacre K. Comparison of filtration efficiency of a N95 filtering facepiece respirator and surgical mask against viral aerosols. *American Journal of Infection Control* 2010;**38**(5):E20.
- Riley 2003** {published data only}
Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. *Science* 2003;**300**(5627):1961–6.
- Rodriguez 2009** {published data only}
Rodriguez CV, Rietberg K, Baer A, Kwan-Gett T, Duchin J. Association between school closure and subsequent absenteeism during a seasonal influenza epidemic. *Epidemiology* 2009;**20**(6):787–92.
- Rosenthal 2005** {published data only}
Rosenthal VD, Guzman S, Safdar N. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. *American Journal of Infection Control* 2005;**33**(7):392–7.
- Safiulin 1972** {published data only}
Safiulin AA. UV sanitation of the air and surfaces for the purpose of preventing in-hospital viral respiratory infections. *Gigiena i Sanitariia* 1972;**37**(10):99–101.
- Sandrock 2008** {published data only}
Sandrock C, Stollenwerk N. Acute febrile respiratory illness in the ICU: reducing disease transmission. *Chest* 2008;**133**(5):1221–31.
- Satter 2000** {published data only}
Sattar SA, Abebe M, Bueti AJ, Jampani H, Newman J, Hua S. Activity of an alcohol-based hand gel against human adeno-, rhino-, and rotaviruses using the fingerpad method. *Infection Control and Hospital Epidemiology* 2000;**21**(8):516–9.
- Schull 2007** {published data only}
Schull MJ, Stukel TA, Vermeulen MJ, Zwarenstein M, Alter DA, Manuel DG, et al. Effect of widespread restrictions on the use of hospital services during an outbreak of severe acute respiratory syndrome. *CMAJ* 2007;**176**(13):1827–32.
- Seal 2010** {published data only}
Seal LA, Slade B, Cargill I, Aust D. Persistence factors in handwashes. *American Journal of Infection Control* 2010;**38**(5):E18–9.
- Seale 2009** {published data only}
Seale H, Corbett S, Dwyer DE, MacIntyre CR. Feasibility exercise to evaluate the use of particulate respirators by emergency department staff during the 2007 influenza season. *Infection Control and Hospital Epidemiology* 2009;**30**(7):710–2.
- Sizun 1996** {published data only}
Sizun J, Baron R, Soupre D, Giroux JD, de Parscau L. Nosocomial infections due to syncytial respiratory virus: which hygienic measures. *Archives de Pediatrie* 1996;**3**(7):723–7.
- Stebbins 2009** {published data only}
Stebbins S, Downs JS, Vukotich CJ. Using nonpharmaceutical interventions to prevent influenza transmission in elementary school children: parent and teacher perspectives. *Journal of Public Health Management and Practice* 2009;**15**(2):112–7.
- Stoner 2007** {published data only}
Stoner MJ, Cohen DM, Fernandez S, Bonsu BK. Physician handwashing: what do parents want?. *Journal of Hospital Infection* 2007;**65**(2):112–6.
- Stukel 2008** {published data only}
Stukel TA, Schull MJ, Guttmann A, Alter DA, Li P, Vermeulen MJ, et al. Health impact of hospital restrictions on seriously ill hospitalized patients: lessons from the Toronto SARS outbreak. *Medical Care* 2008;**46**(9):991–7.
- Svoboda 2004** {published data only}
Svoboda T, Henry B, Shulman L, Kennedy E, Rea E, Ng W, et al. Public health measures to control the spread of the severe acute respiratory syndrome during the outbreak in Toronto. *New England Journal of Medicine* 2004;**350**(23):2353–61.
- Tracht 2010** {published data only}
Tracht SM, Del Valle SY, Hyman JM. Mathematical modeling of the effectiveness of facemasks in reducing the spread of novel influenza a (H1N1). *PLoS One* 2010;**5**(2):e9018.
- Ueno 1990** {published data only}
Ueno T, Saijo K. Prevention of adenovirus infection and antiviral activity of a hand disinfectant, Welpas. *Nippon Ganka Gakkai Zasshi* 1990;**94**(1):44–8.
- van der Sande 2008** {published data only}
van der Sande M, Teunis P, Sabel R. Professional and home-made face masks reduce exposure to respiratory infections among the general population. *PLoS One* 2008;**3**(7):e2618.
- Viscusi 2009a** {published data only}
Viscusi DJ, Bergman M, Sinkule E, Shaffer RE. Evaluation of the filtration performance of 21 N95 filtering face piece

- respirators after prolonged storage. *American Journal of Infection Control* 2009;**37**(5):381–6.
- Viscusi 2009b** *{published data only}*
Viscusi DJ, Bergman MS, Eimer BC, Shaffer RE. Evaluation of five decontamination methods for filtering facepiece respirators. *Annals of Occupational Hygiene* 2009;**53**(8): 815–27.
- Wang 2003** *{published data only}*
Wang JX, Feng HY, Liu D, Zhang ZL, Shan AL, Zhu XJ, et al. Epidemiological characteristics of severe acute respiratory syndrome in Tianjin and the assessment of effectiveness on measures of control. *Chung-Hua Liu Hsing Ping Hsueh Tsa Chih [Chinese Journal of Epidemiology]* 2003;**24**(7):565–9.
- Wang 2005** *{published data only}*
Wang HW, He J, Zhang PH, Tang F, Wang TB, Luan YH, et al. A case-control study on the mxA polymorphisms and susceptibility to severe acute respiratory syndromes. *Chung-Hua Liu Hsing Ping Hsueh Tsa Chih [Chinese Journal of Epidemiology]* 2005;**26**(8):574–7.
- Weber 2004** *{published data only}*
Weber JT, Hughes JM. Beyond Semmelweis: moving infection control into the community. *Annals of Internal Medicine* 2004;**140**(5):397–8.
- Wen 2010** *{published data only}*
Wen Z, Lu J, Li J, Li N, Zhao J, Wang J, et al. Determining the filtration efficiency of half-face medical protection mask (N99) against viral aerosol. *Aerobiologia* 2010;**26**(3): 245–51.
- White 2005** *{published data only}*
White C, Kolble R, Carlson R, Lipson N. The impact of a health campaign on hand hygiene and upper respiratory illness among college students living in residence halls. *Journal of American College Health* 2005;**53**(4):175–81.
- Wilczynski 1997** *{published data only}*
Wilczynski J, Torbicka E, Brzozowska-Binda A, Szymanska U. Breast feeding for prevention of viral acute respiratory diseases in infants. *Medycyna Doswiadczalna i Mikrobiologia* 1997;**49**(3–4):199–206.
- Wilder-Smith 2003** *{published data only}*
Wilder-Smith A, Paton NI, Goh KT. Low risk of transmission of severe acute respiratory syndrome on airplanes: the Singapore experience. *Tropical Medicine and International Health* 2003;**8**(11):1035–7. MEDLINE: 14629772
- Wilder-Smith 2005** *{published data only}*
Wilder-Smith A, Low JG. Risk of respiratory infections in health care workers: lessons on infection control emerge from the SARS outbreak. *Southeast Asian Journal of Tropical Medicine and Public Health* 2005;**36**(2):481–8.
- Wong 2005** *{published data only}*
Wong TW, Tam WW. Handwashing practice and the use of personal protective equipment among medical students after the SARS epidemic in Hong Kong. *American Journal of Infection Control* 2005;**33**(10):580–6.
- Yen 2010** *{published data only}*
Yen M-Y, Lu Y-C, Huang P-H, Chen C-M, Chen Y-C, Lin YE. Quantitative evaluation of infection control models in the prevention of nosocomial transmission of SARS virus to healthcare workers: implication to nosocomial viral infection control for healthcare workers. *Scandinavian Journal of Infectious Diseases* 2010;**42**(6–7):510–5.
- Yu 2004** *{published data only}*
Yu IT, Li Y, Wong TW, Tam W, Chan AT, Lee JH, et al. Evidence of airborne transmission of the severe acute respiratory syndrome virus. *New England Journal of Medicine* 2004;**350**(17):1731–9.
- Zamora 2006** *{published data only}*
Zamora JE, Murdoch J, Simchison B, Day AG. Contamination: a comparison of 2 personal protective systems. *Canadian Medical Association Journal* 2006;**175**(3):249–54.
- Zhai 2007** *{published data only}*
Zhai S, Liu W, Yan B. Recent patents on treatment of severe acute respiratory syndrome (SARS). *Recent Patents on Anti-infective Drug Discovery* 2007;**2**(1):1–10.
- Zhao 2003** *{published data only}*
Zhao Z, Zhang F, Xu M, Huang K, Zhong W, Cai W, et al. Description and clinical treatment of an early outbreak of severe acute respiratory syndrome (SARS) in Guangzhou, PR China. *Journal of Medical Microbiology* 2003;**52**(8): 715–20.

References to studies awaiting assessment

- Aiello 2010b** *{published data only}*
Aiello AE, Coulborn RM, Perez V, Davis BM, Uddin M, Murray GF, et al. A randomized intervention trial of mask use and hand hygiene to reduce seasonal influenza-like illness and influenza infections among young adults in a university setting. *International Journal of Infectious Diseases* 2010;**14**:e320.
- Hubner 2009** *{published data only}*
Hubner NO, Hubner C, Wodny M, Kampf G, Kramer A. Effectiveness of alcohol-based hand disinfectants in a public administration: impact on health and work performance related to acute respiratory symptoms and diarrhoea. *BMC Infectious Diseases* 2009;**9**:10.
- Raboud 2010** *{published data only}*
Raboud J, Shigayeva A, McGeer A, Bontovics E, Chapman M, Gravel D. Risk factors for SARS transmission from patients requiring intubation: a multicentre investigation in Toronto, Canada. *PLoS* 2010;**5**(5):e10717.
- Savolainen-Kopra 2010** *{published data only}*
Savolainen-Kopra C, Haapakoski J, Peltola P A, Ziegler T, Korpela T, Anttila P, et al. STOPFLU: is it possible to reduce the number of days off in office work by improved hand-hygiene?. *Trials* 2010;**11**:69.

Additional references

Aiello 2002

Aiello AE, Larson EL. What is the evidence for a causal link between hygiene and infections?. *Lancet* 2002;**2**(2):103–10.

Bonn 1997

Bonn D. Spared an influenza pandemic for another year?. *Lancet* 1997;**349**(9044):36.

Bootsma 2007

Bootsma MCJ, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. Proceedings of the National Academy of Sciences of the United States of America (PNAS) 2007; Vol. Early edition: 1–6. [doi:10.1073 /pnas.0611071104]

CDC 2005a

Centers for Disease Control and Prevention. Infection Control Guidance for the Prevention and Control of Influenza in Acute-Care Facilities. <http://www.cdc.gov/flu/professionals/infectioncontrol/healthcarefacilities.htm> (accessed 3 March 2006).

CDC 2005b

Centers for Disease Control and Prevention. 2004–2005 Interim Guidance for the Use of Masks to Control Influenza Transmission. <http://www.cdc.gov/flu/professionals/infectioncontrol/maskguidance.htm> (accessed 3 March 2006).

Fraser 2006

Fraser C, Murray A, Burr J. Identifying observational studies of surgical interventions in MEDLINE and EMBASE. *BMC Medical Research Methodology* 2006;**6**:41.

Fung 2006

Fung IC, Cairncross S. Effectiveness of handwashing in preventing SARS: a review. *Tropical Medicine and International Health* 2006;**11**(11):1749–58.

Grimshaw 2004

Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale R, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technology Assessment* 2004;**8**(6:iii-iv):1–72.

Higgins 2002

Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;**21**(11):1539–58.

Higgins 2003

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557–60.

Jefferson 2005a

Jefferson T, Smith S, Demicheli V, Harnden A, Rivetti A, Di Pietrantonj C. Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. *Lancet* 2005;**365**(9461):773–80.

Jefferson 2005b

Jefferson T, Smith S, Demicheli V, Harnden A, Rivetti A. Safety of influenza vaccines in children. *Lancet* 2005;**366**(9488):803–4.

Jefferson 2005c

Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in the elderly: systematic review. *Lancet* 2005;**366**(9492):1165–74.

Jefferson 2005d

Jefferson T. Microbial challenge studies of volunteers—a challenge worth accepting. *Lancet* 2005;**366**(9485):531–3.

Jefferson 2006a

Jefferson T, Demicheli V, Rivetti D, Jones M, Di Pietrantonj C, Rivetti A. Antivirals for influenza in healthy adults: systematic review. *Lancet* 2006;**367**(9507):303–13. [DOI: 10.1016/S0140–6736(06) 67970–1]

Khan 2000

Khan SK, ter Riet G, Popay J, Nixon J, Kleijnen J. Stage II Conducting the review: Phase 5: Study quality assessment. In: Khan SK, ter Riet G, Glanville J, Sowden AJ, Kleijnen J editor(s). *Undertaking Systematic Reviews of Research on Effectiveness. CRD's guidance for carrying out or commissioning reviews. CRD Report No 4*. 2nd Edition. York: NHS Centre for Reviews and Dissemination, University of York, 2000:2.5.1–2.5.10.

Kitamura 2007

Kitamura T, Satomura K, Kawamura T, Yamada S, Takashima K, Suganuma N. Can we prevent influenza-like illnesses by gargling?. *Japanese Society of Internal Medicine* 2007;**46**(18):1623–4. DOI: 10.2169/internalmedicine.46.0104

Lefebvre 2009

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors) editor(s). *Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.2 (updated September 2009). The Cochrane Collaboration. Available from www.cochrane-handbook.org*. Chichester, UK: Wiley-Blackwell, 2009.

Meadows 2004

Meadows E, Le Saux N. A systematic review of the effectiveness of antimicrobial rinse-free hand sanitizers for prevention of illness-related absenteeism in elementary school children. *BMC Public Health* 2004;**4**:50. [doi: 10.1186/1471–2458–4–50]

Monto 1969

Monto AS, Davenport FM, Napier JA, Francis T Jr. Effect of vaccination of a school-age population upon the course of an A2-Hong Kong influenza epidemic. *Bulletin of the World Health Organization* 1969;**41**(3):537–42.

Shute 2003

Shute N. SARS hit home. *US News & World Report* 2003;**134**(15):38–42.

Smith 2006

Smith S, Demicheli V, Di Pietrantonj C, Harnden AR, Jefferson T, Matheson NJ, et al. Vaccines for preventing influenza in healthy children. *Cochrane Database of Systematic Reviews* 2006, Issue 1. DOI: 10.1002/14651858.CD004879.pub3

Thomas 2010

Thomas RE, Jefferson T, Lasserson TJ. Influenza vaccination for healthcare workers who work with the elderly. *Cochrane Database of Systematic Reviews* 2010, Issue 2. DOI: 10.1002/14651858.CD005187.pub3

WHO 2006

World Health Organization Writing Group. Non pharmaceutical interventions for pandemic influenza, national and community measures. *Emerging Infectious Diseases* 2006;**12**(1):88–94.

WHO 2009

World Health Organization. Pandemic H1N1. <http://www.who.int/csr/disease/swineflu/en/> 2009 (accessed 22 July 2009).

References to other published versions of this review**Jefferson 2007**

Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, Hewak B, et al. Interventions for the interruption or reduction of the spread of respiratory viruses. *Cochrane Database of Systematic Reviews* 2007, Issue 4. DOI: 10.1002/14651858.CD006207.pub2

Jefferson 2009

Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. *BMJ online* 2009;**339**:b.3657. DOI: 10.1136/bmj.b367

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Agah 1987

Methods	Prospective cohort study carried out in California hospital during the autumn 1984 to spring 1985 season. The study assessed the efficacy of healthcare workers (HCW) wearing goggle-mask apparatus while visiting and caring for children aged up to 5 with RSV and symptoms of respiratory disease compared to do nothing. Children admitted with a RSV diagnosis were assigned to the 2 arms balanced for age and sex
Participants	168 HCW caring for children < 5 years with differential diagnosis of RSV
Interventions	Mask and goggles (sometimes gowns too) versus normal care
Outcomes	RSV illness reduced from 61% (controls) to 5% (intervention) Laboratory: swabs for RSV diagnosis Effectiveness: RSV illness Safety: n/a
Notes	Risk of bias: low Notes: the authors conclude that wearing mask and goggles significantly reduced transmission to HCWs and other children of RSV (61% versus 5% illness rate). Analysis is also given by number of contacts (data not extracted). A reasonably reported if difficult to conduct study. Standard procedures such as handwashing should not have acted as a confounder given 100% coverage among HCWs

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Methods	Cluster-randomised trial assessing the effects of hand sanitiser and masks with masks or no intervention on ILI symptoms. The trial was conducted in University halls of residence with more than 100 student residents in a US university during the 2006 to 2007 influenza “season”. It lasted 6 weeks The units of randomisation were 7 of the 15 halls. One hall was very large (1240 residents) and the 6 remaining ones which had between 110 and 830 residents were combined into 2 clusters roughly equivalent in size. The 3 clusters were then randomised by random extraction of the clustered halls’ names out of a container. The largest hall (single-cluster) was randomised to the mask and hand sanitiser arm, the 4 halls cluster received masks and the remaining 2 halls were assigned as controls
Participants	Willing, consenting residents aged 18 or more. Recruitment of students began in November 26 but the trial did not go “live” with distribution of intervention materials until 22 January 2007 when the first case of influenza was confirmed on campus by laboratory tests. Enrolment continued until 16 February 2007 and the study was completed on 16 March 2007. During the study period there was a 1-week break when the majority of residents left campus. There were 1327 eligible participants, of which 1297 had a complete baseline survey and at least 1 weekly survey result (367, 378 and 552 in the mask and hand sanitiser, mask only and control groups respectively, giving a total of 1297). It is unclear what the ineligibility criteria were for the 30 missing (1327 minus 1297) but the explanation may be in the appendix
Interventions	Alcohol-based hand sanitiser (62% ethyl alcohol in a gel base) in a squeeze bottle and TECNOL procedure masks with ear loops (KC Ltd) and educational material or masks and educational material or no intervention. Compliance was encouraged within halls and outside. Sleep wearing was optional All participants received basic video-linked instruction on cough etiquette and hand sanitation. At baseline and weekly during the study participants were asked to fill in a web-based survey collecting demographic and ILI symptom data. This was supplemented by direct observation of compliance by staff Compliance with “optimal handwashing” (at least 20 seconds 5 or more times a day) was significantly higher in the sanitiser and mask arm
Outcomes	Laboratory details are described in appendix Effectiveness: ILI, defined as cough and at least 1 constitutional symptom (fever/feverishness, chills, headache, myalgia). ILI cases were given contact nurses phone numbers to record the illness and paid USD 25 to provide a throat swab. 368 participants had ILI and 94 of these had a throat swab analysed by PCR. 10 of these were positive for influenza (7 for A and 3 for B), respectively by arm 2, 5 and 3 using PCR, 7 using cell culture Safety: n/a
Notes	The authors conclude that “These findings suggest that face masks and hand hygiene may reduce respiratory illnesses in shared living settings and mitigate the impact of the influenza A (H1N1) pandemic”. This conclusion is based on a significantly lower level of ILI incidence in the mask and hand sanitiser arm compared to the other 2 arms after adjustment for covariates (30% to 50% less in arm 1 compared to controls in the last 2 weeks of the study) Comparison with the ILI rate of the control arm may not be a reflection of the underlying

	rate of ILI because the intervention arm received instruction on hand sanitation and hand etiquette The play of adjustments is unclear. The intra cluster correlation coefficient is reported in the footer of Table 4. Its very small size suggests lack of clustering within halls The role of the spring break is mentioned in the Discussion as are the results of this study compared to other studies included in our review (Cowling 2008 and MacIntyre 2009) The authors report that 147 of 1297 participants (11.3%) “at baseline” had ILI symptoms and were excluded from analysis. During the 6 weeks of the study 368 of 1150 participants (32%) had ILI. This averages out at about 5% per week. It is unclear what the term “at baseline” means. Presumably this means during the 2 to 3 weeks of participant enrolment. If this is so, the reason for the triggering of the interventions (tied to influenza isolation) are obscure as the trial is supposedly about ILI and an ILI outbreak was already underway “at baseline”	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised but sequence generation not reported
Allocation concealment (selection bias)	Low risk	The residence hall units were randomised by blindly selecting a uniform ticket with the name of each hall out of a container (A. S.M. and A.A.) for randomisation assignment to each study arm
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition is reported as follows: 9, 11 and 19 ineligible and 26, 52 and 21 lost to follow up (respectively by arm). This makes a total of 39 and 99 for each cause of attrition. In total, 1297 (97%) of 1331 participants completed a baseline and at least 1 weekly survey The text reports an ITT analysis with only one ILI episode included by participant No reasons for the attrition of participants and swab volunteers are reported (were the swabs taken from a random sample or not?)
Selective reporting (reporting bias)	High risk	There is no information on the causes of ILI other than the reporting on the 10 influenza PCR-positive swabs of 94 out of 368 students with ILI. This is a very low

		rate (and the Discussion confirms that the influenza season was mild) but investigation of the other known causes of ILI is not even mentioned in the text. This is especially important because stress, alcohol intake levels and influenza vaccination were a significant predictor of ILI symptoms (Table 1). The reason for selective testing and/or reporting of influenza viruses tests over the other causes of ILI are unclear especially as the study objective was focused on ILI. The text also is difficult to follow, weaving the reporting of ILI and influenza without a clear rationale
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Broderick 2008

Methods	Prospective, cohort study carried out in a military recruit training centre during the first 4 weeks of recruit training. Data were collected between February 2004 and March 2005 (duration of recruit training is not reported) It is not clear how the recruits were assigned to 'experimental' (closed) or control (open). Recruits were assigned to units on the basis of arrival order with no particular allocation scheme The study assessed if social distancing would reduce the incidence of febrile respiratory illness (FRI). Data were collected over 4 weeks for each new group of recruits Housing units (n = 196 units) were divided into closed units (n = 30) (experiment/intervention) or open units (n = 166) (control). For description of how the closed units were selected and geographical position in the training centre see notes Microbiological samples from physical structures (tables, surfaces, angles of surfaces, handles) of some units were done. However, it is not mentioned if these units were selected from among the closed or open units
Participants	Male military recruits (n = 13,114), distributed among 196 housing units (166 open units and 30 closed units) took part in the study. Unit size ranged from 44 to 88 recruits per unit. Reported denominators add up to 13488 recruits not 13114 (closed: 329/2099 versus open: 1586/11389). No exclusions were reported. Dimensions of the units are not described (space/subject or space/unit). The average number of subjects/unit in the closed units was not reported 10% of medical convalescent unit (MCU) subjects (762) and 6% of physical conditioning unit (PCU) subjects (395) were positive for adenovirus 4 by PCR
Interventions	To test the effect of social distancing: participants were either assigned (allocation process not clear) to closed or open units. The closed units did not introduce any new participants once their personnel had been assigned (socially-distant); sick recruits were removed but if their symptoms did not require placement in the MCU, the recruits returned to their units. The open units accepted recovering subjects after being discharged from MCU and PCU To test an environmental aetiology: some of the units, which were vacant after 4 weeks of occupation, were swabbed. The MCU was also swabbed. The samples were tested by

	PCR and were cultured
Outcomes	Laboratory: (MicroTest M4 Transport; Remel) polymerase chain reaction (PCR) culture for Ad-4 virus Not used to confirm FRI in all index cases. Adenovirus was the only microorganism tested for and isolated Effectiveness: cases of FRI were defined either by a body temperature of $> 38^{\circ}\text{C}$ and 1 respiratory symptom or by the presence of non-febrile pneumonia Cases were reported as number of cases of FRI per 100 persons per week, averaged over the 4 weeks Safety: n/a
Notes	The institutional review board of the Naval Health Research Centre classified the protocol of this study as a non-research public health endeavour. Given the flaws of the study design (the disparity between the number of closed and open units, testing 2 different 'aetiological' hypothesis using different methodologies and lack of information on how the units were selected), one gets the impression that this study was probably carried out at least retrospectively instead of being carried out as a prospective study as claimed by the authors. The authors conclude that social distancing did not reduce FRI and that environmental contamination rather than person to person transmission is the culprit in the spread of FRI. The method used for social distancing, however, did not exclude those that were little bit sick but did not require placement in the MCU. In other words, sick people were allowed to remain in the closed unit (? as well as in the open units); only apparently healthy recruits were allowed to rejoin the open units after being placed in the MCU and PCU The study put emphasis on the importance of environmental cleaning. In addition to that crowded areas increase the risk of transmission of viruses. In the study, however, it was not clear if open and closed units are similar or different as pathogen reservoir. Also, analysis of closed units according to the population size was not done and information about the location of the closed units (all over the centre or localised in certain (isolated) area) is lacking. Despite these clear limitations this pragmatic study's findings may be interpreted in a variety of different ways. Perhaps the most interesting interpretation is that environmental conditions are determinants of adenoviral infectivity but not entry and exit from a community. In other words virological and presumably bacterial agents persist in the environment, they are not "brought" in and do not "arrive" and do not directly and invariably cause one-on-one disease. This hypothesis challenges the current simplistic interpretation of the postulates of Henle-Koch (one agent = one disease and suggests that the presence of microorganism may only be one of the many variables which determine infectious disease. This interpretation is comforted by the relatively small number of isolates found in studies of ILI causes (so called pie studies) The corresponding author provided the following additional information: each week a new cohort of about 500 recruits arrives at the camp, all of whom arrive by Wednesday. On Thursday the recruits are assigned to 6 platoons (each platoon housed in its own large room - called "housing units" in the article). Each cohort's 6 housing units are numbered from 1 to 6, with no particular distinction between them. Each house is given approximately the same number of recruits. The placement of the recruits into the housing units is based somewhat on the order of their arrival to the camp, but otherwise there are no criteria for placement, although relatives and friends are allowed to be in the

	same platoon. The recruits at MCRD San Diego tend to be from west of the Mississippi. There is no particular order of arrival at the camp from different regions. The number of the closed housing unit assigned in each cohort varied. In the majority of cases it was 1 or 2 Each building contains 4 wings of 3 floors each. From the sky, the buildings form an H shape. The line in the middle of the H connects the sides of the H, and on each side the half above the middle line is one wing and below the middle line is the other wing. If you go on maps.google.com and type in 'san diego ca mcrd' and zoom in on C you can see how big the buildings are. The housing units for each cohort typically occupy 2 wings one building, but occasionally one housing unit will be in a different building. E. g. if there are 6 housing units in a cohort, the cohort will occupy 3 floors of wing A and 3 floors of wing C. The map gives you an idea of the geography of horizontal distance between each wing, and each floor is about 10 feet high. Although the housing units are relatively close to each other, the platoons do not typically interact with each other. They are large permanent buildings each consisting of 12 large rooms and a hallway
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Carabin 1999

Methods	Cluster-randomised controlled trial carried out in daycare centres (DCC) in the Canadian province of Quebec between 1 Sept 1996 and 30 November 1997 (15 months). The aim was to test the effects of a hygiene programme on the incidence of diarrhoea and fecal contamination (data not extracted) and on colds and URIs. The design included before and after periods analysed to assess the Hawthorne effect of study participation on control DCCs. Unit of randomisation was DCC but analysis was also carried out at classroom and single child level. This is a common mistake in C-RCT analysis. DCCs were stratified by URI incidence preceding the trial and randomised by location. Cluster coefficients are not reported
Participants	1729 children aged 18 to 36 months in 47 DCCs (83 toddler classrooms)

Interventions	Training session (1 day) with washing of hands, toy cleaning, window opening, sand pit cleaning and repeated exhortations to handwash	
Outcomes	Laboratory: n/a Effectiveness: diarrhoea and coliform contamination (data not extracted) Colds (nasal discharge with at least one of the following: fever, sneezing, cough, sore throat, earache, malaise, irritability) URTI (cold of at least 2 days' duration) Surveillance was carried out by educators, annotating absences or illness on calendars. Researchers also filled in a phone questionnaire with answers by DCC directors Safety: n/a	
Notes	Risk of bias: high (no description of randomisation; partial reporting of outcomes, numerators and denominators) Notes: the authors conclude that the intervention reduced the incidence of colds (IRR 0.80, 95% CI 0.68 to 0.93). Confusingly written study with unclear interweaving of 2 study designs. For unclear reasons analysis was only carried out for the first autumn. Unclear why colds are not reported in the results. Cluster-coefficients and randomisation process not described	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation of DCC according to region, but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not possible (hygiene session plus educational material versus none)
Incomplete outcome data (attrition bias) All outcomes	High risk	Originally 52 eligible DCCs with 89 classrooms agreed to take part but 5 dropped out (2 closed, 1 was sold, 2 either did not provide data or the data were "unreliable" and 6 classrooms had insufficient data). Forty-three children failing to attend DCC for at least 5 days in the autumn were also excluded. ITT analysis was carried out including an additional DCC whose director refused to let staff attend the training session No correction for clustering made
Selective reporting (reporting bias)	High risk	Denominators unclear and not explained

Methods	Case-control study to test the association between SARS onset and a range of causative and protective variables in Sun Yan Tzen University hospitals in Guanzhou, Southern China The study collected information on cases and controls retrospectively during the first phase of the SARS epidemic in China (March to May 2003) but there is also a prospective element with antibody confirmation of SARS infection. Analysis plan was similar to that of Liu 2009 with a univariate and multivariate analysis conducted to assess risk factors
Participants	Description of cases. Probable SARS cases were defined using the criteria by the China Health Ministry. Criteria for probable and suspected SARS cases included travel to a SARS epidemic area in the 2 weeks before the onset of symptoms or close contact with a probable SARS patient; fever of $\geq 38^{\circ}\text{C}$; chest X-ray abnormalities; normal or decreased leukocyte count; and no response to treatment by antimicrobial drugs. In this study what appears to have happened is that available Sun Yan Tzen University hospitals HCWs who were willing to be interviewed were bled and those with raised IgG against SARS-CoV were included as cases. Cases enrolled were 90 out of the possible 112 who had SARS (80%) and 758/846 controls (89%). The choice criterion for interview of cases and controls was availability i.e. being "off duty" during the survey. It is unclear what this means and why such bias was knowingly introduced Description of controls. Controls were SARS-CoV negative HCW who had worked in the 2 hospitals attending SARS cases
Interventions	An extensive number of exposure and interventions variables were elicited and quantified with discrete scores. Definitions are absent in most cases <i>Use of personal protective and control measures</i> Number of gowns worn 0 = single, 1 = double Number of multilayered cotton mask worn 0 = single, 1 = double Number of pairs of gloves worn 0 = single, 1 = double Frequency of wearing shoe cover 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of wearing cap 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of face shield in SARS ward 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of wearing goggles while performing operation for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time <i>Health-related behaviours</i> Frequency of washing uncovered skin after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of washing hands after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of washing nasal cavity after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time Frequency of washing oral cavity after caring for SARS patients 0 = never, 1 = sometimes, 2 = often, 3 = every time <i>SARS patient care</i> Special training for SARS 0 = no, 1 = yes Performing tracheotomy 0 = no, 1 = yes Performing tracheal intubations 0 = no, 1 = yes Caring for "Super Spreading Patient" 0 = no, 1 = Yes Avoiding face to face while caring for patient 0 = never, 1 = sometimes, 2 = often, 3 =

	every time <i>Other relevant control measures</i> Method of air ventilation in offices and SARS wards 1 = artificial central ventilation (windows were closed in wards), 2 = natural ventilation (windows were opened in wards) , 3 = natural ventilation and additional electronic exhaust fan (windows were opened in wards, at the same time, electronic exhaust fans were used for improving air circulation in wards) Type of equipment for washing hands 1 = automatic tap, 2 = non-automatic tap, 3 = other	
Outcomes	N/A	
Notes	The authors conclude that “Some measures, particularly good air ventilation in SARS wards, may be effective in minimising or preventing SARS transmission among HCWs in hospitals”. The study is biased by the selection of cases and controls (enrolment only of available personnel) and the non-eligibility (and lack of mention) of HCW who died of SARS (which may be up to 20% of people who were ill during the first wave of SARS). The design and analysis are very similar to those of Ma 2004/Liu 2009 and the design also lacks focus. i.e. it does not test a defined hypothesis, but trawls through large numbers of variables looking for associations. There is no attempt at matching cases with controls and part of the design is prospective (IgG estimation). As a consequence the design distinction between a case-control and a cohort study is blurred. There is no mention of whether interviewers were blinded to case or control status of interviewees Data extracted are from the univariate analysis table 3 which is the table reporting both numerators and denominators for cases and controls. Table 4 (multivariate logistic analysis) reports the significant multiple protective associations: caring for super spreading patient and avoiding face to face contact while caring for SARS patient (OR 0.30, 0.15 to 0.60) and wearing gloves coupled with methods of ventilation (various ORs for the various combinations intensity of wearing and ventilation methods, all significant). In the light of so many biases it is difficult to interpret the data but there does seem to be a gradient favouring multiple interventions	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A

Selective reporting (reporting bias)	Unclear risk	N/A
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Cowling 2008

Methods	Cluster-randomised controlled trial carried out in Hong Kong SARS between February and September 2007. The study assessed the effects of non-pharmaceutical interventions on the household transmission of influenza over a 9-day period. ILI cases whose family contacts had been symptom-free for at least 2 weeks rapid tested for influenza A and B were used and randomised to 3 interventions carried out. Randomisation was carried out in 2 different schedules (2:1:1 for the first 100 households and subsequently 8:1:1) but it is unclear why and how
Participants	946 index subjects aged 2 years or more in 122 clusters (households). 116 households were included in the analysis, 6 were excluded because subsequent laboratory testing (culture) were negative. There were 350 household contacts in the analysis but there 370 household contacts at randomisation. Attrition is not explained. Index cases were defined as subjects presented with at least 2 influenza-like symptoms of at least 48 hour duration (such as fever more or equal to 38 degrees, cough, headache, coryza , sore throat, muscle aches and pains) and positive influenza A+B rapid test
Interventions	Households were randomised to either wearing face masks with education (as the control group plus education about face mask use) or handwashing with special medicated soap (with alcohol sanitiser) with education (as the control group plus education about handwashing) or education about general healthy lifestyle and diet (control group). The soap was distributed in special containers which were weighed at the start and the end of the study. Interventions visits to the households were done on average 1 day after randomisation of index case household
Outcomes	Laboratory: QuickVue RTI MDCK culture Samples were harvested using NTS, but the text refers to a second procedure from June 2007 onwards testing for non-influenza viruses but no data were reported Effectiveness: secondary attack ratios (SAR): SAR is the proportion of household contacts of an index case who subsequently were ill with influenza (symptomatic contact individuals with at least 1 NTS positive for influenza by viral culture or PCR) Three clinical definitions were used for secondary analysis: 1. Fever more or equal to 38 degrees or at least 2 of following symptoms, headache, coryza , sore throat, muscle aches and pains 2. At least 2 of the following S/S: fever more or equal to 37.8 degrees, cough, headache, sore throat and muscle aches and pains 3. Fever of more or equal to 37.8 degrees plus cough or sore throat Safety: no harms were reported in any of the arms
Notes	The authors conclude that "The secondary attack ratios were lower than anticipated, and lower than reported in other countries, perhaps due to differing patterns of susceptibility, lack of significant antigenic drift in circulating influenza virus strains recently, and/or issues related to the symptomatic recruitment design. Lessons learnt from this pilot have

	informed changes for the main study in 2008”	
	Although billed as a pilot study the text is highly confusing and at times contradictory. The intervention was delivered at a home visit up to 36 hours after the index case was seen in the outpatients. This is a long time and perhaps the reason for the failure of the intervention. Practically, the intervention will have to be organised before even seeking medical care - i.e. people know to do it when the kid gets sick at home	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated by a biostatistician “A pre-specified table of random numbers will be used to assign one of the three interventions to the household of the index case.”
Allocation concealment (selection bias)	Low risk	The households of eligible study index patients were allocated to 3 groups in a 1:1:1 ratio under a block randomisation structure with randomly permuted block sizes of 18, 24 and 30 by using a random-number generator. Allocation was concealed from treating physicians and clinics and implemented by study nurses at the time of the initial household visit
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and people who administered the interventions were not blinded to the interventions, but participants were not informed of the specific nature of the interventions applied to other participating households
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout was accounted for. Dropout from randomised population was high: 32% in control group, 37.5% in hand hygiene group and 39.4% in the face masks and hand hygiene group. Reasons for dropout distributed evenly over the 3 groups Authors report follow up as proportion of patients remaining in the study after initial dropout
Selective reporting (reporting bias)	High risk	The choice of season, change in randomisation schedules and unexplained dropouts among contacts, the use of QuickVue

Cowling 2008 (Continued)

		which proved unreliable, reporting bias on non-influenza isolates make this study at high risk of bias
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Cowling 2009

Methods	Cluster-randomised controlled trial
Participants	Households in Hong Kong From 45 outpatient clinics in both the private and public sectors across Hong Kong, they enrolled persons who reported at least 2 symptoms of acute respiratory illness (temperature 37.8 °C, cough, headache, sore throat, or myalgia); had symptom onset within 48 hours; and lived in a household with at least 2 other people, none of whom had reported acute respiratory illness in the preceding 14 days. After participants gave informed consent, they provided nasal and throat swab specimens. 2750 patients were eligible and tested between 2 January through 30 September 2008. Included were 407 people with influenza-like illness who were positive for influenza A or B virus by rapid testing (index patients) and 794 household members (contacts) in 331 households
Interventions	Participants with a positive rapid test result and their household contacts were randomly assigned to 1 of 3 study groups: control (lifestyle measures - 134 households), control plus enhanced hand hygiene only (136 households) and control plus face masks and enhanced hand hygiene (137 households) for all household members. No detailed description of the instructions given to participants
Outcomes	Influenza virus infection in household contacts, as confirmed by reverse transcription polymerase chain reaction (RT-PCR) or diagnosed clinically after 7 days “The primary outcome measure was the secondary attack ratio at the individual level: that is, the proportion of household contacts infected with influenza virus. We evaluated the secondary attack ratio using a laboratory definition (a household contact with a nose and throat swab specimen positive for influenza by RT-PCR) as the primary analysis and 2 secondary clinical definitions of influenza based on self-reported data from the symptom diaries as secondary analyses.” Statistical analysis: adjusted for clustering Results: no significant difference in secondary attack ratio between groups in total population. Statistically significant reduction in RT-PCR confirmed influenza virus infections in the household contacts in 154 households in which the intervention was applied within 36 hours of symptom onset in the index patient. Adherence to hand hygiene between 44% and 62%. Adherence of index patient to wearing a face mask between 15% and 49%
Notes	“In an unintentional deviation from that protocol, 49 of the 407 randomly allocated persons had a household contact with influenza symptoms at recruitment (a potential co-index patient). We also randomly assigned 6 of 407 persons who had symptoms for slightly more than 48 hours.” The authors conclude that “Hand hygiene and face masks seemed to prevent household transmission of influenza virus when implemented within 36 hours of index patient symptom onset. These findings suggest that non-pharmaceutical interventions are important for mitigation of pandemic and interpandemic influenza.”

Cowling 2009 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated by a biostatistician "A pre-specified table of random numbers will be used to assign one of the three interventions to the household of the index case."
Allocation concealment (selection bias)	Low risk	The households of eligible study index patients were allocated to 3 groups in a 1:1:1 ratio under a block randomisation structure with randomly permuted block sizes of 18, 24 and 30 by using a random-number generator. Allocation was concealed from treating physicians and clinics and implemented by study nurses at the time of the initial household visit
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and people who administered the interventions were not blinded to the interventions, but participants were not informed of the specific nature of the interventions applied to other participating households
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout was accounted for. Dropout from randomised population was high: 32% in control group, 37.5% in hand hygiene group and 39.4% in the face masks and hand hygiene group. Reasons for dropout distributed evenly over the 3 groups Authors report follow up as proportion of patients remaining in the study after initial dropout
Selective reporting (reporting bias)	Unclear risk	In general good reporting

Cowling 2010

Methods	Retrospective cohort study carried out to test whether entry screening practices delayed the onset of endogenous (i.e. not linked with travel of travel contacts) cases of nH1N1 during the recent influenza pandemic in countries which had introduced them compared to countries which had not
Participants	35 countries which reported more than 100 cases of nH1N1 influenza to WHO by 6 July 2009 and for which entry policies could be ascertained or date of first untraceable local case (n = 26 countries). Participants excluded Mexico and US where transmission seemingly occurred earlier

Cowling 2010 (Continued)

Interventions	Dates and types of entry screening: temp check prior to disembarkation, health questionnaires from traveller with H1N1 cases, observation of arrivals for symptoms and thermal body imaging. There was wide variation in implementation with China and Japan implemented all 4, and 5 other nations none (Table 1)
Outcomes	Laboratory: n/a Effectiveness: dates of first imported pandemic influenza case and confirmation of first untraceable case (identified by Google and sundry searches) Safety: n/a
Notes	The authors conclude that entry screening provided an additional 1 to 2 weeks' delay with distributions delay ranging from 0 to 30 days (the CIs of median days of delay overlap) . The authors question the cost-effectiveness of entry screening given the uncertainty of its effects and the enormous amounts of resources required to implement it This an interesting broad-brush study, heavily dependent on web-based searches but with a wide-ranging scope reflected in the multilingual capabilities of the study group. Its many weaknesses are known to the authors and are discussed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Derrick 2005

Methods	Prospective cohort study testing the performance of 1, 2, 3, 4 and 5 surgical masks worn in layers against the droplet filtration capacity of a N95 respirator. The study is described as cross-over trial when all volunteers wore the combinations of layers, but this is not further described
Participants	6 volunteers who wore the masks and had their droplet count taken
Interventions	Pleated rectangular 3-ply surgical mask
Outcomes	Laboratory

Derrick 2005 (Continued)

Notes	Risk of bias: high (report too brief to allow assessment) Notes: the authors conclude that the best combination of 5 surgical masks scored a fit factor of 13.7, well below the minimum level of 100 required for a half face respirator. The reduction in particle count went from 2.7 for a single mask to 5.5 for 5 masks worn at the same time. Multiple surgical masks filter ambient particles poorly. They should not be used as a substitute for N95 respirator unless there is no alternative. Cautiously the authors state that they cannot comment on the capacity of 5 layers of masks to stop infections such as SARS as the infective count of the SARS-CoV is unknown Fascinating small study with no details of assignment so it was classified as a cohort study. Unfortunately there is no indication of how comfortable 5 masks are to wear in a layer and no description of the volunteers	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Dick 1986

Methods	Prospective cohort study involving men ~ 18 years of age. The objective of the study was to determine whether rhinovirus 16 colds could be stopped from spreading with the use of an highly virucidal paper handkerchief (CMF tissues) containing citric acid and other virucidal ingredients. 20 to 25 men ~ 18 years of age were inoculated intranasally with a safety tested R16. The laboratory-induced cold was in all aspects comparable to natural colds. 8 of them with the most severe colds (donors) played cards with 12 antibody-free men (recipients) in a experiment room. Four experiments were conducted, in experiments B and C volunteers used CMF tissues to prevent spreading of R16 colds. In the 2 control experiments (A and D) volunteers were permitted to use cotton handkerchiefs
Participants	Males ~ 18 years of age with a laboratory-induced R 16 cold (donors) and 12 antibody-free men (recipients)
Interventions	Use of virucidal paper handkerchief (CMF tissues), containing citric acid and other virucidal ingredients to stop the spreading of R16 colds versus normal cotton handkerchiefs

Dick 1986 (Continued)

Outcomes	Laboratory: serological evidence (serum samples or viral isolation) Effectiveness: rhinovirus colds Safety: n/a
Notes	Risk of bias: low Notes: the authors concluded that the use of CMS tissues has been successful, because it determined a complete interruption of transmission of R16 among participants, stopping the spreading in an environment in which possibilities for transfer of virus were constant, and in which the rate of transmission was predictably high under standard conditions (42% of cotton handkerchief users developed colds, but no user of virucidal tissues did so)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Doherty 1998

Methods	Retrospective cohort study carried out in North Staffordshire hospital (UK) during 2 periods: from 1 November 1994 to 31 January 1995 and from 1 November 1995 to 31 January 1996. The study assessed the use at admission of assigning children to a cohort once a rapid enzyme immunoassay or immunofluorescence testing had identified RSV-positive patients. The incidence of RSV illness was compared in cohorted and uncohorted children. The authors believed that this procedure would aid clinical management and minimise cross-infection from affected to susceptible patients. Nasopharyngeal aspirates were obtained from infants and young children with an acute respiratory illness. Aspirates were sent for rapid diagnostic testing. RSV-positive patients were cohorted into 6-bedded bays on the paediatric ward. All carers observed standard routines (handwashing and gown wearing)
Participants	Children less than 3 years of age with an acute respiratory illness on admission. During the study periods a total of 222 patients in 1994 to 1995 and 291 patients in 1995 to 1996 had positive rapid tests

Doherty 1998 (Continued)

Interventions	RSV diagnosis and cohorting versus normal care
Outcomes	Laboratory: aspirates for RSV diagnosis Effectiveness: RSV illness (developed at least 5 days since admission) Safety: n/a "RSV infection reduced" (but data tabled do not support this conclusion)
Notes	Risk of bias: high (poor descriptions) Notes: the authors conclude that cohorting has been shown to reduce nosocomial transmission of RSV infections (no OR or other measures of strength are reported: "nosocomial transmission was minimised"). The study presents many inconsistencies between text and table and data were not extracted. The objective of the study is not well-defined. Part of the results is in the discussion. Most of all it is unclear who the intervention and control arms were (i.e. cohorting of RSV-infected children to prevent infection in whom?)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Methods	Prospective, cluster open-label cross-over cohort study of programmed use of a hand sanitiser in conjunction with at-will soap-and-water handwashing conducted in a private elementary school in California. The aim of the study was to assess the effectiveness of the SAB sanitiser at reducing illness absenteeism in a school setting. Subjects were grouped by classroom without formal randomisation. 7 classes received the instant sanitiser, while the remaining 7 classes were assigned to the control group. Male-to-female ratios and age distributions of the 2 groups did not differ significantly Prior to study commencement all students participated in an educational programme about germs and the importance of handwashing to prevent illnesses. Children in the hand sanitiser group received a spray to use under teacher supervision to supplement normal, at-will handwashing with soap and water. The control group was instructed to wash hands with water and soap, and it was not supervised. Data were collected for 10 weeks. After this period, there was a 2-week wash-out period, during which neither group of students used SAB sanitiser. Then SAB sanitiser was distributed to the student group that had previously served as the control and the study proceeded for another 4 weeks
Participants	420 children in a private elementary school in California aged 5 to 12 years; cluster, open-label, cross-over cohort study over 10 weeks
Interventions	Educational programme plus the SAB (surfactant, allantoin and benzalkonium chloride) spray hand sanitiser in 1 oz bottles fitted with a pump spray top and with at-will soap-and-water handwashing versus nothing
Outcomes	Laboratory: serological evidence: n/a Effectiveness: days of absences from school for respiratory illness (and gastrointestinal illness - data not extracted) Safety: n/a Respiratory illness and gastrointestinal illness: reduced absenteeism by 41.9%; respiratory illnesses by 49.7%
Notes	Risk of bias: medium Notes: the authors conclude that daily use of the SAB instant hand sanitiser with at-will handwashing using soap and water significantly decreased absences due to acute communicable illness. Use of the sanitiser reduced illness absenteeism by 41.9% (reduction in respiratory illnesses of 49.7% over the 10-week period of the study). The authors also described some limitations of the study, as limited socio-economic diversity in the study population, limitation to a single study site and lack of blinding. Further soap-and-water washing was not monitored. Generalisability of the results is questionable as all participants underwent the educational programme

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A

Dyer 2000 (Continued)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Falsey 1999

Methods	Prospective cohort study conducted at 3 adult daycare centres in Rochester, New York. The study assessed the value of a staff educational programme combined with the use of a portable virucidal hand foam for the reduction of respiratory infections in daycare participants. The authors report in the same paper an ecological study of the incidence of ILI in 3 previous seasons (1992 to 1996) which does not report numerators and denominators and was not extracted
Participants	In December 1995 when the study started there were centre 1: 69 elderly and 36 staff members; centre 2: 67 elderly and 45 staff members; centre 3: 68 elderly and 16 staff members
Interventions	Addition of virucidal hand foam as a supplement versus normal handwashing and educational programme
Outcomes	Laboratory: serological evidence and virology cultures (Table 1 reports a series of isolated pathogens, with no tie in with actual cases) Effectiveness: viral pathogens: influenza A/B, RSV, coronavirus, parainfluenza, rhinovirus Safety: n/a
Notes	Risk of bias: low Notes: the authors conclude that the educational programme for staff was associated with an almost 50% decrease in the infection rate in daycare attendees. The programme was effective only in the last of the 4 years of the programme (rates of infection in daycare patients fell from 14.5 to 10.4 per 100 person-months to 5.7 per 100 person months, $P < 0.001$). This is a conclusion based on an ecological study of the incidence of ILI in 3 previous seasons which the authors report in the same paper, but which does not report numerators and denominators and was not extracted. The lower infection rate is likely to reflect the combination of interventions and education, which increased staff awareness and more broadly changed behaviour. There was no apparent additional benefit from the virucidal foam. This is one of the few identified studies reporting circulating viruses in the daycare setting, both in staff and patients. The decline in influenza-like illness episodes across the 4 study years is reflected in the decline in viral isolates, suggesting that aspecific measures such as handwashing are effective against the main respiratory viruses

Risk of bias

Falsey 1999 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Farr 1988a

Methods	The study was a 6-month cluster-randomised, controlled, double-blind trial of the efficacy of virucidal nasal tissues in the prevention of natural cold, and it was conducted in Charlottesville, Virginia, USA. Many of the families were enrolled, because one or more members worked at the State Farm Insurance Company; the remaining families were recruited from the Charlottesville community by advertisement in a local newspaper. Families were randomly assigned by the sponsoring company to receive boxes of treated tissues, placebo tissues or no tissues. The randomisation was performed by computer. Study participants and investigators were unaware of the type of tissues which each family was randomised to receive. Blinding efficacy was tested using a questionnaire: the mothers in each family were asked twice if she believed her family was using virucidal or placebo tissues Participants in the treated and placebo groups were instructed to use only tissues received through the study, while families in the additional control group without tissues were allowed to continue their usual practice of personal hygiene. Each family member kept a daily listing of respiratory symptoms on a record card. A nurse epidemiologist visited each family monthly to encourage recording
Participants	186 families, 58 in the active group, 59 in the placebo group and 69 in the no tissues group. A total of 302 families were originally recruited, 116 families who did not comply with the study protocol, lost their surveillance cards, could not complete the protocol were excluded from the analysis
Interventions	Use of virucidal tissues versus placebo tissues versus no tissues. The treated tissues were impregnated with malic and citric acids and sodium lauryl sulphate, while placebo tissues contained saccharin
Outcomes	Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: n/a

Notes	Notes: the authors conclude that virucidal tissues have only a small impact upon the overall rate of natural acute respiratory illnesses. The total illness rate was lower in families using virucidal tissues than in both of the other 2 study groups, but only the difference between active and placebo groups was statistically significant (3.4 illness per person versus 3.9 for placebo group, P = 0.04 and 3.6 for no tissues control group P = 0.2, and overall 14% to 5% reduction). The questionnaire results suggest that some bias may have been present since a majority of mothers in the virucide group believed they were receiving the “active” tissues. Another possible explanation of the low effectiveness of virucidal tissues is poor compliance by children in the use of virucidal tissues. A well-designed and honestly reported study	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“The randomisation was performed by computer in each trial.”
Allocation concealment (selection bias)	Unclear risk	“In trial I, families were randomly assigned by the sponsoring company to receive boxes of treated tissues, placebo tissues or no tissues.” “Families with one or two children were randomised in one stratum, and families with three or more children were randomised in a second stratum in trial I.” Concealment of allocation not described
Blinding (performance bias and detection bias) All outcomes	Low risk	“Study participants and investigators were unaware of the type of tissues which each family was randomised to receive in both trials. In trial I, the mother in each family was asked twice if she believed her family was using active or placebo tissues, first after three months and then at the end of the study.”
Incomplete outcome data (attrition bias) All outcomes	High risk	“A total of 116 of the 302 families were excluded from the analysis. Families were excluded if they lost their surveillance cards or did not conscientiously record data, did not comply with the study protocol, or simply could not complete the protocol for family reasons. It was discovered that families with five or more members had so many colds that it was not possible to distinguish primary and secondary illnesses. These large families were therefore excluded from the

Farr 1988a (Continued)

		analysis in trial I and were excluded from enrolment in trial II.”
Selective reporting (reporting bias)	Low risk	All indicated outcomes are reported

Farr 1988b

Methods	The study was a 6-month randomised, controlled, double-blind trial of the efficacy of virucidal nasal tissues in the prevention of natural cold and it was conducted in Charlottesville, Virginia. Families were recruited from the Charlottesville community by advertisement in a local newspaper. Families were randomly assigned by the sponsoring company to receive either virucidal tissues, or placebo-treated tissues. Stratified randomisation was performed by computer and the strata were defined by total number in the family. Study participants and investigators were unaware of the type of tissues which each family was randomised to receive. Each family member kept a daily listing of respiratory symptoms on a record card. A nurse epidemiologist visited each family monthly to encourage recording. In addition a study monitor visited each family bimonthly to further encourage compliance and reporting of symptoms
Participants	98 families, 58 in the active group and 40 in the placebo group. 231 families were initially recruited, 222 completed the trial, data of 98 families were analysed. The others were excluded from the analysis since they complained of side effects (sneezing, etc.) or reported not using the tissues regularly
Interventions	Use of virucidal tissues versus placebo tissues. The treated tissues were impregnated with malic and citric acids and sodium lauryl sulphate, while placebo tissues contained succinic acid. Participants in the treated and placebo groups were instructed to use only tissues received through the study
Outcomes	Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: n/a
Notes	Notes: the study suggests that virucidal tissues have only a small impact upon the overall rate of natural acute respiratory illnesses. The total illness rate was lower in families using virucidal tissues than in the other study group, but the difference between active and placebo groups was not statistically significant. There was a small non-significant drop in illness rates across families (5%). The tissues appeared ineffective as the drop was confined to primary illness unaffected by tissue use. Placebo (succinic acid) was not inert, and it was associated with cough and nasal burning. This impacted on allocation concealment. A well-designed and honestly reported study marred by transparent allocation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“The randomisation was performed by computer in each trial.”

Farr 1988b (Continued)

Allocation concealment (selection bias)	Unclear risk	“In trial II, families were randomly assigned by the sponsor to receive either virucidal tissues or placebo treated tissues.” “In trial II, stratified randomisation was again used, but this time the strata were defined by total number in the family (i.e., one stratum for two-member families, another stratum for three-member families, and a final one for four-member families).” Concealment of allocation not described
Blinding (performance bias and detection bias) All outcomes	Low risk	“Study participants and investigators were unaware of the type of tissues which each family was randomised to receive in both trials.”
Incomplete outcome data (attrition bias) All outcomes	High risk	“A total of 222 (of 231) families completed trial II; 9 families were terminated early (table 1). In 124 families, one or more family members reported not using the tissues regularly and/or reported having significant side effects. The data from these families were not analysed, leaving 58 families (177 persons) and 40 families (114 persons) for analysis in the virucide and placebo groups, respectively.”
Selective reporting (reporting bias)	Low risk	All indicated outcomes are reported

Foo 2006

Methods	Retrospective cohort survey carried out in Singapore to assess the harm associated with the use of the personal protective equipment in healthcare staff working in a “SARS-designated hospital” from March 2003 to middle 2004. Three departments from the hospital were surveyed the National Skin Centre (NSC), Department of Emergency (A&E) and the intensive care unit (ICU) Control group: unclear Control group: none
Participants	340 healthcare staff were surveyed, 322 responded (60 from the NSC, 77 from the TTSH A&E, and 185 from the TTSH ICU)
Interventions	Use of personal protective equipment (PPE), namely, masks, gloves and gowns. Adverse skin reactions to PPE
Outcomes	Laboratory: none Effectiveness: not applicable

	Safety: adverse skin reactions (ASR) from the use of 3 types of PPE (masks (respirator, surgical or paper masks), plastic gloves and disposable gowns) developed with prolonged use (8.4, 9.4 and 8.8 months, respectively)	
Notes	The authors conclude that prolonged use of PPEs (N95 respirators, rubber gloves) is associated with high frequency of ASR. The authors reported that there were no significant differences in adverse skin reactions to masks and gloves due to sex, race or profession. Some differences were reported by age as follows: • Those who developed acne with masks were younger (mean of 29.5 years) compared with those who did not (mean of 33.2; P < 0.001) • Those who developed dry skin with gloves were younger (mean of 28.7 years) compared with those who did not (mean of 33.2; P < 0.002) • Those who developed itch with gloves were younger (mean of 29.5 years) compared with those who did not (mean of 33.2; P < 0.001) Survey results show that acne, itch and rash are the most common harms reported after wearing a N95 respirator (59.6%, 51.4% and 35.8%) and that dry skin, itch and rash were reported by (73.4%, 56.3% and 37.5%, respectively) glove users. Other harms were reported by very small numbers of users (4 or below). This study, although a retrospective survey is important as it suggests that barrier intervention-using carries harms and such harms may affect compliance with the intervention	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Methods	The purpose of this study was to evaluate whether the use of a disposable plastic goggle designed to cover the eyes and nose could help reduce the rate of nosocomial infections during an outbreak of RSV infection. The rates of RSV infection in staff members and infants were determined on an infant and toddler ward during a seven-week study. Two 3-week study periods were compared: period 1, during which all staff members used the goggles, and period 2, where no goggles were worn. The respiratory infection control procedures were the same during both periods of study: handwashing, isolation and cohorting. In reality although on report, Gala and colleagues are conducting 2 studies. The first is a non-concurrent cohort study, in which 2 different population of children are assessed separated by a 1-week 'wash-out' period and the intervention (goggles) on staff. The play of confounders here is too heavy and uncontrolled to include the data in the study. The second is a controlled before and after on the 40-odd members of staff (32 of whom took part in both periods). Here the play of confounders should be partly reduced. We extracted data relating to the second study only	
Participants	74 children and 40 staff members in period 1; 77 children and 41 staff members in period 2. During the study 151 children were admitted to the ward; their mean age was 12.9 months, 59% were boys. During period 174 infants were examined, 15 were admitted with RSV infections, the remaining 59 constituted the group potentially susceptible to a nosocomial RSV infection. Seventeen infants were hospitalised for sufficient time for a nosocomial infection and in 1 nosocomial RSV infection was detected. During period 277 babies were studied, 17 of whom were admitted with RSV infection. Of the remaining 60, 39 children were excluded, 21 were considered susceptible, and in 9 of them nosocomial RSV infection was detected. Forty staff members were examined in period 1 and 41 during period 2. During period 2, 2 of the ward staff acquired RSV infection and were not considered susceptible	
Interventions	Use of a disposable plastic eye-nose goggle and respiratory infection control procedures versus only respiratory infection control procedures (cohorting, isolation and handwashing)	
Outcomes	Laboratory: serological evidence Effectiveness: RSV infection (symptoms and laboratory confirmation) Safety: n/a	
Notes	Risk of bias: high Notes: the use of the disposable eye-nose goggles appeared to be associated with a significant decrease in nosocomial RSV infections (6% versus 42% of contacts when the goggles were used compared to when they were not). The expense of such goggles will have to be determined and compared with the cost of nosocomial infections. The study has an orgy of confounders, is it difficult to see how such studies can be carried out without disrupting patient care? Why not randomise staff to goggles or standard care?	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A

Gala 1986 (Continued)

Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Gwaltney 1980

Methods	The study assessed the effectiveness of aqueous iodine applied to the fingers in blocking hand transmission of experimental infection with rhinovirus from one volunteer to another. Healthy, young adult volunteers were recruited from the general population at the University of Virginia, Charlottesville. Volunteers were not informed about the contents of the hand preparation until after the study. Two experiments were conducted to evaluate the virucidal activity of aqueous iodine applied to the fingers immediately before viral contamination. Another 2 experiments were conducted to determine whether there was sufficient residual activity of aqueous iodine after 2 hours to interrupt viral spread by the hand route. Volunteers who were donors of virus for the hand exposures were challenged intranasally on 3 consecutive days with strain HH rhinovirus. Recipients were randomly assigned to receive iodine or placebo. The donors contaminated their hands with nasal secretions by finger to nose contact before the exposure. Hand contact was made between a donor and a recipient by stroking of the fingers for 10 seconds. Donors and recipients wore masks during the exposure period
Participants	15 and 20 volunteers in 2 experiments
Interventions	Treatment of fingers with iodine versus placebo. The virucidal preparation used was aqueous iodine (2% iodine and 4% potassium iodide). The placebo was an aqueous solution of food colours
Outcomes	Experimental rhinovirus infection reduced ($P = 0.06$) Laboratory: serological evidence Effectiveness: rhinovirus infection (based on serology, isolation and clinical symptoms) with high score clinical illness. Score was published elsewhere Safety: N/A
Notes	Risk of bias: high (poor description of randomisation process, concealment, or allocation) Notes: the study suggests that aqueous iodine applied to the fingers was effective in blocking transmission by hand contact of experimental infection with rhinovirus for up to 2 hours after application (1 out of 10 volunteers were infected compared to 6 out of 10 in the placebo preparation arm, $P = 0.06$ with Fisher's exact test). The effectiveness of iodine treatment of the fingers in interrupting viral transmission in volunteers recommends its use for attempting to block transmission of rhinovirus under natural conditions. Although the cosmetic properties of 2% aqueous iodine make it impractical for

Gwaltney 1980 (Continued)

	routine use, it can be used as an epidemiologic tool to study the importance of the hand transmission route and to develop an effective cosmetically acceptable hand preparation. A summarily reported study	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Hall 1981a

Methods	Cohort study to determine the possible modes of spread a RSV to young adult volunteers working on a paediatric ward who were exposed in different manners to infants with RSV. Volunteers were divided into 3 groups: "cuddlers", exposed to an infected infant over 2 to 4 hours by caring for the baby in the usual manner, wearing gowns, but no mask or gloves; "touchers", exposed with the infant out of the room by touching surfaces contaminated with the baby's secretions; "sitters", exposed to an infected baby by sitting at a distance of more than 6 feet from an infant's bed, and they wore gowns and gloves, but no masks. In order to control for possible differences in infectivity among infants, a volunteer from each of the 3 groups was exposed to each infant, or to this environment in the case of touchers. In addition, volunteers from each group were exposed to more than one infant. After exposure volunteers were followed for 12 days
Participants	31 volunteers: 7 in the cuddler group, 10 in toucher group and 14 in the sitter group
Interventions	Exposure to infants admitted with bronchiolitis or pneumonia during a community outbreak of RSV isolation
Outcomes	Laboratory: serological evidence Effectiveness: RSV infection demonstrated by viral isolation and serology. Clinical symptom diary collected with questionnaires. Symptomatic, asymptomatic and febrile symptomatic data reported separately Safety: n/a

Hall 1981a (Continued)

Notes	Risk of bias: low Notes: the authors concluded that the spread of RSV may occur by close contact with direct inoculation of large droplets or by self-inoculation after touching contaminated surfaces. Infection does not appear to occur after more distant contact requiring small particle aerosols (0 infected out of 14 “sitters”, those that sat away from RSV infected infants, compared with 5 out of 7 who cuddled and 4 out of 10 who touched the infected infants). Ancillary procedures that may be helpful include the care of contaminated surfaces and gowns, cohorting of staff and infants, and limiting the traffic in and out of the infants’ room. With limited facilities, isolation rooms might best be reserved for uninfected infants with underlying disease who, should they acquire nosocomial RSV infection, are at risk for severe disease	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Methods	Controlled before and after study designed to evaluate the efficacy of infection-control procedures with the use of masks and gowns compared with procedures not using mask and gowns on the rate of nosocomial RSV infection in both infants and staff. The study, conducted at Strong Memorial Hospital in Rochester, NY, USA, in 1979, was begun 12 days after the hospital admission of the first infant infected by RSV, and was continued for the next 2 months. All patients and staff on the ward for children less than 3 years of age were included. During the first 4 weeks (period 1) of the study the infection-control procedures for infants with respiratory illness included handwashing and the use of mask and gowns by the staff on entering the room, with a change of gowns between contacts with each infant. After 4 weeks the wearing of gowns and masks was discontinued and handwashing alone was used for the final 5 weeks of the study. Throughout the study handwashing, cohorting and isolation were employed and emphasised. The number of nosocomial infections in patients and staff for period 1 were compared with the period 2 (last 4 weeks of the study). Infections that occurred in the interval week were not counted	
Participants	162 patients suspected with RSV infections from infected infants; 78 admitted in the period 1 and 84 in period 2. The age range was 2 weeks to 3 years. 55% were male. Of 78 (period 1), 24 were admitted for RSV infections and the remaining 24 became the contacts. (Due to lack of comparability of children and an unclear text children data were not extracted) 39 ward personnel were included, 30 in the period 1 and 27 of these were also studied during period 2 along with 9 other personnel. Thus a total of 36 staff members were studied during period 2	
Interventions	Use of gowns and masks and standard infection-control procedures (handwashing, cohorting, isolation) versus standard infection-control procedures only to prevent transmission of RSV infections from infected infants	
Outcomes	Laboratory: serological evidence Effectiveness: RSV infection demonstrated by symptoms, viral isolation and serology Safety: n/a	
Notes	Risk of bias: high Notes: the authors concluded that the use of masks and gowns as additional infection-control procedures for RSV infection shows no appreciable benefit in preventing nosocomial spread of RSV to infants or to the ward personnel. The nosocomial infection rate in the 2 periods was not significantly different in either the infants or staff (32% infection versus 41%). Both of the study periods appeared to be equal in terms of potential for transmission or exposure to RSV. The number of infants admitted during both periods was similar. Furthermore these 2 groups of contacts were alike in age and types of underlying diseases. The routine use of masks and gowns does not seem warranted in view of the considerable cost. A very poorly reported study with an unclear eligibility procedure and a lack of description of denominators. Why not use randomisation?	
Risk of bias		
Bias	Authors' judgement	Support for judgement

Hall 1981b (Continued)

Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Heymann 2004

Methods	Controlled before and after study to evaluate the effect of school closure on the occurrence of respiratory infection among children ages 6 to 12 years and its impact on healthcare services. The study was conducted in Maccabi healthcare services, which has a nationwide network of > 3000 independent physicians connected by a unified computer system. The authors assembled a retrospective cohort of all 6 to 12 year old children comprising 186,094 children. The computerised data were examined for three 2-week periods: before school closure, during closure and after closure. The occurrence of respiratory tract infections was determined according to recorded diagnoses, including cough, upper respiratory tract infection, common cold, sore throat and viral infection
Participants	186,094 children aged 6 to 12 years
Interventions	Effect of a school closure on the occurrence of respiratory infection during an “influenza” outbreak
Outcomes	Laboratory: no Effectiveness: respiratory tract infections Safety: n/a
Notes	Risk of bias: high Notes: the authors concluded that school closure was temporally associated with 42% decreased morbidity from respiratory tract infections, a consequent 28% decrease in visits to physicians and to emergency departments and a 35% reduction in purchase of medications. Limits of this study are: the fact that in Israel 33.8% of the population are children, hence these results may not be applicable to high-income countries with lower percentage of children. In addition there may be a difference in parental attitudes toward respiratory illness symptoms in other cultures that affect health care utilisation. Another reason for such a difference may be the basic structure of the health system in Israel, where comprehensive health insurance is universal and provided by the law. Finally there is limited availability of over-the-counter medications, and to obtain symptomatic therapeutic agents children are generally seen by a physician. The biggest limit to this study is not mentioned by the authors: the assumption that the circulation of respiratory

Heymann 2004 (Continued)

	viruses is constant throughout the study period. Although in the Discussion the authors mention some surveillance data on national diffusion of an H3N2 epidemic but this took place in December 1999 Observed effects may be due to school closure or they may be due to lower circulation of the viruses	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Isaacs 1991

Methods	Retrospective and prospective cohort study was conducted to evaluate the effectiveness of cohorting and educational programme (handwashing) in reducing the incidence of nosocomial respiratory syncytial virus infections Data on all children with RSV infection on any of the paediatric wards in winter of 1986 to 1987 were retrospectively collected. In order to define the population at risk of developing RSV infection it was determined the number of children under 2 years of age hospitalised on the 2 paediatric wards and the paediatric intensive care unit and the number they spent in hospital. For the next 2 winters (1987 to 1988 and 1988 to 1989) the same data were prospectively collected. In addition some interventions were made to try to reduce the incidence of hospital-acquired RSV infection. Children admitted with suspected RSV infection were nursed in a specific area until the result of an indirect immunofluorescent test. It was not possible to cohort babies on the paediatric intensive care unit. Staff were instructed on the importance of handwashing and this was reinforced on ward rounds. An educational leaflet was prepared and given to the parents of every child admitted with the infection
Participants	Children < 2 years of age: 425 in period 1; 840 in period 2; 552 in period 3
Interventions	Isolation and handwashing versus normal care
Outcomes	Laboratory: indirect immunofluorescence on nasopharyngeal secretions or by culture of secretions Effectiveness: RSV infection

	Safety: n/a	
Notes	Risk of bias: high (poor descriptions) Notes: the authors concluded that handwashing and cohorting reduced at least 66% in the number of hospital acquired infections due to RSV in the 2 intervention winters. One minor problem with cohorting was that babies could not remain in the accident and emergency department until a diagnosis of RSV was virologically confirmed. Hence they were cohorted on the basis of a clinical diagnosis of bronchiolitis. The authors also underline the importance of a more rapid antigen test for RSV. It is doubtful whether the non-exposed cohort is similar to its hospital peers, especially because there are several cardiac children in the exposed cohort. The biggest limit to this study is mentioned by the authors in the Discussion: the assumption that the circulation of RSV is constant throughout the study period. Exposure however is not the same in the 3 seasons and observed effect may be due to cohorting or to the different viral circulation	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Jacobs 2009

Methods	Open randomised controlled trial lasting 77 days from January 2008 to test "superiority" of face masks in preventing URTI. This term appears as an acronym in the introduction and is not explained. It is assumed it stands for "upper respiratory infections" but it is preceded in the text by the term "common cold" which is also lacking a definition. Randomisation was carried out in blocks within each of 3 professional figures (physicians, nurses and "co-medical" personnel)
Participants	33 HCWs mainly females aged around 34 to 37 in a tertiary healthcare hospital in Tokyo, Japan. HCW with "predisposing conditions" (undefined) to "URTI" and those taking antibiotics were excluded A baseline descriptive survey was carried out including "quality of life" 1 participant dropped out at end of week 1 but no reason is reported nor the allocation arm

Interventions	Surgical mask MA-3 (Osu Sangyo, Japan) during all phases of hospital work (n = 17) or no mask (n = 15) (except when specifically required by hospital SOPs)	
Outcomes	Laboratory; n/a Effectiveness: URTI is defined on the basis of a symptoms score with a score >14 being a URTI according to Jackson's 1958 criteria ("Jackson score"). These are not explained in text although the symptoms are listed in Table 3 (any, sore throat, runny nose, stuffy nose, sneeze, cough, headache, ear ache, feel bad) together with their mean and scores SD by intervention arm Safety: the text does not mention or report harms. These appear to be indistinguishable from URTI symptoms (e.g. headache which is reported as of significantly longer duration in the intervention arm). Compliance is self-reported as high (84.3% of participants)	
Notes	The authors conclude that "Face mask use in healthcare workers has not been demonstrated to provide benefit in terms of cold symptoms or getting colds. A larger study is needed to definitively establish non-inferiority of no mask use" This is a small, badly reported trial. The purpose of trials is to test hypotheses not to prove or disprove "superiority" of interventions. There is no power calculation and CIs are not reported (although there is a mention in Discussion). No accurate definitions of a series of important variables (e.g. URTI, runny nose etc.) are reported and the Jackson scores are not explained, nor their use in Japanese personnel or language validated Intervention arm data not extracted because of the uncertainty of its meaning	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Open randomised controlled trial, but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	"Mask and no mask groups were formed using block randomisation of subjects within their respective job categories: nurses, doctors, and co-medical personnel." Concealment of allocation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible (mask wearing or not)
Incomplete outcome data (attrition bias) All outcomes	Low risk	One dropout in each group accounted for. "Analyses were performed following the principles of intention-to-treat."
Selective reporting (reporting bias)	High risk	NB: influenza vaccine coverage in mask group was 100% and only 81% in the non-mask wearing group

Kimel 1996

Methods	Prospective cohort study conducted in a school of Chicago, USA, to evaluate the effectiveness of a handwashing programme in reducing the absenteeism caused by flu-like illness. The school was located in a predominantly white, middle to upper middle class suburb. All 4 kindergarten and 5 first-grade classes were included in the study. No significant differences were found between participating classes for size, male-female ratio, percentage of low-income students, or students with chronic health problems. Teachers were surveyed to determine classroom handwashing activities. The influenza season usually occurs during December and January. The handwashing programme was planned for presentation just prior to this time. The effectiveness of the programme was determined by comparing absentee rates among participants and non-participating classes (the control group). Absentee rates were determined by reviewing the computerised daily school absence logs. Entries that listed flu-like symptoms were counted. A take-home handwashing chart was also given to each student to encourage follow-through with handwashing at home
Participants	199 children of kindergarten and first grade schools
Interventions	Handwashing and educational programme versus no intervention
Outcomes	Laboratory: no Effectiveness: flu-like illness Safety: n/a Absenteeism from influenza-like illness was approximately double in the control arm (P = 0.01)
Notes	Risk of bias: medium Notes: the authors concluded that handwashing education can decrease absenteeism even among kindergarten and first grade students. This study did not control for health and hygiene practices at home or exposure to ILI outside of school. Furthermore the student population at the school was generally healthy, probably because families were able to provide adequate health and hygiene resources. Another problem of the study is that the flu season was later than usual (February), and this represented a confounding variable. The teacher surveys indicated problems with handwashing facilities

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A

Kimel 1996 (Continued)

Selective reporting (reporting bias)	Unclear risk	N/A
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Kotch 1994

Methods	Pair-matched cluster-randomised, controlled trial conducted in the period 19 October 1988 to 23 May 1989 in 24 childcare centres in North Carolina, USA. The trial tested the effects of a handwashing and environment sterilising programme on diarrhoea (data not extracted) and ARIs. Child daycare centres had to care for 30 children or less, at least 5 of whom had to be in nappies and intending to stay open for at least another 2 years. Randomisation is not described, nor are cluster coefficients reported
Participants	389 children aged 3 years or less in daycare for at least 20 hours a week. There were some withdrawals but the attrition on participants is not stated, only that in the end data for 31 intervention classrooms and 36 control classrooms were available. There were 291 children aged up to 24 months and 80 over 24 months that took part. The text is very confusing as 371 seem to be the total of the number of families that took part. No denominator breakdown by arm is reported and numerators are only reported as new episodes per child-year
Interventions	Structured handwashing and environment (including surfaces, sinks, toilets and toys) disinfecting programme with waterless disinfectant scrub
Outcomes	Laboratory: N/A Effectiveness: ARI (coughing, runny nose, wheezing, sore throat or earache) Safety: N/A
Notes	Risk of bias: high (poor reporting of randomisation; outcomes; numerators and denominators) Notes: the authors conclude that the fully adjusted RR for prevention of ARIs was 0.94 (-2.43 to 0.66). A poorly reported study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Pair-matched cluster-randomised, controlled trial", but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Centres were matched in pairs and then randomly allocated to either intervention or control programmes. Allocation concealment not reported
Blinding (performance bias and detection bias)	High risk	Not possible (intervention was training session)

Kotch 1994 (Continued)

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	High risk	18 families were dropped, denominator not clear
Selective reporting (reporting bias)	High risk	Denominators not clearly reported

Krasinski 1990

Methods	Controlled before and after study conducted in Bellevue Hospital Center, New York, USA, to determine the effectiveness of screening for RSV and assignment to a cohort at admission to reduce nosocomial transmission of RSV infections. Children who were 3 years of age and older were admitted to a paediatric ward that is equipped with private rooms for the control of communicable diseases. Children younger than 3 years of age were admitted to a separate ward without private rooms, where as many as 4 children shared a room. All paediatric patients hospitalised on or before 31 December 1986 were regarded as potentially infected with RSV and were constituted as an RSV-infected cohort. A second cohort, free of infection with RSV, was established on the toddlers' ward to segregate high-risk patients from RSV-infected patients. Patients requiring hospital admission and assignment to the high-risk cohort were screened for evidence of RSV infection by means of a rapid ELISA method. No gloves or masks were used in the RSV cohort	
Participants	All hospitalised paediatric patients regarded as potentially infected with RSV	
Interventions	RSV screening cohorting and service education programme versus do nothing	
Outcomes	The authors concluded that screening and subsequent cohorting reduced RSV infections (from 5.33 infections per 1000/patient days of care to 1.23 infections per 1000/patient days after introduction of screening). There was an attempt at correlation between RSV admissions and RSV community circulation	
Notes	Risk of bias: medium Notes: the authors concluded that screening and subsequent cohorting reduced RSV infections (from 5.33 infections per 1000/patient days of care to 1.23 infections per 1000/patient days after introduction of screening). There was an attempt at correlation between RSV admissions and RSV community circulation	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A

Krasinski 1990 (Continued)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Krilov 1996

Methods	Controlled before and after study carried out in a 16 classrooms of special needs school for Down Syndrome children in New York State. The study took place between November 1991 and November 1993. The 'before' period between November 1991 and October 1992, followed by a 1-month washout period during which the intervention was introduced, followed by 12 months of 'after' period (December 1992 to November 1993)
Participants	33 children aged 6 weeks to 5 years took part in the 'before' and 38 in year 2 ('after' period) . During the study period there were about 110 children in the school but the parents of the majority did not agree to replying to 2-weekly questionnaires, so their children were not entered in the study. In addition 5 sets of questionnaires in the 'before' and 2 in the 'after' periods did not contain sufficient data (6 months' worth) and were excluded. Despite this there were no significant differences between 'before' and 'after' children. The authors also describe viral circulation during the study periods from isolates in the local hospital. All community isolates were constant with the exception of adenovirus which doubled in the 'after' period of the study
Interventions	Training and sanitary programme with handwashing, disinfection of school buses, appliances and toys. In addition a person designated a study monitor carried out intensive monitoring of classroom behaviour and reinforced messages. Disinfection took place with Reckitt & Colman products (sponsors of the study)
Outcomes	Laboratory: viral isolates from surrounding community (non-random samples) Effectiveness: ARI (cough, runny nose, sore throat, wheezing or rattling in the chest, ear ache). Vomiting and diarrhoea (data not extracted). Follow up was carried out on the basis of parents' questionnaire Safety: N/A
Notes	Risk of bias: high (disinfectants provided and study sponsored by manufacturer) Notes: the authors concluded that respiratory illnesses decreased from a median of 0.67 to 0.42 per child per month ($P < 0.07$), physician visits, 0.50 versus 0.33 ($P < 0.05$) , mean course of antibiotics prescribed 0.33 versus 0.28 ($P < 0.05$) and days of school missed because of respiratory infections 0.75 versus 0.40 ($P < 0.05$). Respiratory illnesses decreased from a median of 0.67 to 0.42 per child per month. Small study with a serious selection bias and generalisability problems
Risk of bias	

Krilov 1996 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Ladegaard 1999

Methods	RCT with cluster-randomisation to intervention or control. Out of 10 institutions they excluded 2 because they wanted institutions to be comparable in uptake area (that means housing and income). Interventions were given to children, parents and teachers at the institutions	
Participants	Children 0 to 6 years old	
Interventions	Multifaceted: information, t-shirts to the children with: “Clean hands - yes, thank you”, performance of a fairytale “The princess who did not want to wash her hands”, exercise in handwashing, importance of clean and fresh air. The aims of the intervention were: - to increase the hygiene education of the daycare teachers - to motivate the children by practical learning to have a better hand hygiene - to inform the parents about better hand hygiene	
Outcomes	34% decrease in 'sickness' (probably mostly gastroenteritis)	
Notes	Risk of bias: limited data only available Notes: the authors conclude that there was a 34% decrease in sickness in the intervention arm, this is probably overall sickness as gastroenteritis is part of the outcomes (data not extracted). Limited data only available from translation by Jørgen Lous	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described

Ladegaard 1999 (Continued)

Allocation concealment (selection bias)	Unclear risk	Randomisation by “lottery”, the same as “flip the coin” Concealment not reported
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	High risk	No total numbers of children included in each arm reported
Selective reporting (reporting bias)	High risk	Limited data reported, especially denominators missing

Larson 2010

Methods	Cluster block-randomised, controlled trial carried out between 20 November 2006 and 20 June 2008 in an upper Manhattan immigrant Latino neighbourhood (“19 month data collection period”). The study aimed at assessing the effects of education versus education and hand sanitiser use versus education and hand sanitiser use and common mask use against upper respiratory infections over a period of under 2 years. Follow up was through an automated telephone system with a small financial incentive (USD 20) for those with 75% or more compliance. Those reporting an ILI received a visit within 48 hours for swabbing An index case was someone who at the “onset day of illness nobody else in the household had been symptomatic within the previous five days” A secondary case for each episode “was any member of the household who developed symptoms within five days following the index case”, “The secondary attack rate was defined as the number of secondary cases recorded within 5 days of the onset of symptoms in the index case divided by the number of household members minus one” The text implies that the unit of observation was the episode (“study subjects contributed more than one episode in which they were considered to be the index case”)
Participants	Recruitment and allocation were carried out by household. These had to have at least 3 people living in the household, with at least 1 being a preschool or elementary school child, speaking English or Spanish, having a telephone willingness to complete symptom assessments and having bimonthly home visits and not using alcohol-based hand sanitiser routinely 617 households were randomised, 211 to the education, 205 to the hand sanitiser and 201 to the hand sanitiser and mask groups. The participants were 2708, mostly adult Latino immigrants to the USA Intraclass correlation coefficients are reported on page 179 of the manuscript
Interventions	Written Spanish or English language educational materials regarding the prevention and treatment of URIs and influenza or the same educational materials and hand sanitiser (Purell, J&J), in large (8- and 4-ounce) and small (1-ounce) containers to be carried by individual household members to work or school or the same interventions as well as regular surgical face masks (Procedure Face Masks for adults and children, Kimberly-

	Clark) with instructions for both the caretaker and the ill person to wear them when an ILI occurred in any household member. Replenishment of intervention stocks was done at the bimonthly home visit Caretakers had to wear a mask for 7 days when within 3 feet of a symptomatic case. These were also encouraged to wear masks within 3 feet of any household member. Reinforcing phone calls were made 3 times in 6 days The text clearly reports active influenza vaccine promotion during the bi-monthly visits ("The home visit to each household was made every 2 months to minimise study dropout, reinforce adherence to the assigned intervention, replenish product supplies and record use of supplies, answer questions, and correct ongoing misconceptions. At each visit, new educational materials regarding URTI prevention and treatment and influenza vaccination were distributed." (PDF page 3). Also just before the Discussion as follows: "Influenza vaccination rates: There was an increase between the baseline and exit interview in all three groups that reported 50% of more of members receiving influenza vaccine (pre- versus post-intervention for each group: 21.1% and 40.8% in the Education group, 19.0% and 57.1% in the hand sanitiser group, and 22.4% and 43.5% in the hand sanitiser and face mask group ($P = 0.001$). Additionally, those in the hand sanitiser group reported a significantly greater increase than the other 2 groups, controlling for baseline rates ($P = 0.002$)" Coverage was unequal across groups, no information on the progressive impact of the vaccine, or indeed the nature of the vaccine(s) is reported. Apparently the first season was mild and the vaccine mismatched, compliance with the trial interventions was low in Arm 3 and a local epidemic of <i>S. aureus</i> meant that the control group started washing hands The authors report no effect on reporting rates of vaccine coverage by arms but with so many confounders who knows?
Outcomes	Laboratory: PCR carried out on samples from deep nasal swabs for influenza and the most common other pathogens (RSV, rhinovirus, enterovirus, parainfluenza viruses etc.). The text describing the results of the swabbing is confusing but in general appears to be non-random "Households reported 669 episodes of ILI (0 to 5 per individual)". Of the 234 deep nasal swabs obtained, 33.3% ($n = 78$) tested positive for influenza; 43.6% ($n = 34$) were influenza A and 56.4% ($n = 44$) were influenza B. Among the 66.7% who tested negative for influenza, 30.8% (48/156) tested positive for other viruses: 7 for respiratory syncytial virus, 9 for parainfluenza, 11 for enterovirus, 10 for rhinovirus, 6 for adenovirus, and 5 for metapneumovirus. Swabs were not obtained from the remaining 435 reported ILI episodes for the following reasons: 72.0% ($n = 313$) did not meet the CDC definition of an ILI and were therefore included in the URTI symptom count, 21.4% of episodes ($n = 93$) were reported after 48 hours of ILI onset or the participant refused to be swabbed, and the research staff were unable to reach the participant in 6.7% of episodes ($n = 29$) As no definition of URTI is given it is unclear what kind of biases are introduced by the non-swabbing of the 313/435 "not meeting CDC definition". Effectiveness: ILI (CDC definition): "temperature of 37.8°C or more and cough and/or sore throat in the absence of a known cause other than influenza" URTIs only referred to as "Viral upper respiratory infections (URTIs)" Safety: N/A

Notes	The authors conclude that “the Hand Sanitizer group was significantly more likely to report that no household member had symptoms (P,0.01), but there were no significant differences in rates of infection by intervention group in multivariate analyses. Knowledge improved significantly more in the Hand Sanitizer group (P,0.0001). The proportion of households that reported >50% of members receiving influenza vaccine increased during the study (P,0.001). Despite the fact that compliance with mask wearing was poor, mask wearing as well as increased crowding, lower education levels of caretakers, and index cases 0-5 years of age (compared with adults) were associated with significantly lower secondary transmission rates (all P,0.02). In this population, there was no detectable additional benefit of hand sanitiser or face masks over targeted education on overall rates of URTIs, but mask wearing was associated with reduced secondary transmission and should be encouraged during outbreak situations. During the study period, community concern about methicillin-resistant <i>Staphylococcus aureus</i> was occurring, perhaps contributing to the use of hand sanitiser in the Education control group, and diluting the intervention’s measurable impact”. The study is at high risk of bias. Randomisation and reasons for dropout are not described. Differentials in cluster characteristics across arms point to randomisation not having worked and the confounding effects of a post-randomisation staphylococcal scare is difficult to judge. Symptom-driven follow up gives no idea of the effects on asymptomatic ILI/influenza. Poor definitions (URTI?). There are unexplained dropouts and the analysis plan is unclear. Finally the very small number of cases of influenza and an unclear swabbing attrition may introduce further elements of confounding	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“Cluster block randomised, controlled trial”, but sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	“Households were block randomised into one of three groups:” Allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	High risk	In 211 control group HH 26 dropped out and 37 did not consent In 205 hand sanitiser group HH 21 dropped out and 36 did not consent In 201 hand sanitiser and face mask group HH 19 dropped out and 35 did not consent Reasons for dropout not described

Selective reporting (reporting bias)	Unclear risk	617 of 772 eligible households were randomised HH in groups comparable
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Lau 2004a

Methods	Case-control study carried out in Hong Kong, SARS of China during 4 April to 10 June 2003, at the height of the SARS outbreak. The aim was to describe the defined and undefined sources of SARS cases groups and assess the protective effects of various public health measures Defined sources were classified as being a healthcare worker in a hospital, living in Amoy Gardens (a known focus of infection) having had a contact with a member of the household with SARS of earlier onset, hospital in patients infected with SARS by other hospital inpatients and contacts of SARS cases before the onset of their own symptoms The undefined sources group of cases were all the other categories Cases in general were identified and interviewed on the phone. Households with more than 1 index case were considered as having 2 index cases. Of the 1690 identified cases, 1214 from 996 households were enrolled in the study. 140 cases could not be contacted as they had a wrong phone number, 163 were uncontactable after at least 5 attempts, 163 refused to take part and 10 did not speak either Chinese or English. 17 were further excluded because they were aged less than 16. 22 questionnaires were unusable. (This makes 1175, obviously the 17 minors are included in the case-control study, as adding them makes a total of 1192)
Participants	Description of cases: 330 probable cases of SARS selected as follows. From 1192 people with probable SARS reported to the Department of Health in the territory of HK up to 16 May 2003, 1175 were entered in the case-control analysis. SARS cases were defined as Xray evidence of pulmonary infiltration consistent with pneumonia with a temperature of > 38°C or a history of such in the previous 2 days and at least 2 of the following: history of chills in the previous 2 days new or increased cough, breathing difficulty, general malaise of myalgia, typical signs of consolidation and known exposure to SARS. The authors say that this definition is the same the WHO's case definition of probable SARS. At interview, risk factors were elicited and identified. There were 727 cases in the defined source category and 347 in the undefined sources category (330 after exclusion of 17 minors) Description of controls: 660 controls of undefined origin and with no description of selection
Interventions	Natural exposure to SARS during a serious epidemic
Outcomes	Community transmission of SARS reduced OR 0.30 (95% CI 0.23 to 0.39)
Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that community transmission was of less importance than previously thought and public health measures worked. The following risk factors were significantly associated with SARS (matched multivariate analysis OR with 95% CIs): - Visit to mainland China 1.95 (1.11 to 3.42) - Visited Prince of Wales Hospital 7.07 (1.62 to 30.75)

Lau 2004a (Continued)

- Visited other hospitals 3.70 (2.54 to 5.39) - Visited Amoy Gardens 7.63 (3.77 to 15.43) The following activities/interventions had a significant protective function: - Thorough disinfection of living quarters 0.41 (0.29 to 0.58) - Wore a mask in public places frequently 0.36 (0.25 to 0.52) - Washed hands 11 or more times a day 0.58 (0.38 to 0.87) Potentially a very interesting study possibly rigorously conducted let down by a very confusingly written text. The biggest problem is lack of clarity as to who the controls were. This may be a reflection of the pressure of carrying out a study in the midst of a serious epidemic		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Leclair 1987

Methods	Controlled before and after study conducted in children's hospital of Boston, USA, to determine whether increased compliance with a policy of glove and gown isolation precautions could reduce the high rate of nosocomial RSV infection on an infant and toddler ward. All patients admitted to the 28-bed infant and toddler medical ward during 3 consecutive RSV seasons (1982 to 1985) were included in the study. When patients with known or suspected RSV infection were admitted, an attempt was made to place them in single rooms or to group them together, but infected patients were frequently required to share rooms with susceptible patients during the winter months, when the prevalence of RSV on the wards is highest. The RSV season was defined as the 24 weeks each year starting at the beginning of November and continuing through the end of April. All the documented cases of RSV infection occurred during that period, and all the patients and patient-days during that interval on the study ward were recorded. RSV infections were classified as nosocomial if symptoms developed 5 or more days after the patient's admission to the hospital. All cases of RSV infection were confirmed virologically. During the first half of the study nursing staff wore both gloves and gowns for only 20 of 52 observed contacts. During and after the second compliance survey, compliance rapidly increased: nursing staff wore both gloves and gowns for 73 of 90 of their contacts	
Participants	695 patients aged from 5 days to 4 years and 11 months. The distribution of ages was similar in the 2 periods. 37 acquired nosocomial RSV infections	
Interventions	Infection-control intervention to increase use of gloves and gowns versus no intervention	
Outcomes	Laboratory: yes Effectiveness: RSV infection Safety: N/A	
Notes	Risk of bias: low Notes: the authors concluded that the incidence of nosocomial RSV infection rose with the intensity of hospital exposure and that this rise was markedly different in the periods before and after intervention. The use of gloves and gowns can reduce the nosocomial transmission of RSV, particularly with increasing exposure to patients shedding the virus (RR for pre and post-intervention periods infection rates 2.9, 1.5 to 5.7). Compliance by the staff improved dramatically after the intervention and it continued even after the end of the study, probably because the favourable results of the intervention were well-publicised, the head nurse introduced an educational programme emphasising the appropriate application of isolation precautions, and gowns and gloves became more accessible to care givers. The study, although prone to selection bias, is better designed than some of it peers as there is an attempt at adjusting for different levels of RSV circulation by sub-analysis by virus shedding days by the infected participants	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A

Leclair 1987 (Continued)

Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Leung 2004

Methods	Prospective cohort study conducted during 13 March to 29 June 2003 in the paediatric department of the Prince of Wales Hospital at the height of the SARS epidemic in Hong Kong, China. The aim of the study was to test the effectiveness of procedures to stop transmission of SARS from infected children to carers and visitors
Participants	26 HCWs in close contact with probable or suspected SARS and 88 HCWs in contact with patients in other study areas during the study period
Interventions	Triage and UHR-S isolation and strict infection control procedures versus triage and UHR-S isolation and less strict infection control procedures Healthcare workers were exposed to 9 children with probable SARS and 29 with suspected SARS admitted into the Ultra High Risk SARS (UHR-S) areas with a mean age of 8.9 years, 88 children with pneumonia but no SARS contact with a mean age of 8.2 admitted to the isolation cubicle of the Ultra High Risk Infection (UHR-I) area, 227 with febrile illness and normal chest radiograph aged 4.9 years treated in an open cubicle in the UHR-I area and 274 non-febrile children with a mean age of 7.5 years admitted into the High Risk (HR) area. The study tested the effectiveness of triage and UHR-S isolation + strict infection control procedures versus triage and UHR-S isolation + less strict infection control procedures Triage at admission aimed at identifying children aged less than 18 who: - were febrile or afebrile with a known SARS contact who were admitted to the UHR-S area - with a positive CXR and a SARS contact who were admitted to the UHR-S area - with CXR changes but no SARS contact who were admitted to the UHR-I area - were febrile or afebrile but no SARS contact who were admitted to the HR area Very strict infection control measures were implemented on entry and exit from the UHR-S area (handwashing, gown, caps, goggles, mask, upper and trousers of cloth operating theatre garments and N95 face respirator for HCWs, all measures but no goggles or undergarments for visitors and handwashing and mask for patients) Less strict infection control measures were implemented on entry and exit from the UHR-I area (handwashing, gown, goggles, mask, upper and trousers of cloth operating theatre garments and N95 face respirator for HCWs, and handwashing and mask for visitors and patients), Even less strict infection control measures were implemented on entry and exit from the HR area (handwashing, gown, caps, goggles, mask, upper and trousers of cloth operating

Leung 2004 (Continued)

	theatre garments and mask of N95 face respirator for HCWs and handwashing and paper mask for visitors and patients) Enforcement was directed by a police nurse in the UHR areas	
Outcomes	Laboratory: laboratory confirmation of SARS Effectiveness: probable or suspected SARS according to WHO definitions Safety: N/A	
Notes	Risk of bias: low Note: the authors conclude that the measures worked well as no HCW or visitor became ill. This is a remarkably well-conducted and clearly reported study in the midst of a major infectious disease outbreak with a previously unknown agent. The Prince of Wales Hospital had previously witnessed an outbreak in which an index patient had infected 138 healthcare workers. All the more remarkable as the paediatric department had not been built as isolation facility and had to be rapidly reorganised	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Liu 2009

Methods	The paper is a re-analysis and publication in English of Ma 2004 , a case-control study carried out shortly after the SARS outbreak at the Armed Forces Hospital (AFH) in Beijing in which 16 HCW died. The data from Ma 2004 had been published in Chinese only. The paper assesses relationships between protective and risk factors in cases and controls using a 2-step analysis procedure: univariate analysis and then multivariate analysis for those associations found significant up to the 10% level
Participants	Description of cases - 51 HCW (age mean 29.5 years) who were admitted to AFH during 5 March to 17 May 2003 with clinical features fitting WHO's SARS criteria. All enrolled analysed cases subsequently proved to be IgG SARS positive (1 case was excluded because he/she was negative). Probable cases of SARS are defined as: documented fever (temperature > 38°C), presence of cough, shortness of breath or breathing difficulty, and

	a significant history of exposure to a SARS patient not more than 10 days prior to onset of symptoms, plus radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR) (World Health Organization criteria, 2003). The text mentions that cases were 76% (51 of the 67) “survived” staff in the AFH Description of controls; 426 HCW (age mean 31.4 years) working in AFH during the same period as cases with self-reported exposure to SARS but had no symptoms (the text says “uninfected”). All enrolled analysed controls subsequently proved to be IgG SARS negative and their exposure within 1 month of a SARS case was confirmed. These are 90% of AFH employees exposed to SARS
Interventions	Exposure and risk or protective factors were subsequently elicited by questionnaire and interviews in June to July 2003: gender, age, ethnic group, educational level, co-morbidity, smoking status, alcohol intake, contact date, occupation, department, contacts with SARS and exposure time. None of these factors proved to be significant in a multivariate analysis. At univariate analysis 17 variables were significantly associated with SARS, 10 of which were protective (i.e. negative association): - wearing a 12-layer cotton surgical mask - wearing 16-layer cotton surgical mask (and wearing layers of mask) - wearing glasses - wearing gloves - wearing goggles - wearing multiple layers of protective clothing - taking “prophylactic medicine” (such as “antivirals” and vitamin supplements), performing nose washes after contact and having training prior to exposure N95 mask use was non-significant probably because of the rarity of its use At multivariate analysis level, 12 and 16-layer mask non-use and not undergoing training, not taking medicine and not wearing multiple layers of masks were found to be associated with SARS onset
Outcomes	Laboratory: all clinically diagnosed hospital-acquired SARS cases confirmed by + SARS-CoV IgG ELISA and all controls confirmed by a - SARS-CoV IgG ELISA Effectiveness: univariate and multivariate analysis among the 28 variables elicited in questionnaires and by interview
Notes	The authors conclude that “this study identified exposure to high-risk procedures (such as chest compression), and contact with respiratory secretions to be significant risk factors for SARS infection among HCWs in a hospital in Beijing. These results also provide confirmation that personal protective measures against droplet spread, such as wearing multiple layers of mask, are effective against the nosocomial spread of SARS” The main points to bear in mind when interpreting this study are: - the possibility of selection bias in cases (only living cases were recruited whereas we know that 16 HCWs in AFH died) - protective variables are not well-defined (i.e. the make or type of masks used, whether fitted or not) - information on the 10 protective interventions (variables) was elicited post hoc with a possibility of recall bias (mentioned by the authors in their Discussion) - the lack of reporting of numerator and denominator data for cases and controls - the apparent lack of mention of data assessment and analysis blinded to case or control

Liu 2009 (Continued)

	status - failure to attempt matching between cases and controls and the partly prospective nature of the study design	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Loeb 2009

Methods	Open non-inferiority randomised, controlled trial carried out to compare the surgical mask with the N95 respirator in protecting healthcare workers against influenza. The trial was carried out between 2008 (enrolment started in September and follow up on 12 January 2009) and 23 April 2009 (when all HCWs were told to wear a N95 respirator for all HCWs caring for febrile patients because of the appearance of novel A/H1N1). The trial trigger was the beginning of the influenza season defined as isolation of 2 or more viruses in a district in the same week. Following the 2003 SARS outbreak all Ontario nurses caring for febrile patients (38 °C or more and new onset cough or SOB) had to wear surgical masks. The randomisation (carried out in blocks of 4 by centre) then consisted of either confirmation to same-maker surgical mask wear or N95 respirator wear. Investigators and laboratory staff were blind to allocation status, but for obvious reasons (the visible difference in interventions), participants were unblinded. "The criterion for non-inferiority was met if the lower limit of the 95% confidence interval (CI) for the reduction in incidence (N95 respirator minus surgical group) was greater than -9%". So this is the non-inferiority margin. It is assumed that the "minus surgical group" means minus surgical mask group
Participants	Consenting nurses (n = 446 randomised) aged a mean of 36.2 years working full time (> 37 hours/week) in 23 acute units (a mix of paediatric, A&E and acute medical units) in 8 hospitals in Ontario, Canada. 225 were randomised to the surgical mask and 221 to the N95 respirator. There were 13 and 11 dropouts respectively from each arm (all accounted for) plus 21 and 19 lost to follow up. 11 in each arm gave no reason, the others are accounted for. There were no deaths. The final total of 212 and 210 was included in the analysis. Table 1 reports the demographic data of participants by arm, which appear

	comparable
Interventions	Surgical masks (as standard wear by the standard distributor) or fit-tested N95 respirator. All nurses wore gloves or gowns in the presence of a febrile patient
Outcomes	Laboratory RT-PCR paired sera with 4-fold antibody rise from baseline (only for unvaccinated) nurses Effectiveness: follow up (lasting a mean of around 97 days for both arms) was carried out twice-weekly on a web-based instrument. Nurses with new symptoms were asked to swab a nostril if any of the following signs or symptoms had developed: fever (temperature > 38°C), cough, nasal congestion, sore throat, headache, sinus problems, muscle aches, fatigue, earache, ear infection or chills The text defines influenza with laboratory-confirmation and separately reports criteria for swab triggering and a definition of ILI ("Influenza-like illness was defined as the presence of cough and fever: a temperature > 38°C"). But this is not formally linked to influenza in the text as it appears that primary focus was the detection of laboratory-confirmed influenza (either by RT-PCR or serology) Additional outcome data sought were work-related absenteeism and physician visits for respiratory illness Secondary outcomes included detection of the following non-influenza viruses by PCR: parainfluenza virus types 1, 2, 3 and 4; respiratory syncytial virus types A and B; adenovirus; metapneumovirus; rhinovirus-enterovirus; and coronaviruses OC43, 229E, SARS, NL63 and HKU1 Audits to assess nurse compliance with the interventions were carried out in the room of each patient cared for. The text reports that 50 and 48 nurses in the surgical mask and N95 groups respectively had laboratory confirmation of influenza infection, indicating non-inferiority. Interestingly non-inferiority seemed to be applicable both to seasonal viruses and nH1N1 viruses (as 8% and 11.9% were serologically positive to nH1N1). This finding is explained either by seeding or cross reaction with seasonal H1N1. Equivalent conclusions could be drawn for nurses with complete follow up. Non-inferiority was applicable also to other ILI agents identified. None of the 52 persons with positive isolates met the criteria for ILI All cases of ILI were confirmed as having influenza (9 and 2 respectively). This means that all the 11 cases of ILI had influenza but that most of those with a laboratory diagnosis of influenza did not have cough and fever. For example the text reports that "Of the 44 nurses in each group who had influenza diagnosed by serology, 29 (65.9%) in the surgical mask group and 31 (70.5%) in the N95 respirator group had no symptoms". By implication of the 88 nurses with antibody rises 28 had symptoms of some kind, i.e. two-thirds were asymptomatic. Absenteeism was 1 versus 39 episodes in the mask versus respirator arms. No episodes of LRTI were recorded. The number of family contacts with ILI were the same for each arm (45 versus 47). Physician visits were similar in both groups Safety: no AEs are reported
Notes	The authors conclude that "Among nurses in Ontario tertiary care hospitals, use of a surgical mask compared with a N95 respirator resulted in non-inferior rates of laboratory-confirmed influenza" This a well-designed and conducted trial with credible conclusions. The only comment is that the focus in the analysis on influenza (symptomatic and asymptomatic) is not

	well-described, although the rationale is clear (interruption of transmission)	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Randomisation was performed centrally . . .”
Allocation concealment (selection bias)	Low risk	“...by an independent clinical trials coordinating group such that investigators were blind to the randomisation procedure and group assignment and was stratified by centre in permuted blocks of 4 participants.”
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcome assessment blinded: “It was not possible to conceal the identity of the N95 respirator or the surgical mask since manipulating these devices would interfere with their function. Laboratory personnel conducting hemagglutinin inhibition assays, polymerase chain reaction (PCR), and viral culture for influenza were blinded to allocation.”
Incomplete outcome data (attrition bias) All outcomes	Low risk	21 of 225 randomised in mask group and 19 of 221 randomised in N95 group were lost to follow up, reasons reported Study stopped early: “We had planned to stop the study at the end of influenza season. However, because of the 2009 influenza A(H1N1) pandemic, the study was stopped on April 23, 2009, when the Ontario Ministry of Health and Long-Term Care recommended N95 respirators for all healthcare workers taking care of patients with febrile respiratory illness.”
Selective reporting (reporting bias)	Low risk	All outcomes reported

Longini 1988

Methods	Cluster-controlled, double-blind, randomised trial to assess the efficacy of virucidal tissues in interrupting family transmission of rhinovirus and influenza virus. The study was carried out in the community of Tecumseh, Michigan, USA during the period 25 November 1984 to 28 April 1985. However, the authors only report results for the period 13 January to 23 March 1985, when a high circulation of influenza A H3N2 and rhinovirus was detected
Participants	296 households were enrolled but for “technical reasons” 5 household were eliminated from the analysis. The analysis was carried out in households with 3 to 5 members. The authors report data on 143 households randomised to virucidal tissues and 148 to placebo tissue. Average age in households was around 22 and the difference between arms was not significant. Randomisation was carried out by the sponsor and tissues were pre-packed in coded boxes with no other identifying features and delivered to households at the beginning of the study period
Interventions	Disposable 3-layered virucidal tissues (citric and malic acids with sodium lauryl sulphate in the middle layer) or placebo (succinic acid in the middle layer) tissues. They were used to blow the nose and for coughing or sneezing into Households were also stratified by level of tissue use. Tissue use was significantly higher in the intervention arm (82% versus 71%)
Outcomes	Laboratory: yes - viral culture from nasal and throat swabs from symptomatic participants Effectiveness: ARI (with a proportion of laboratory-confirmed diagnosis in non-randomly chosen participants with symptoms lasting 2 days or more) Follow up and surveillance was carried out using a telephone questionnaire Safety: N/A
Notes	Risk of bias: high (inappropriate choice of placebo) Notes: the authors conclude that virucidal tissues were up to 36.9% effective in preventing transmission of ARIs as measured by secondary attack rates (18.7% versus 11.8%). This was not significant but may well have been affected by the lack of do-nothing community controls. This a well-designed, well-written study despite the unexplained attrition of 5 families, the lack of reporting of cluster coefficients and the differential in tissue use between the 2 arms which raises questions about the robustness of double-blinding. Particularly notable is the discussion on the low generalisability of results from the study from the placebo arm given that even the inert barrier of the tissues is a likely to have limited spread. Also the lengths to which the authors went to obtain allocation concealment and maintenance of double-blind conditions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“Treated and placebo tissues were randomly assigned ...” Sequence generation not reported
Allocation concealment (selection bias)	Low risk	“Treated and placebo tissues were randomly assigned by the sponsor to 296 partici-

Longini 1988 (Continued)

		pating households stratified by household size, such that roughly half the households would receive treated tissues. Thus, the investigators were unaware of the assignment of treated tissues.”
Blinking (performance bias and detection bias) All outcomes	Low risk	“The type of tissue was identified by code, and the boxes in which tissues were contained were not marked with any specific identifiers. Therefore, the study was double-blinded.”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	296 HH eligible. “The final sample used for analysis consisted of 143 households in the treatment group and 148 households in the placebo group.”
Selective reporting (reporting bias)	High risk	“The analysis of secondary spread was restricted to households of three to five members for technical reasons, which eliminated five households.” “The two groups were almost identical in composition.”

Luby 2005

Methods	Partly double-blind, cluster-randomised controlled trial carried out during 15 April 2002 to 5 April 2003 in Karachi, Pakistan. The trial assessed the effects of mother and child handwashing on the incidence of respiratory infections, impetigo (data not extracted) and diarrhoea (data not extracted) Randomisation took place by computer-generated random numbers in 3 phases: - 25 neighbourhoods were assigned to handwashing and 11 to standard practice - 300 households assigned to using antiseptic soap - 300 households assigned to using plain soap - 306 households assigned to standard practice - 1523 children younger than 15 years assigned to using antiseptic soap - 1640 children younger than 15 years assigned to using plain soap - 1528 children younger than 15 years assigned to standard practice Soaps were identical weight, colour and smell and were packed centrally with a coded packing case matched to households containing 96 bars. Neither field workers nor participants were aware of the content. Control arm households were visited with the same frequency as intervention household but were given books and pens. Codes were held centrally by the manufacturer and broken after the end of the trial to allow analysis
Participants	Householders of slums in Karachi. Of the 1523 children younger than 15 years assigned to using antiseptic soap 117 dropped out (1 died, 51 were born in and 65 aged out) = 1406; 504 were aged less than 5 Of 1640 children younger than 15 years assigned to using plain soap 117 dropped out (3 died, 44 were born in and 70 aged out) = 1523; 517 were aged less than 5

	1528 children younger then 15 years assigned to standard practice 125 dropped out (3 died, 40 were born in and 82 aged out) = 1403; 489 were aged less than 5	
Interventions	Instruction programme and antibacterial soap containing 1.2% triclocarban, or ordinary soap to be used throughout the day by householders or standard procedure	
Outcomes	Laboratory: N/A Effectiveness: - Number of new respiratory illness per person per week - Pneumonia (cough or difficulty in breathing with a respiratory rate of > 60 min in children less than 60 days old, > 50 min in those less than 1 year old and > 40 min for those aged 1 to 5 years) Follow up was weekly with household interview and direct observation. Children aged less than 5 were weighed and the report presents stratification of results by child weight Safety: N/A	
Notes	Risk of bias: low (cluster coefficients and analysis by unit of randomisation provided) Notes: the authors conclude that “handwashing” neighbourhoods has significantly less episodes of respiratory disease than controls (e.g. 50% less cough). “Handwashing” children aged less than 5 had 50% less episodes of pneumonia than controls (-65% to -35%). However there was no difference in respiratory illness between types of soap. The report is confusing, with a shifting focus between children age groups. The impression reading is of an often re-written manuscript. There is some loss of data (for example in the results by weight, i.e. risk group) because of lack of clarity on denominators. Despite this, the trial is a landmark	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation took place by computer-generated random numbers in 3 phases:
Allocation concealment (selection bias)	Low risk	“One of the investigators (SL) who did not participate in recruiting neighbourhoods or households programmed a spreadsheet to randomly generate the integers of a 1 or a 2. He applied the random numbers sequentially to the list of neighbourhoods. Neighbourhoods with a 1 were assigned to control, and those with a 2 were assigned to handwashing promotion. Random assignment continued until neighbourhoods consisted of at least 600 handwashing promotion households and 300 control households were assigned.”

Luby 2005 (Continued)

Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	89% of the study population followed up, but no data on the clusters
Selective reporting (reporting bias)	Low risk	"At baseline, households in the three intervention groups were similar."

Macartney 2000

Methods	Controlled before and after study with economic evaluation (data not extracted) carried out over 8 RSV seasons in 1988 to 1996. The study assessed the impact of a programme for the interruption of transmission of RSV in a children hospital in Philadelphia, USA. Analyses are presented both by risk group (exposure to patients by days of viral shedding) and as aggregate. Only for the latter numerators and denominators are provided, whereas for the former figures are presented in bar chart format
Participants	Children with community-acquired RSV infection and the inpatient children exposed to them (1604 in 4 seasons before and 2065 in the "after the intervention" seasons. Children were aged around 1 year and those with risk factors were equally spread (51% versus 54%) in the 2 periods
Interventions	Education with high index of suspicion for case-finding with barriers (but no goggles or masks) and handwashing for patients and staff with contact precautions for RSV + patients for 2 weeks with isolation (when possible) with cohorting of patients and staff with enhanced surveillance with restriction of visits with discouragement of staff with ARIs from working unprotected in SCBU
Outcomes	Laboratory: ELISA confirmation of RSV infection on all children admitted with respiratory symptoms. In a proportion of cases RSV culture was undertaken, although this had a minimal practical impact as any child with respiratory symptoms was considered as a RSV case Effectiveness: clinically-defined RSV cases contracted nosocomially (with symptoms appearing after at least 6 days from admission) Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that 10 RSV infections were prevented per season (RR for post-intervention compared to pre-intervention periods 0.61, 95% CI 0.53 to 0.69). The study is well-reported and the conclusions appear reasonable, but no information is given on the background rate of infection and the impact of the intervention on HCW morbidity is not analysed

Risk of bias

Macartney 2000 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

MacIntyre 2009

Methods	Prospective cluster-randomised trial carried out in Sydney, Australia, to assess the use of surgical masks, P2 masks and no masks in preventing influenza-like illness (ILI) in households. The study was carried out during the 2 winter seasons of 2006 and 2007 (August to the end of October 2006 and June to the end of October 2007). "Gaussian random effects were incorporated in the model to account for the natural clustering of persons in households"
Participants	290 adults from 145 families; 47 households (94 enrolled adults and 180 children) were randomised to the surgical mask group, 46 (92 enrolled adults and 172 children) to the P2 mask group, and 52 (104 enrolled adults and 192 children) to the no-mask (control) group
Interventions	Use of surgical masks and P2 mask versus no mask. The P2 mask is described as very cumbersome
Outcomes	Laboratory: serological evidence Effectiveness: Influenza-like illness (ILI) (described as fever, history of fever or feeling feverish in the past week, myalgia, arthralgia, sore throat, cough, sneezing, runny nose, nasal congestion, headache) However, a positive laboratory finding for influenza converts the ILI definition into one of influenza Safety:N/A
Notes	The authors conclude that adherence to mask use significantly reduced the risk for ILI-associated infection, but < 50% of participants wore masks most of the time. We concluded that household use of face masks is associated with low adherence and is ineffective for controlling seasonal respiratory disease. Compliance was by self-report - therefore likely to be an underestimate

The primary outcome was ILI or lab-positive illness. This showed no effect. Sensitivity analysis by adherence showed that under the assumption that the incubation period is equal to 1 day (the most probable value for the 2 most common viruses isolated, influenza (21) and rhinovirus (26)), adherent use of P2 or surgical masks significantly reduces the risk for ILI infection, with a hazard ratio equal to 0.26 (95% CI 0.09 to 0.77; $P = 0.015$). No other covariate was significant. Under the less likely assumption that the incubation period is equal to 2 days, the quantified effect of complying with P2 or surgical mask use remains strong, although borderline significant; hazard ratio was 0.32 (95% CI 0.11 to 0.98; $P = 0.046$). The study was underpowered to determine if there was a difference in efficacy between P2 and surgical masks (Table 5). The study conclusion appears to be a post-hoc data exploration. Regardless of this the study message is that respirator use in a family setting is unlikely to be effective as compliance is difficult unless there is a situation of real impending risk.		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participating households were randomised to 1 of 3 arms by a secure computerised randomisation process."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Study participants and trial staff were not blinded, as it is not technically possible to blind the mask type to which participants were randomised. However, laboratory staff were blinded to the arm of randomisation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	143 families of 145 randomised were analysed; 2 families in the control group were lost to follow up during the study. No reason was given for this
Selective reporting (reporting bias)	Low risk	No differences between groups at baseline

Madge 1992

Methods	Prospective cohort study conducted in 4 medical wards of the Royal Hospital for Sick Children in Glasgow, UK, to evaluate the effectiveness of 4 infection control procedures in preventing nosocomial infection with RSV. This is an interruption of transmission study. Every child up to 2, irrespective of clinical presentation, had respiratory secretions tested for RSV antigen within 18 hours of admission. Nosocomial infection was assumed if a child become RSV positive 7 days or more after admission. Children after discharge from hospital were not studied
Participants	No special precaution group 152 (winter 1); gowns/gloves 337 (winter 1 and 2); cohort nursing 265 (winter 1 and 2); cohort nursing and gowns/gloves 310 (winter 1 and 2); 1001 (winter 3)
Interventions	Stepwise intervention programmes: gowns/gloves; cohort nursing + gowns/gloves; cohort nursing, versus no special precautions. The procedures evaluated in the 2 winter periods were gowns/gloves; cohort nursing + gowns/gloves; cohort nursing, versus no special precautions. In the third year the most effective strategy was introduced into all ward areas and its efficacy in clinical practice was assessed. There was not separate area for managing children with infections
Outcomes	Laboratory: yes - culture, antibodies titres, serological studies Effectiveness: RSV infections (seroconversion within 7 days of admission) Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that combined with rapid laboratory diagnosis, cohort nursing and the wearing of gowns and gloves for all contacts with RSV-infected children can significantly reduce the risk of nosocomial RSV infection (odds reduced to between 1.27% to 75.6%). One confounding effect that was not accounted for in the study design was a possible "ward effect". For practical reasons, 2 wards (3 and 4) continued with the same policy over the first 2 years of the study. Since it was also necessary apply policies to whole wards there is a possibility that ward 4 might have been especially effective at implementing their assigned policy

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A

Madge 1992 (Continued)

Selective reporting (reporting bias)	Unclear risk	N/A
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Makris 2000

Methods	Prospective cohort study carried out in 8 private, freestanding long-term care facilities located in New Jersey and Delaware, to determine the impact of an ongoing infection control intervention programme in reducing the incidence of nosocomial infections. The 8 facilities were selected on the basis of similarity with respect to admission rate, size, acuity levels, availability of services, overall infection rates, in-house environmental service departments. Resident populations were comparable in terms of age, sex and underlying disease. The 8 facilities were grouped into 4 sets of matched pairs. Within each pair, each home was designated at random as either a test site or a control site. The results was that 4 facilities (2 urban and 2 suburban, with a total of 443 beds), were selected as test sites and another 4 facilities, 2 urban and 2 suburban, with a total of 447 beds, were selected as control sites
Participants	443 beds (patients) in the test group, 447 beds (patients) in the control group. We assumed number of beds as number of participants
Interventions	Infection-control education programme reinforcing handwashing and other hygienic measures versus normal care
Outcomes	Laboratory: no Effectiveness: upper respiratory infections Safety: N/A
Notes	Risk of bias: high (internal inconsistencies) Notes: the authors conclude that infection control education measures that reinforce handwashing and other hygienic measures helps reduce the number of organisms present on hands and surfaces and may have contributed to the non-significant reduction of URTIs (the opposite is reported in the paper: incidence density rate of 4.15/1000 patient days in the test homes versus 3.15/1000 patient days in the control homes) showed in this study. We assumed number of beds as number of participants to the study, but we do not know the characteristics of the patients (age, sex, underlying conditions, etc.). The authors confuse a cohort design with a before and after design and in the report they confusingly use both terms and reach conclusions not supported by the evidence presented

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A

Makris 2000 (Continued)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Master 1997

Methods	Prospective cohort study conducted in an elementary school, Detroit, to evaluate the effect of a mandatory scheduled handwashing programme on absenteeism due to acute communicable illness (including upper respiratory disease). Classrooms were divided into either control or experimental groups without formal randomisation. Six classrooms were assigned to the handwashing group and 8 classrooms were assigned to the control group. Data were collected for 37 school days. Information about absent children was recorded daily by the school secretary. Symptoms were used to classify students as having respiratory or gastrointestinal illness. Upper respiratory infections and gastrointestinal symptoms (data not extracted) were not considered mutually exclusive	
Participants	14 classrooms including 305 healthy, predominantly upper middle-class children ranging from ages 5 to 12. All grade levels from kindergarten through fifth grade were included. Six classrooms (143 students) were the handwashing group and 8 classrooms (162 students) were the control group	
Interventions	Handwashing programme versus usual practice. Children in the handwashing group were asked to wash their hands after arrival at school, before eating lunch, after lunch recess, and before going home. Children in the control group washed at their normal frequency. All children in both groups washed with the school soap, which was not antibacterial	
Outcomes	Laboratory: no Effectiveness: upper respiratory infections (URTI) - cough sneeze, pink eye, headache, mononucleosis, acute exacerbation of asthma, sinus trouble, fever alone, bronchitis Safety: N/A	
Notes	Risk of bias: high Notes: the authors conclude that handwashing among children can be effective in preventing transmission of disease, but the difference in days of absence is statistically significant only for gastrointestinal symptoms (RR for ARIs 0.79, P = 0.756). Limitations in the study design are: use of a discrete population without socio-economically diverse backgrounds, use of a single institution, lack of blind assessment, low specificity of symptoms, and lack of accurate symptom definition	
Risk of bias		
Bias	Authors' judgement	Support for judgement

Master 1997 (Continued)

Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Morton 2004

Methods	Cross-over study to evaluate the effectiveness of an alcohol gel as an adjunct to regular handwashing for decreasing absenteeism among elementary children by reducing specific communicable diseases such cold, flu and conjunctivitis. The study was conducted in an elementary school in New England, US. In the cross-over design classrooms in each grade level were randomised to begin as the experimental group (alcohol gel) or the control group (regular handwashing). A study protocol for hand hygiene was introduced following the germ unit education. The handwashing product was a soap and water alternative that is approximately 60% ethyl alcohol. In phase 1 (46 days) children in 9 classrooms were in the experimental group, and children in 8 classrooms were in the control group. After a 1 week washout period when no children had access to the alcohol gel, Phase 2 (47 days) started, and the classroom that had participated before as an experimental group passed in the control group and vice versa. Data were collected by the parents that informed the secretary or the school nurse of the reasons for a child's absence, including symptoms of any illness. Respiratory illnesses were defined by symptoms of URTI	
Participants	253 children, 120 girls and 133 boys, from kindergarten to 3rd grade. 32 children dropped out (10 due to skin irritation and 22 because of lack of parental consent)	
Interventions	Use of an alcohol gel as an adjunct to regular handwashing and educational programme versus regular handwashing and educational program	
Outcomes	Laboratory: no Effectiveness: days of absences from school for respiratory illness Safety: N/A	
Notes	Risk of bias: high (no description of randomisation; partial reporting of outcomes, numerators and denominators) Notes: the authors conclude that significantly fewer children became ill while using the alcohol gel as an adjunct to regular handwashing than when using regular handwashing only (decreased school absenteeism of 43% with the use of alcohol gel on top of handwashing). The authors also described, as a limitation of the study, the fact that the school	

Morton 2004 (Continued)

	nurse served as the data collector, and this could be perceived as bias in measurement of the outcome variable Randomisation and allocation are not described, there are no cluster coefficients reported and attrition is not taken into consideration during the analysis. Unit of randomisation and analysis are different. No reporting by arm. No ORs, no CIs reported	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Murphy 1981

Methods	Prospective cohort study carried out in the Children's Hospital, Denver, to examine the effect of using gowns, masks and handwashing on the acquisition of symptomatic respiratory infections by medical personnel caring for infants with respiratory disease
Participants	58 people of nursing, medical, respiratory therapy personnel; 30 in the handwashing group, 28 in the handwashing, masks and gowns. Seventy HCWs initially were available for enrolment, 9 refused to take part and 3 withdrew
Interventions	Handwashing versus handwashing, masks and gowns
Outcomes	Laboratory: yes Effectiveness: viral infections (including RSV) Safety: N/A
Notes	Risk of bias: medium Notes: the authors conclude that there was no difference between the 2 groups with respect to number of viral infections (i.e. 4/30 in the handwashing group versus 5/28 in the handwashing gown and masking group ($P > 0.20$). The findings cannot demonstrate any effect of adding the use of both gown and mask to the usual handwashing routine on the development of illness in personnel caring for infants with respiratory disease. Possible reasons for lack of effect are: the heavy exposure all adults have to respiratory viral illness in the community at large; poor compliance to the study protocol, modes of

Murphy 1981 (Continued)

	virus spread which would not be blocked by the use of mask and gown	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Niffenegger 1997

Methods	Prospective 2-centre cohort study assessing the effects of a handwashing programme in Indiana, USA. Two centres were enrolled for the August to December 1994 (21 weeks) study: a test and a control centre
Participants	Eight teachers and 26 children (aged 3 to 5) in the test group and 12 children and 8 teachers in the control group. According to the authors, age, experience gender and socioeconomic variables were equally distributed between the 2 groups, but data are not shown. No attrition is mentioned
Interventions	Three weekly cycles of teachings, handwashing routine encouragement for children, parents and staff and correct sneezing and coughing procedure. Follow up was weekly filling in of a teacher report. It is unclear from the text what happened in the control site, or indeed if they were fully aware of the project
Outcomes	Laboratory: N/A Effectiveness: colds and ARIs no better defined Safety: N/A
Notes	Risk of bias: high (wide range of incidence of infections) Notes: the authors conclude that during the first 11 weeks of the study the test centre had double the incidence of colds compared to the control centre this is explained by the author as caused by the influx of new children bringing in new viruses in the test centre. In the second period the reverse was true, explained as the stabilising of the population and the taking effect of the programme. The list of potential confounders and biases is countless. For example there is only a very cursory description of participants in both arms and the role of teachers especially in the control centre is not explained

Niffenegger 1997 (Continued)

The test group had significantly fewer colds than the control group ($P < 0.05$)		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Nishiura 2005

Methods	Case-control study carried out during the SARS outbreak (26 February 2003 to 28 April 2003) in Hanoi, Vietnam. The study aimed at assessing the relationship between SARS infection and behaviour. The study population was based at the Hanoi French Hospital (HFH) and followed the outbreak during 3 phases. The first phase (26 February to 4 March 2006) in which an index case and 9 suspected secondary cases were admitted/cared for. The second phase (8 March to 11 March 2003) in which outpatients were closed and staff no longer returned home as the outbreak spread and the third phase (11 March 2003 to 28 April 2003) in which the HFH was closed to all other than SARS cases who were isolated
Participants	Description of cases: 29 surviving people with laboratory confirmed SARS cases either admitted and retained or transferred to other hospitals. Nine cases did not take part (5 died, 1 refused and 3 had relocated). Twenty-eight were HCWs employees of the HFH and 1 a relative of a patient. Substantial exposure and behaviour were documented through observation and questionnaires Description of controls: 90 people aged > 20 who provided written consent with substantial SARS exposure, 57 of whom were HFH employees
Interventions	Handwashing before contact with SARS patient Handwashing after contact with SARS patient Masks Gloves Gowns All measures combined Analysis by epidemic stage is reported

Nishiura 2005 (Continued)

Outcomes	SARS infection	
Notes	Risk of bias: low Notes: the authors conclude that masks (OR 0.3, 95% CI 0.1 to 0.7) and gowns (OR 0.2, 95% CI 0.0 to 0.8) were significantly associated with protection during phase 1 but in Phase 2 masks (OR 0.1, 95% CI 0.0 to 0.3) and all measures (OR 0.1, 95% CI 0.0 to 0.3) were associated with protection probably because of the increased awareness of the danger of the outbreak and increase use of measures - this is confirmed by the results of the mathematical model in the second part of the study. A well-written and reported study	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Ou 2003

Methods	Retrospective cohort study carried out in selected precincts of Haidian district of Beijing, People's Republic of China between March and May 2003 during the epidemic of SARS (attack rate 19/100,000 population in the period March to July). Precincts were chosen on the basis of the highest number of quarantines. The study aimed at assessing the risk of acquiring SARS among quarantines. A better definition of the risk would help in future to identify better candidates for quarantine and target resources accordingly. The study was based on a questionnaire-based survey on the reasons for quarantine. SARS diagnosis for contacts was independently carried out from lists	
Participants	171 SARS cases (29% of total) were identified in the precincts and 1210 persons (23%) quarantined from the selected districts (contacts). These were sampled from a total population of 2.24 million, with 5.186 quarantines. Response rate was 85% (1.028 quarantines who completed the questionnaire, of which 232 developed probable SARS while in quarantine)	

Interventions	Quarantine at home or hospital for 14 days post-exposure (reduced to 10 and then to 3). Quarantine is defined as the separation and or restriction of movement of persons who due to recent exposure to a communicable disease risk acquiring the disease and transmitting to third parties. A contact was defined as: - Healthcare worker not using personal protective equipment (PPE) when caring for/ assessing a SARS case: - other persons caring for a SARS case - persons sharing accommodation with a SARS case - persons visiting a SARS case - persons working with a SARS case - classmates or teachers of a SARS case - persons sharing the same means of public transport with a SARS case All quarantined were followed up daily and were admitted to hospital if they developed fever (38 °C or more)	
Outcomes	Laboratory: no Effectiveness: definition of SARS was based on criteria of Chinese Ministry of Health. Definition was clinical and not based on laboratory isolation of the SARS-CoV Safety: N/A	
Notes	Risk of bias: high Notes: the authors conclude that only those quarantined who actually had home or hospital contact with a symptomatic SARS patient developed the illness (attack rate 31.1, 95% CI 20.2 to 44.4 for carers, 8.9%, 95% CI 2.9 to 22.1 for visitors, 4.6%, 95% CI 2.3 to 8.9 for those who lived with a SARS case) but not those living in the same building or working with them and not contacts of any SARS case during the incubation period. Fever was also not a good reason to quarantine people (attack rate nil) . Quarantine also appeared to prevent transmission, although there were numerous cases in which quarantine was not required. There are several limitations to the conclusion of the study Non-random basis for the sample, selection bias of the sample and responders, recall bias of responders and the absence of a laboratory-confirmed diagnosis may have affected the conclusion one way or another Overall, not enough denominator data, non-exposed data are given to allow data extraction or calculate OR	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A

Ou 2003 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Pang 2003

Methods	Ecological study describing and analysing the effects of public health measures on the SARS epidemic between 5 March and 29 May 2003 in Beijing, China. Data were collected from centralised notification and close contact databases
Participants	2521 probable SARS cases mostly hospitalised aged around 33 (407 or 16% were HCWs) and 192 of these who died out of a total population of 13.6 million people. The peak took place on 25 April with 173 hospitalised cases
Interventions	SARS was made notifiable on 9 April and contact tracing commenced a day later. On 18 April 62,363 of the estimated 85,000 Beijing HCWs received training in the management of SARS cases and were issued gowns, gloves, masks. By 17 April, 123 fever clinics were opened, however these were contiguous to hospitals and it is thought that some transmission occurred By 21 April quarantine of close contacts was underway (these were only allowed to leave quarantine in exceptional circumstances and only wearing a mask) and fever check at airports were begun the day after. By 24 April all schools and universities closed. Two days later public meeting places (bars, libraries etc) were closed. From 27 April all SARS cases were placed in designated hospital wards and by 8 May SARS cases were only sent to designated hospitals. By 1 May a SARS hospital of 1000 beds built in 1 week was opened and received only SARS cases (40% of total cases). The last cases were registered on 26 May. The highest attack rate (14.5%) of quarantined people was those of spouses of SARS cases
Outcomes	Laboratory: laboratory testing for the presence of SARS-CoV was not part of the case definition Effectiveness: probable SARS cases (close contact of a SARS sufferer with signs and symptoms of febrile respiratory disease and chest X-ray changes, or person visiting of residing in an area with recent SARS activity and with signs and symptoms of febrile respiratory disease and chest X-ray changes and lack of response to antibiotics or person visiting of residing in an area with recent SARS activity and with signs and symptoms of febrile respiratory disease and chest X-ray changes and normal or decreased WBC count) Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that in virtue of the shape of the epidemic curve it is likely that the combination of measures taken before the 25 April helped contain the spread of SARS. Although there may be alternative explanations this appears to be the most likely explanation of the facts. Hospitals were seen early on as sources of transmission of the SARS Co-V. The authors seem to doubt the direct effectiveness of entry port (for example, airports, stations, etc.) checks (12 cases identified out of over 13 million people

	screened). They think screening was more useful to keep away sick people	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Pelke 1994

Methods	Controlled before and after study conducted in a neonatal intensive care unit (NICU) of Kapiolani medical centre, Honolulu, Hawaii, to assess the effect of gowning on RSV and other infections, on traffic and handwashing patterns. Alternate 2-month gowning and no-gowning cycles were established in a 24-bed NICU for 8 months. One entire 4-month cycle was repeated to eliminate the potential for seasonal variables and outbreaks. All the people entering into the NICU (physicians, nursing staff, ward clerks, families and visitors) wore gowns. During the no-gowning periods nursing staff wore hospital-issued pantsuit, washed at home through ordinary methods and worn from home. Ward clerks, physicians, hospital staff, families and visitors wore street clothes without gowns. Throughout the entire 8-month period, there was the recommendation for all staff and visitors to enforce initial 2-minute hand-scrub. Nails were cleaned before scrubbing, and a minimum 15-second handwash between infants or equipment was expected. Surveillance cultures were done weekly on all patients. Without the knowledge of the NICU staff, a neonatal research nurse scheduled observations of traffic patterns, while ostensibly reviewing charts, to determine if a lack of gowning procedures encourage more traffic. Handwashing compliance was studied, again without staff awareness, by 30 minutes direct observation. Follow up of infection rates was planned through standard infection control surveillance
Participants	230 infants, aged 22 to 42 weeks, with birth a weight of 464 to 6195 grams. Overall there were 330 infants admitted to NICU during the study period. Thus 17% of participants had no RSV cultures taken. The reasons given are vague (transfer or death)
Interventions	Use of gowns and standard procedures (handwashing) versus standard procedures

Pelke 1994 (Continued)

Outcomes	Laboratory: serological evidence: yes Effectiveness: RSV infection Safety: N/A
Notes	Risk of bias: medium (17% loss to follow up) Notes: the authors conclude that gowning did not protect NICU infants from any type of infection or affect mortality (1.21 versus 1.38/100 patient-days of gowning and no-gowning periods respectively). Gowning procedures did not deter staff or visitors from entering the unit, since traffic was also unchanged between periods. Finally the results showed no change in handwashing patterns between periods. Besides the advantage of eliminating a potentially unnecessary ritual that may be perceived as a psychological barrier to families visiting their infants, other benefits to discontinuing gowning include saving staff time involved in various gowning procedures and costs. If gowns are eliminated, it is recommended to perform careful follow up. The study conclusions must be taken with caution given the likely selection bias introduced by the missing 17% of children

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Roberts 2000

Methods	Open cluster-RCT carried out between March and November 1996 (the southern hemisphere winter season) in 23 child care centres caring for a minimum of 50 children 10 hours a day, 5 days a week in Australia. The study assessed the effects of an Australian national handwashing programme compared to standard procedure. Randomisation was according to a random number table and cluster coefficients are reported
Participants	Children (299 in the intervention arm and 259 in the control arm) aged 3 or younger attending the centres at least 3 days a week. Attrition was 51 children in the intervention arm and 72 children in the control arm due mainly to staff leaving the centres

Roberts 2000 (Continued)

Interventions	Handwashing programme with training for staff and children. It is unclear whether any extra hand cleansing agents were used, as GloGerm (?) is mentioned when it was used in a preliminary study
Outcomes	Laboratory: N/A Effectiveness: ARI (runny nose, cough and blocked nose) Follow up was via a parental phone interview every 2 weeks Safety: N/A
Notes	Risk of bias: low (cluster coefficients and analysis by unit of randomisation) Notes: the authors conclude that although there was no overall decrease in respiratory illness (RR 0.95, 95% CI 0.89 to 1.01), in children up to 24 months the decrease was significant (RR 0.90, 95% CI 0.83 to 0.97). The authors speculated that this was because maximum benefits are likely from this age group because of their limited ability to wipe their nose and hands without a structured programme. Analyses by 3 compliance levels are also reported. A so-so reported and well-conducted trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was according to a random number table
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind the intervention
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Recruitment rate 88% (23 of 26 CCCs); loss to follow up not clear as no denominator given
Selective reporting (reporting bias)	Low risk	Centres comparable at baseline

Ryan 2001

Methods	Retrospective and prospective, controlled, before and after study carried out at the US Navy's Great Lakes recruit training centre in Illinois. Rates of respiratory disease were retrospectively calculated for recruits undergoing training for 3 periods: 1996, before the implementation of "Operation Stop Cough" and 1997 and 1998. To compare rates of respiratory illness with a similar community the authors also looked at the incidence of respiratory illness in a population of phase II sailors undergoing the second part of their training in the same camp. In addition a compliance questionnaire was also carried out during the latter 2 years of the study
Participants	Recruits undergoing training (44,797 in 1996; 47,300 in 1997; and 44,128 in 1998) mainly men, aged around 19 to 20 and a control population of phase II training sailors (no precise denominators given but around 10,000 yearly) who did not have a programme of handwashing
Interventions	Structured top-down programme of handwashing at least 5 times daily
Outcomes	Laboratory: N/A Effectiveness: respiratory illness detected from sick parade records and outgoing recruits questionnaire on a sample survey Safety: N/A
Notes	Risk of bias: low Notes: the authors conclude that implementation of the control programme has seen near-halving of incidence of ARIs (based on 3 stratified samples of recruits infrequent handwashers had more self-reported episodes of ARIs (4.7 versus 3.2 per recruit, OR 1.5, 95% CI 1.2 to 1.8) and reported more hospitalisations (OR 10.9, 95% CI 2.7 to 46.2). Despite dramatic results, implementation was and continues to be difficult

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Sandora 2005

Methods	Single-blind, cluster-randomised controlled trial carried around the Boston area, USA, in the period November 2002 to April 2003. The trial tested the effects of using a hand sanitiser and a programme of instruction on the transmissions of GI infections (data not extracted) and ARIs in families. Units of randomisation were childcare centres and were carried out on enrolment by an investigator using random block size generated by computer. Assignment was single-blind (i.e. investigator blinded to the status of the centre). Cluster correlation was 0.01
Participants	292 families with 1 or more children aged 6 months to 5 years who were in child care for 10 or more hours a week. There were 155 children in 14 centres allocated to the intervention arm and 137 children in 12 centres allocated to the control arm. The mean age was 3 to 2.7 years. Attrition was respectively 15 (3 lost to follow up and 12 who discontinued the intervention) and 19 (8 lost to follow up and 11 who discontinued the intervention). ITT analysis was carried out
Interventions	Alcohol-based hand sanitiser with bi-weekly hand hygiene educational materials over 5 months versus bi-weekly educational material on healthy diet
Outcomes	Effectiveness: ARI (2 of the following symptoms for 1 day or 1 of the following symptoms for 2 days: runny nose, cough, sneezing, stuffy or blocked nose, fever, sore throat). An illness episode had to be separated by 2 symptom-free days from a previous episode. A secondary illness was when it followed a similar illness in another family member by 2 to 7 days Follow up was by means of bi-weekly phone calls to care givers Safety: dry skin (71 reports), stinging (11 reports), bad smell (7 reports), dislike (2 reports), allergic reaction (2 reports), slippery feel (1 report) and irritation (20 reports)
Notes	Risk of bias: low Notes: the authors conclude that although the rate of GI illnesses was significantly lower in the intervention group, the incidence rate ratio - IRR was not significantly different for ARIs (0.97, 95% CI 0.72 to 1.30). Compliance and droplet route spread may account for this apparent lack of effect. A well-reported trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Random assignments were generated by computer using a permuted-blocks design with random block sizes."
Allocation concealment (selection bias)	Low risk	"Assignments were concealed in opaque envelopes, and centers were assigned to control or intervention groups by a study investigator as they were enrolled."
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not possible

Sandora 2005 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition was 15 in intervention arm (3 lost to follow up and 12 who discontinued the intervention) and 19 in the control arm (8 lost to follow up and 11 who discontinued the intervention). ITT analysis was carried out
Selective reporting (reporting bias)	Unclear risk	Well-reported

Sandora 2008

Methods	Cluster-randomised, controlled trial carried out in a single elementary school system located in Avon, Ohio, USA to assess the effectiveness of a multifactorial infection-control intervention, including alcohol-based hand sanitiser and surface disinfection, in reducing absenteeism caused by gastrointestinal and respiratory illnesses among elementary school students. The study also aimed to describe the viral and bacterial contamination of common surfaces in the school classroom and to assess the impact of an environmental disinfectant on the presence of selected viruses and bacteria on these surfaces. Clustering was described as "teams of 3-4 classes depending on the class year"
Participants	A total of 363 students in 15 different classrooms were eligible to participate and received letters about the study. A total of 285 of these students provided written informed consent and were randomly assigned to the intervention group (146) or to the control group (139). No students were lost to follow up or discontinued the intervention during the study period. Baseline demographic characteristics were similar in the intervention and control groups. Most families were white and non-Hispanic and in excellent or very good health at baseline
Interventions	Alcohol-based hand sanitiser to use at school and quaternary ammonium wipes to disinfect classroom surfaces daily for 8 weeks versus usual handwashing and cleaning practices
Outcomes	Laboratory: Serological evidence: no Swabs for bacteria and viruses from 3 types of classroom surfaces were taken Effectiveness: Respiratory illness defined as days absent as measured by a (blinded) school worker who routinely recorded reason for absenteeism either for gastrointestinal or respiratory causes Safety: N/A
Notes	The authors conclude that multifaceted intervention that included alcohol-based hand sanitiser use and disinfection of common classroom surfaces reduced absenteeism from gastrointestinal illness among elementary school students. The intervention did not impact on absenteeism from respiratory illness. In addition, norovirus was detected less frequently on classroom surfaces in the group receiving the intervention. The study is good quality with low risk of bias. The authors checked compliance by counting discarded wipes. Reasons given for the apparent lack of effect against ARIs but good

Sandora 2008 (Continued)

	effect on GI illness are that disinfecting the classroom surfaces (daily at lunchtime with alkali) was important - as well as the alcohol wipes. The authors measured the norovirus concentration on surfaces and found this reduced. Other reasons may be that droplets are not affected by this method or that contamination of hands by respiratory infections is likely to be continuous (in orofaecal transmission is mostly at the time of defecation)	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“The allocation sequence was generated by computer ...”
Allocation concealment (selection bias)	Unclear risk	“...and teams were assigned to study groups by a study investigator (Dr Shih).” Blinding of allocation cannot be guaranteed
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	No students were lost to follow up or discontinued the intervention during the study period
Selective reporting (reporting bias)	Unclear risk	Well-reported

Satomura 2005

Methods	Randomised controlled trial, randomisation was achieved by simple computer-generated random digit. Allocation was concealed using sealed opaque envelopes. Not clear if there was a central randomisation centre. Post hoc exchange of envelopes was prevented by writing both the name of each subject and the number on the envelope he/she drew before breaking the seal. Participants were not blinded to the intervention, however, disease incidence was determined by 1 study physician who was not informed of the results of assignment. Analysis was done based on the intention-to-treat principle. The study targeted community healthcare all over Japan and was conducted between December 2002 and March 2003 for a follow-up period of 60 days	
Participants	Three hundred and eighty-seven participants at 18 sites were recruited. Included in the analysis 384, follow up was completed on 338 participants. Attrition was fully explained for URTI analysis, however, 2 subjects were not accounted for in the ILI analysis. Forty-six participants did not complete the follow up due to either discontinuation of diary use (n = 9) or contracting influenza-like illness (ILI) (n = 37) Of the 37 participants with ILI, 11 were in povidone-iodine group, 12 in water group and 14 in control. Analysis was performed on 35 participants (Kitamura 2007)	

Interventions	Participants were randomised to 1 of the following: water gargling, n = 122 (20 mL of water for about 15 seconds 3 times consecutively, at least 3 times a day); povidone-iodine gargling, n = 133 (20 mL of 15 to 30 times diluted 7% povidone-iodine (as indicated by the manufacturer) in the same way as water gargling); and control, n = 132 (retain their previous gargling habits) All groups were asked to fill a daily gargling diary (standardised form to record: gargling habits, handwashing and influenza complaints) The frequency of gargling in the water group was higher (3.6), frequency of handwashing was similar between the 3 groups URTI symptom was classified according to Jackson methods. Diary recording was continued throughout the follow-up period and for 1 week after the onset of URTI. ILI were reported separately
Outcomes	Laboratory: none Effectiveness: primary outcome: incidence of first URTI. Index cases were defined as all of the following conditions: (1) both nasal and pharyngeal symptoms, (2) severity of at least 1 symptom increased by 2 grades or more, and (3) worsening of a symptom of 1 increment or more for > 3 days Secondary outcome: severity of URTI of the incident cases was assessed by grading each symptom during the initial 7 days after the onset of URTI in numeric scores: none = 0, mild = 1, moderate = 2 and severe = 3 ILI was defined as both developing a fever of 38 °C or higher, and worsening arthralgia in addition to some respiratory symptoms (Kitamura 2007) Safety: no harm was reported. However, 2 patients in the povidone group switched to water gargling (analysed in their assignment group)
Notes	The authors conclude that simple water gargling is effective to prevent URTIs among healthy people. However, no significant difference was observed against ILIs Study was well-conducted, blinding would have added to the validity of the results. In addition, the study was not powered enough to detect significant preventative effect against ILI The study demonstrated that in addition to handwashing, simple gargling even with simple water can reduce URTI but not ILI. However, during periods of endemic influenza, multiple inexpensive and simple modalities (handwashing, masks, gargling) can be utilised together to reduce infection and transmission. Overall, the reporting of the 2 combined studies together is highly confusing. In the first study (Satomura 2005) the main outcome is URTI defined as fever and arthralgia. The second study (which is a presentation of further data from the 2005 publication in the guise of a short report) introduces the outcome ILI with a definition similar to that of URTI in the first study but referring to the earlier outcome as common cold. Also of note is reporting of significance without confidence intervals. Overall this potentially important study should be repeated with a larger denominator Medium risk of bias because of confused reporting and absence of double-blinding
<i>Risk of bias</i>	

Satomura 2005 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Group assignment was based on simple computer-generated random digits..."
Allocation concealment (selection bias)	Low risk	"By an individual drawing of sealed opaque envelopes, subjects were randomly assigned to the following three groups" "allocation was completely concealed from study administrators"
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	338 of 385 randomised followed up; reasons reported
Selective reporting (reporting bias)	Unclear risk	Confusing reporting

Seto 2003

Methods	Case-control study Hong Kong, China, conducted during the period 15 March to 24 March 2003 in 5 hospitals. The study aims were to assess the effectiveness of protective procedures for contracting SARS in HCWs exposed to 11 index cases in 3 of the 5 hospitals during the SARS epidemic
Participants	Description of cases: 13 HCWs infected with confirmed SARS within 2 to 7 days of exposure with no community exposure, 4 males and 9 females 2 doctors, 6 nurses, 4 healthcare assistants and 1 domestic staff who came into contact with SARS index cases. Only one used no protection measures and all omitted at least one of the protective measures required (handwashing, masks, gloves, gowns). Cases were identified through notification, which has been active since early February A SARS cases was defined as having fever of 38 °C or more, radiological infiltrates, and 2 of either: new cough, malaise, signs of consolidation Description of controls: 241 staff from the 5 hospitals who were not infected. The authors report that use of measures was elicited using questionnaires, 365 of which were returned (85% response rate). Non-responders were likely to be on leave or night shift. Data for 102 staff were excluded because they had no exposure to SARS
Interventions	Exposure was defined as coming within 0 to 91 metres (3 feet) of an index case with SARS symptoms when providing care. Recommended measures were handwashing, masks, gloves and gowns
Outcomes	SARS

Seto 2003 (Continued)

Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that the 69 staff reporting use of all 4 measures were not infected, whereas all infected staff had omitted at least one measure. Simple analysis showed that masks, gowns and handwashing (OR 5, 95% CI 1 to 19) were effective but only masks (OR 13, 95% CI 3 to 60) were significant at logistic regression, possibly through lack of power. No blind assessment of cases and control data was carried out and 15% attrition of questionnaires may have introduced bias. The study was published as research letter in the Lancet, so possible lack of space may have affected reporting clarity
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Simon 2006

Methods	Prospective cohort surveillance study conducted in the University Children's Hospital in Bonn, Germany, to assess the global efficacy of a complex intervention programme to contain nosocomial transmission of RSV infections. This is a before-after design, with a multifactorial intervention carried out in one hospital
Participants	6548 paediatric patients admitted at the University Children's Hospital in the period of study (2200 in 1999 to 2000; 2298 in 2000 to 2001; 1959 in 2001 to 2002). 283 RSV infections were documented in 278 hospitalised paediatric patients: 138 in 1999 to 2000, 89 in 2000 to 2001, 56 in 2001 to 2002. Of the general population 244 events were ambulatory RSV infections and 39 nosocomial RSV infections
Interventions	Intervention strategy aimed at increasing vigilance to identify and isolate RSV-infected patients together with enforced contact precautions versus standard procedures. Interventions are not described very well: vigilance + cohorting versus vigilance versus standard practice
Outcomes	Laboratory: All RSV infections were confirmed by antigen detection or cell culture using MS cells

Simon 2006 (Continued)

	Effectiveness: RSV infections no better defined clinically
	Safety: N/A
Notes	Risk of bias: low The authors conclude that the multi-factorial prevention strategy (early diagnosis, a strict cohorting and contact isolation policy, and prospective surveillance) probably contributed significantly to the reduced risk of nosocomial RSV infections in the hospital. In the pre-intervention period there were 39 cases (13.8%) nosocomial infections with an incidence density of 0.99/1000 patient-days; following the introduction of the surveillance and prevention policy there was a 9-fold decrease of the incidence (1.67 versus 0.18/1000 patient-days)
<i>Risk of bias</i>	
Bias	Authors' judgement Support for judgement
Random sequence generation (selection bias)	Unclear risk N/A
Allocation concealment (selection bias)	Unclear risk N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk N/A
Selective reporting (reporting bias)	Unclear risk N/A

Snydman 1988

Methods	Controlled before and after study conducted during the winters of 1983-84 (retrospectively), 1984 to 1985 and 1985 to 1986 (prospectively) to assess whether the introduction of infection control measures halted transmission of RSV in a special nursery in Boston, USA. Record review for the retrospective part and prospective study for the 2 seasons following the introduction of infection control measures
Participants	HCW and patients in the special care baby unit
Interventions	From the 1984 to 1985 season the following were introduced: Active surveillance Extensive cohorting of patients and staff Respiratory precautions on suspicion of respiratory case Gown, mask and gloves used on contact

Snydman 1988 (Continued)

	Restricted visiting policy Segregation of cases	
Outcomes	Laboratory: RSV culture Effectiveness: RSV cases with symptoms and laboratory confirmation Safety: N/A	
Notes	Risk of bias: high Notes: the authors conclude that there were 7 cases in the season “before” and no cases in the following seasons (no transmission per 1000 patient days in the post-intervention period compared 8 per 1000 patient-days in the pre-intervention period). No denominators are provided (hence no data can be extracted) and exposure is generically quantified by aggregate patient-days of exposure. It is unclear how the circulation of RSV outside related to the claimed success of the measures, as no information is provided	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Somogyi 2004

Methods	Prospective cohort study of 9 observations (3 each when using 3 different masks). The authors observed and photographed droplet dispersal while a volunteer breathed out 3 times in 3 different types of mask
Participants	1 volunteer
Interventions	Three masks, 2 without air filter and allowing external exhalation, 1 with manifold and air filter
Outcomes	Effectiveness: plume of droplets as observed and photographed: masks were poor at preventing droplet spread

Somogyi 2004 (Continued)

Notes	Risk of bias: low Notes: the authors conclude that the mask with manifold and air filter did not allow dispersal of droplets and was far safer in an epidemic such as SARS to contain the spread. Simple, safe and effective study	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Teleman 2004

Methods	Case-control study assessing risk and protective factors in HCWs during the SARS outbreak in Singapore (1 to 22 March 2003)
Participants	Description of cases: 36 HCWs admitted with probable SARS (according to WHO definition) during 1 to 31 March 2003. Six others were too ill to speak and 2 others died Description of controls: 50 HCWs working on the same wards who had definite exposure to SARS (physical proximity of 1 metre or less of a patient subsequently diagnosed as having SARS) but did not develop SARS
Interventions	Data on personal details and symptoms and exposure were gathered via a closed phone questionnaire. The 2 groups were comparable for demographic and epidemiological characteristics except that non-Chinese ethnic groups were twice as common among controls The following risk factors were assessed: - Distance from source of infection < 1 metre - Duration of exposure 60 or more minutes - Wearing N95 respirator - Wearing gloves - Wearing gown - Touched patients - Touched patients' personal belongings - Contact with respiratory secretions - Performed venepuncture

	Performed or assisted in intubation Performed suction of body fluids Administered oxygen Handwashing after each patient	
Outcomes	SARS	
Notes	Risk of bias: low Notes: the authors conclude that 3 factors were associated with significant risks or protection: Wearing N95 respirator OR 0.1 (95% CI 0.02 to 0.86) Contact with respiratory secretions OR 21.8 (95% CI 1.7 to 274.8) Handwashing after each patient OR 0.07 (95% CI 0.008 to 0.66) A well-reported study, let down by the failure to indicate whether assessment of risk factors had been carried out blindly to cases or control status. We wonder how much of the non-significance for certain factors is due to lack of statistical power	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Methods	Double-blind randomised controlled trial conducted by Hill Top Research, Inc. Winnipeg, Canada, to assess the efficacy of acids with virucidal activity for the inactivation of virus and prevention of experimental rhinovirus colds. Subjects in good health, aged 18 to 60, were recruited from Winnipeg and surrounding communities for participation. Qualified subjects were randomised to treatment with vehicle (62% ethanol, 1% ammonium lauryl sulfate and 1% Klucel), vehicle containing 3.5% salicylic acid or vehicle containing 1% salicylic acid and 3.5% pyroglutamic acid. The volunteers' hands were disinfected and then test product was applied to both hands of each subject. Fifteen minutes after application, the fingerprints of each hand were contaminated with Rhinovirus type 39. The volunteers touched conjunctiva and the nasal mucosa only with the right hand. Viral contamination of the fingers was assessed in the left hands of the volunteers, and viral infection was assessed by culture of nasal lavage specimens and blood samples	
Participants	85 volunteers, 31 control group, 27 used vehicle with 3.5% salicylic acid, 27 used vehicle with 1% salicylic acid and 3.5% pyroglutamic acid	
Interventions	Use of salicylic acid versus salicylic acid and pyroglutamic acid versus “placebo” substance	
Outcomes	Laboratory: yes Effectiveness: rhinovirus type 39 infection Safety: N/A	
Notes	Risk of bias: unclear (no description of randomisation process, concealment or allocation) Notes: the authors concluded that organic acids commonly used in over-the-counter skin care and cosmetic products have substantial virucidal activity against rhinovirus. These preparations provided effective residual antiviral activity on the hands. The virucidal effect of these hand treatments resulted in a reduction in the incidence of rhinovirus infection in the treated volunteers (P = 0.025). The utility of this observation in the natural setting remains to be determined. The volunteers were not allowed to use their hands in the interval between the hand treatment and the virus challenge, so the effect of normal use of the hands on the virucidal activity of these organic acids is not known. Similarly, the virus challenge method used in these experiments may not simulate the natural setting in all aspects. The effect of nasal secretions that would be transferred with the virus in the natural setting on the activity of the acids or on the transmission of virus was not tested in the model We are unsure as to the practical significance of this study and the generalisability of its results to the real world. Poorly-reported study	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“randomised” Sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not reported

Turner 2004a (Continued)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	“double blind” but no description
Incomplete outcome data (attrition bias) All outcomes	Low risk	All accounted for (short study)
Selective reporting (reporting bias)	High risk	Poorly reported

Turner 2004b

Methods	Double-blind, randomised controlled trial conducted by Hill Top Research, Inc. Winnipeg, Canada, to assess the residual virucidal activity of a skin cleanser wipe and its effectiveness in preventing experimental rhinovirus colds. Subjects in good health and from 18 to 60 were recruited from Winnipeg and surrounding communities for participation The residual activity of a skin cleanser wipe containing 4% pyroglutamic acid formulated with 0.1% benzalkonium chloride was tested. The negative control treatment was 62% ethanol. Benzalkonium chloride had been previously tested and was found to have no virucidal activity. Volunteers were randomly assigned to use the control preparation or the active preparation. The study material was applied to hands with a towelette. Fifteen minutes later, when the fingers were completely dry, the fingertips of each hand of the control subjects and the volunteers in the active treatment group were contaminated with rhinovirus type 39. An additional volunteer in the active group were challenged with virus 1 hour after application and the final group of volunteers was challenged 3 hours after application. Viral infection was assessed by culture of nasal lavage specimens and blood samples	
Participants	122 volunteers, 30 control group, 92 active group (30 tested after 15 minutes, 30 after 1 hour, 32 after 2 hours)	
Interventions	Use of a skin cleanser wipe containing 4% pyroglutamic acid formulated with 0.1% benzalkonium chloride versus skin cleanser wipe containing ethanol	
Outcomes	Laboratory: yes Effectiveness: rhinovirus type 39 infection Safety: N/A	
Notes	Risk of bias: unclear (no description of randomisation process, concealment or allocation)	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“randomised” Sequence generation not described

Turner 2004b (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	“double blind” but no description given
Incomplete outcome data (attrition bias) All outcomes	Low risk	All accounted for (short study)
Selective reporting (reporting bias)	High risk	Poorly reported

Wang 2007

Methods	Prospective cohort, surveillance study carried out to identify risk factors for development of SARS among quarantined persons in Taiwan. Two types of quarantine were implemented during the SARS outbreak in Taiwan: level A and level B quarantine. Level A quarantine was designed for persons who had known and, at times, had close exposure to persons infected with SARS in healthcare facilities and other community and domestic areas. Level B quarantine was designed for travellers who sat on the same flight within 3 rows of a person infected with SARS or were returning from World Health Organization-designated SARS-affected areas	
Participants	During the study period 52,255 persons were placed under level A quarantine and 95,271 persons were placed under level B quarantine	
Interventions	Exposure to level A quarantine versus level B	
Outcomes	Laboratory: Serological evidence: yes Effectiveness: SARS (definition not reported) Safety: N/A	
Notes	The authors conclude that focusing quarantine efforts on persons with known or suspected exposure can greatly decrease the number of persons placed under quarantine, without substantially compromising its yield and effectiveness. This is an important study, as it implies that risk banding can increase effectiveness and efficiency of quarantine procedures. The risk of bias is high as most of the answers to the NOS items are clearly no, however it is very difficult to get answers to a question such as the effectiveness of quarantine using any other design	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Wang 2007 (Continued)

Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

White 2001

Methods	Double-blind, placebo-controlled, cluster-randomised trial that took place in 3 schools in California during March to April 1999. The study assessed the incremental value of using an alcohol hand rub together with water and soap handwashing. Both arms had been given an educational programme starting 2 weeks prior to the beginning of the trial. Randomisation was by classroom and the placebo hand rub was indistinguishable from the active ingredient. Details of randomisation are not given
Participants	Of the 72 classes originally recruited, lack of compliance (use of supplementary product at least 3 times a day), reduced the classes to 32 (16 in both arms) with 769 participants aged 5 to 12
Interventions	Pump-activated antiseptic hand rub with benzalkonium chloride (SAB) (Woodward Laboratories) or inert placebo that “virtually” looked the same in batches of 4 colour-coded bottles containing both. School staff, parents and participants were blinded
Outcomes	Laboratory: testing of virucidal and bactericidal activity of the active compound Effectiveness: ARI (cough, sneezing, sinus trouble, bronchitis, fever, red eye, headache, mononucleosis, acute exacerbations of asthma) Gastrointestinal and other illnesses (data not extracted) Follow up and observation was carried out by classroom staff and illnesses were described by parents Safety: 7 students dropped out because of mild sensitivity to the rub
Notes	Risk of bias: high (no description of randomisation; partial reporting of outcomes, numerators and denominators) Notes: the authors conclude that addition of the rub led to a 30% to 38% decrease of illness and absenteeism (RR for illness absence incidence 0.69, RR for absence duration 0.71). Very high attrition, unclear randomisation procedure, educational programme and use of placebo hand rub make generalisability of the results debatable. No confidence intervals reported

Risk of bias

White 2001 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised trial", but sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blind, placebo-controlled, cluster-randomised trial. Randomisation was by classroom and the placebo hand rub was indistinguishable from the active ingredient
Incomplete outcome data (attrition bias) All outcomes	High risk	Partial reporting of outcomes, numerators and denominators
Selective reporting (reporting bias)	High risk	Poor reporting

White 2003

Methods	Prospective, open, cohort study carried out at the University of Colorado, Boulder campus during 8 weeks in the autumn-winter of 2002. The study aimed at assessing the effects of hand hygiene on URTIs and absenteeism. Allocation was by residence hall with 2 halls doing “knowledge studies” being allocated, one to each arm	
Participants	430 students aged around 18 mainly females were recruited but only 188 in the intervention cluster and 203 in the control cluster completed at least 3 weeks’ follow up. Students were recruited with cash incentives. No reasons for attrition are given	
Interventions	Education programme and alcohol gel adjunct to handwashing in residence halls versus standard hygiene	
Outcomes	Laboratory: in vitro testing of the antibacterial and antiviral properties of the hand rub Effectiveness: URTI (at least 2 symptoms with one of them lasting at least 2 to 3 days. List of symptoms as follows: sore throat, stuffy nose, ear pain, painful/swollen neck, cough, chest congestion, sinus pain, fever, working days lost). Weekly surveys were carried out before during and after the study Safety: N/A	
Notes	Risk of bias: medium Notes: the authors conclude that the intervention resulted in significantly fewer symptoms (reductions of 14.8% to 39.9 %) and absenteeism (40% reduction). Unexplained attrition and unknown effect of cash incentives. Relatively unclear definition of illness with a hint of a sensitivity analysis in the footer to a table	
Risk of bias		
Bias	Authors’ judgement	Support for judgement

White 2003 (Continued)

Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Wu 2004

Methods	Case-control study carried out on the Beijing SARS outbreak to assess the reasons for the insurgence of SARS cases in people who had no apparent contact with a SARS case
Participants	Description of cases: 94 probable or suspected SARS cases (Ministry of Health of China definitions) hospitalised during the period 28 April 2003 to 9 June 2003, aged 14 or more and non-HCWs with no known or reported no close contact with probably or suspected SARS cases. Fifty percent of cases were males with a median age of 29 years. The definition changed after 3 May to include those with symptoms who travelled to or resided in areas with known recent SARS activity but did not necessarily have contact with an index case. No laboratory confirmation of SARS was included in the definition which was purely practical (i.e. clinical-anamnestic). However antibody titres were taken several weeks after symptoms had abated. Close contacts (which played a part in the earlier case definition) were defined as persons who shared utensils, meals, residence hospital room or transportation vehicle with a suspected SARS or those who visited or came into contact with body fluids up to 14 days prior to the development of the index case's symptoms. Cases and controls were interviewed during the period 3 to 16 June Description of controls: 281 controls selected each by telephone random number change of last digits of the cases' phone numbers. This was aimed at providing neighbouring matching. Controls were interviewed by 4 July 2003 Seven controls (2 matched sets) were excluded because they were aged less than 14 and 7 matched sets were excluded because the case was reclassified as a HCW Cases and controls were interviewed for the 2 weeks preceding symptoms
Interventions	Always wearing a mask Intermittently wearing a mask Washing hands Owning a pet Visiting a farmer's market Visited clinics, eaten out or taken taxis
Outcomes	SARS

Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that cases were more likely than controls to have chronic pathologies (OR 4.1, 95% CI 1.8 to 9.3) or have visited fever clinics (OR 13.4, 95% CI 3.8 to 46.7), eaten out (OR 2.3, 95% CI 1.2 to 4.5) or taken taxis more than once a week (OR 3.2, 95% CI 1.3 to 8.0). In other words, unrecognised sources of transmission were present in the community. Always wearing a mask use was strongly protective (70% reduction in risk OR 0.3, 95% CI 0.2 to 0.7) and even wearing one intermittently with a smaller significant reduction in risk (OR 0.5, 95% CI 0.2 to 0.9) and so was always washing hands after returning home (OR 0.3, 95% CI 0.2 to 0.7) and owning a pet (OR 0.4, 95% CI 0.2 to 0.9) and visiting a farmer's market (OR 0.4, 95% CI 0.2 to 0.8). Of great interest is the role of fever clinics in spreading the disease, probably because of poorly-implemented isolation and triage procedures. A fascinating study
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Yen 2006

Methods	Prospective cohort study performed in a 67-bed military hospital in Taiwan to assess the effectiveness of the integrated infection control strategy by comparing the rate of SARS transmission in HCWs in the study hospital with that in other major hospitals in Taiwan without the integrated infection control strategy
Participants	Healthcare workers (HCWs) of a 67-bed military hospital, that was the study hospital. Eighty-six hospitals were used as comparison hospitals with a total of 746 negative pressure isolation rooms (NPIR beds), caring for SARS patients without the integrated infection control strategy. All HCWs in this group were trained before the SARS epidemic in Taiwan through a national regulation for a standard nosocomial infection control programme, with infectious diseases physicians/infection control nurses available in each regional and tertiary hospital

Yen 2006 (Continued)

Interventions	Integrated infection control strategy (consisting of patient traffic into hospital, zone of risks and extensive installation of alcohol dispensers for glove-on hand-rubbing) versus standard nosocomial infection control programme
Outcomes	Serological evidence: yes Effectiveness: SARS (definition?) Safety: N/A
Notes	Risk of bias: high The authors conclude that the integrated infection control strategy appeared to be effective in reducing the incidence of HCWs contracting SARS. Point estimates? 95% CIs. The advantages included rapid implementation without negative pressure isolation rooms, flexibility to transfer patients, and re-enforcement for HCWs to comply with infection control procedures, especially handwashing. The efficacy and low cost are major advantages, especially in countries with large populations at risk and fewer economic resources

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

Yin 2004

Methods	Case-control study carried out in 10 hospitals of Guangdong province, China, comparing the rate of usage of protective measures in HCWs with SARS and without SARS. The rate of exposure to SARS between 2 groups was similar. The data were obtained by questionnaire. Limited information is available from the abstract and from partial translation of the original text in Chinese
Participants	Description of cases: 77 HCWs who had contracted SARS Description of controls: 180 HCWs who had not contracted SARS Both cases and controls had been working in isolation units and took part in delivering

	first aid and caring for SARS patients. No significant differences were noted between cases and controls for a series of variables	
Interventions	Mouth mask Thick mouth mask (more than 12 layers of cloths) Use one-off paper mouth mask Never use mouth mask Wear eye mask if necessary Protecting for nose and eyes mucosa Wear shoe gloves Wear barrier gown Wear hand gloves Rinse out mouth Take bath and change clothes before home Check mouth mask Intake oseltamivir phosphate orally Never eating and smoking in the ward Handwashing and disinfection Using nose clamp Intake herbal Banlangen (Indigowoad Root) orally	
Outcomes	SARS	
Notes	Risk of bias: medium (inconsistencies in the text: lack of description of controls) Notes: the authors conclude that the combination of mouth mask, barrier gown, gloves, goggles, footwear, rinse out mouth and take bath and change clothes before provided significant protection and that there was a dose-response relation with the more inter-ventions used in combination the better the protection. Single measures such as wearing of a mask (OR 0.78, 95% CI 0.60 to 0.99), goggles (OR 0.20, 95% CI 0.10 to 0.41) and footwear (OR, 0.58 95% CI 0.39 to 0.86) were effective Limited information is available from the abstract and from partial translation of the original text in Chinese	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A
Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A

Yin 2004 (Continued)

Selective reporting (reporting bias)	Unclear risk	N/A
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Yu 2007

Methods	Case-control study to analyse the risk factors associated with nosocomial outbreaks of SARS in hospital wards in Guangzhou and Hong Kong, China. The study was designed with the individual hospital wards as the units for data collection and analysis. Case wards were hospital wards in which super spreading events of SARS occurred, and control wards were hospital wards in which patient(s) with SARS were admitted, but no super spreading events occurred. A super spreading event is defined as the development of ≥ 3 new cases of SARS in a ward during the period from 2 to 10 days after the admission of an identifiable index patient or as the development of a cluster of ≥ 3 new cases of SARS in a ward during a period of 8 days but without any known sources of SARS
Participants	Eighty-six wards in 21 hospitals in Guangzhou and 38 wards in 5 hospitals in Hong Kong were included in the study. One ward in Guangzhou and 2 wards in Hong Kong did not participate and they were excluded from the analysis
Interventions	Information related to 2 factors was collected: (1) environmental and administrative factors and (2) host factors. Environmental and administrative factors included physical factors, procedural or situational factors, and administrative factors pertaining to each ward. Host factors included symptoms, severity or dependency (for activities of daily living and behaviour changes), treatment or intervention, and comorbidity of the identified index patient in a case ward or in the first patient with SARS admitted in a control ward
Outcomes	Laboratory: serological evidence: no Effectiveness: SARS (no definition) Safety: N/A
Notes	The authors conclude that environmental risk factors were significantly associated with the occurrence of a super spreading event (clustering of ≥ 3 cases) included minimum distance between beds of ≤ 1 m and performance of resuscitation in the ward. Use of BIPAP ventilation and use of oxygen were the significant risk factors associated with the host patient. Of the administrative factors, allowing staff with symptoms to work also increased the risk. Providing adequate washing or changing facilities for staff was protective As disaggregate data are not reported we did not extract numerator/denominator data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	N/A

Allocation concealment (selection bias)	Unclear risk	N/A
Blinding (performance bias and detection bias) All outcomes	Unclear risk	N/A
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	N/A
Selective reporting (reporting bias)	Unclear risk	N/A

AEs: adverse events

AFH: Armed Forces Hospital

ARI: acute respiratory infection

ASR: adverse skin reactions

A&E: accident and emergency

BIPAP: Bilevel Positive Airway Pressure

CCC: Child Care Centre

CI: confidence intervals

CDC: Centers for Disease Control and Prevention

CMF: citric acid; malic acid; sodium lauryl sulfate (a virucidal mixture added to tissue paper)

CoV: coronavirus

C-RCT: cluster-randomised controlled trial

CXR: chest X-ray

DCC: daycare centre

FRI: febrile respiratory illness

GI: gastro-intestinal

HCW: healthcare worker

HFH: Hanoi French Hospital

HH: hand hygiene

HR: high risk

ICU: intensive care unit

ILI: influenza-like illness

IRR: incident rate ratio

ITT: intention-to-treat

LRTI: lower respiratory tract infection

m: metre

MCU: medical convalescent unit

MDCK: Madin Darby canine kidney cell line

MS: monkey-derived cell line

N/A: not applicable

NICU: neonatal intensive care unit

NOS: Newcastle-Ottawa Scales

NTS: National Skin Centre

OR: odds ratio

PCR: polymerase chain reaction

PCU: physical conditioning unit

PPE: personal protective equipment

RCT: randomised controlled trial
 RDS: respiratory distress syndrome
 RR: risk ratio
 RTI: respiratory tract infection
 RT-PCR: reverse-transcriptase polymerase chain reaction
 RSV: respiratory syncytial virus
 SAB: surfactant, allantoin and benzalkonium chloride
 SARS: severe acute respiratory syndrome
 SD: standard deviation
 SOPs: standard operating procedures
 S/S: signs/symptoms
 SOB: shortness of breath
 SCBU: special care baby unit
 UHR-I: ultra high-risk infection
 UHR-S: ultra high-risk SARS
 URTI: upper respiratory tract infection
 WBC: white blood cell
 WHO: World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abou El Hassan 2004	Topic completely extraneous
Amirav 2005	Randomised controlled trial of aerosol treatment
Anderson 2004	Mathematical model with interesting discussion of interaction between public health measures
Anonymous 2002	News item
Anonymous 2003	No data presented
Anonymous 2004	News item
Anonymous 2005a	News item
Anonymous 2005b	News item
Anonymous 2005c	News item
Apisarnthanarak 2009	Intervention bundle not broken down
Apisarnthanarak 2010	Participants took antivirals
Aragon 2005	Descriptive paper (non-comparative). Has no viral outcomes

(Continued)

Barros 1999	Correlational study between incidence of upper respiratory tract infection (URTI) and factors such as overcrowding
Bauer 2009	Historical comparison with RSV gammaglobulin among interventions
Bell 2004	Has unpublished entry exit screening data and extensive references but no comparative data
Bellissimo-Rodrigues 2009	Intervention is chlorexidine
Ben-Abraham 2002	Exclude - bacterial illness only
Black 1981	Diarrhoea only outcome
Borkow 2010	No human beings involved
Bouadma 2010	Hospital based ventilator routine
Breugelmans 2004	Description of risk factors in aircraft
Cai 2009	Compliance study
Cantagalli 2010	Outcome outside inclusion criteria
Carbonell-Estrany 2008	Immunoglobulin intervention and descriptive review
Carter 2002	News item
Castillo-Chavez 2003	Editorial
Cava 2005a	Survey of quarantinees' views
Cava 2005b	Personal experiences of quarantine
CDC 2003	Case reports
Chai 2005	Letter - about MRSA
Chaovanich 2004	Case report
Chau 2003	No original retrievable data. Mathematical model fitting expected to observed cases with quarantine in the SARS of Hong Kong
Chau 2008	Audit of infection control procedures and compliance with guidelines
Chen 2007	An assessment of the impact of different handwashing teaching methods. No clinical outcomes
Cheng 2010	Confounded by antiviral use for post-exposure prophylaxis

(Continued)

Chia 2005	Knowledge survey
Clynes 2010	Letters
Cowling 2007	Epidemiology, non-comparative, non-interventions study
Daniels 2010	Commentary
Daugherty 2008	No free data presented
Davies 1994	Antibody titres as outcomes with so many biases that interpretation of study is problematic
Day 1993	No acute respiratory infection outcome data
Day 2006	Mathematical model; no new data
Dell'Omodarme 2005	Probabilistic and Bayesian mathematical model of screening at entry
Desenclos 2004	Description of transmission
DiGiovanni 2004	Qualitative study of compliance factors in quarantine
Doebbeling 1992	RCT respiratory data not present. Only 3 viruses isolated in total with no viral typing available
Dwosh 2003	Case series
Edmonds 2010	Lab study
Fendler 2002	Cohort study badly biased with differential health profiles and healthcare workers dependency in intervention and control semi-cohorts. No attempt at adjusting for confounders was made. No denominators available
Flint 2003	Description of spread in aircraft and non-comparative data
Fung 2004	Non-comparative
Garcia 2010	Commentary
Gaydos 2001	Editorial linked to Ryan 2001
Gensini 2004	Interesting historical review
Giroud 2002	Non-clinical outcomes
Glass 2006	Mathematical model - no original data presented
Goel 2007	Non-comparative study

(Continued)

Gomersall 2006	Non-comparative study
Gore 2001	Summary of Dyer 2000 (already included)
Gostin 2003	Not an analytical study
Gralton 2010	Review
Guinan 2002	It would appear that 9 classes took part and “acted as their own controls”, but it is not clear if there was cross-over of classes or not. In addition the outcome is combined gastrointestinal/respiratory. The clue lies in the presence of a nested economic analysis which shows considerable savings in time for staff and pupils if the soap is used: in other words this is a (covert) publicity study
Gupta 2005	Economic model - no new data
Gwaltney 1982	No breakdown of cases by arm given
Han 2003	Non-comparative
Hayden 1985	This is a RCT with laboratory-induced colds, small numbers and uncertain numerators but almost certainly because of the unique laboratory conditions (placebo tissues not being a placebo at all) of impossible generalisation. It was a pilot to the far bigger trial by Farr 1988a ; Farr 1988b
Hendley 1988	Inappropriate intervention
Hens 2009	Model
Heymann 2009	Already in review as Heymann 2004
Hilburn 2003	No ARI/viral outcomes (e.g. URTIs)
Hilmarsson 2007	Animal study
Hirsch 2006	Study tested pharmacological interventions
Ho 2003	Descriptive review
Hsieh 2007	Mathematical model
Hugonnet 2007	Letter without any data
Jiang 2003	Two papers probably the same paper in different versions: Jiang SP, Huang LW, Wang JF, Wu W, Yin SM, Chen WX, et al. [A study of the architectural factors and the infection rates of healthcare workers in isolation units for severe acute respiratory syndrome]. [Chinese] Chung-Hua Chieh Ho Ho Hu Hsi Tsa Chih [Chinese Journal of Tuberculosis & Respiratory Diseases]. 26(10):594-7, 2003 Oct
Johnson 2009	Outcomes are non-clinical

(Continued)

Jones 2005	Historical account
Kaydos-Daniels 2004	Not an analytical study
Kelso 2009	Model
Khaw 2008	Assessing the efficacy of O ₂ delivery
Kilabuko 2007	Aetiological study
Kosugi 2004	Non-comparative study
Lam 2004	Outcomes were generic (infection rates). No laboratory data available for viral diagnosis
Lange 2004	No data presented
Larson 2004	Inappropriate outcomes
Larson 2005	Cluster-RCT comparing the effects of 2 hand hygiene regimens on infection rates and skin condition and microbial counts of nurses' hands in neonatal intensive care units. Outcomes were generic (for example, pneumonia and microbial counts of participants' skin). No laboratory data available for viral diagnosis
Lau 2004b	Attitude survey
Lau 2005	Herbal remedy effectiveness assessment
Lee 2005	Descriptive study of risk and protective factors of transmission in households. No assignment took place
Lee 2010	Cohort study; unclear numbers were vaccinated against influenza
Lipsitch 2003	Mathematical model fit to evidence
Luckingham 1984	Historical report on Tucson experience during Spanish flu pandemic
Ma 2004	Case-control study of risk factors for SARS
MacIntyre 2010	Commentary on Cowling 2009
Malone 2009	Model
Marin 1991	Viral resistance study
McSweeney 2007	Historical description
Mielke 2009	Review

(Continued)

Mikolajczyk 2008	No intervention
Monsma 1992	Non-comparative study
Nishiura 2009	Model
O'Callaghan 1993	Letter linked to Isaacs 1991
Olsen 2003	Description of transmission
Ooi 2005	Descriptive study but with interesting organisational chart
Orellano 2010	Confounded by antiviral use
Panchabhai 2009	Pharma intervention
Pang 2004	Descriptive study of Beijing outbreak. Some duplicate data in common with Pang 2003
Pittet 2000	Analysis of relationship between handwashing compliance campaign and nosocomial bacterial infections (e.g. MRSA)
Prasad 2004	Letter about retrospective cohort - behavioural
Rabenau 2005	In vitro test of several disinfectants
Reynolds 2008	Describes the psychological effects of quarantine
Richardson 2010	Non-clinical study
Riley 2003	Mathematical model fit to evidence
Rodriguez 2009	A "reasonable attempt at minimizing bias" (see inclusion criteria) does not include absenteeism
Rosenthal 2005	Outcomes were generic (for example, pneumonia, URTIs). No laboratory data available for viral diagnosis
Safulin 1972	Non-comparative set of studies with no clinical outcomes
Sandrock 2008	Review
Satter 2000	Experiment assessing virucidal activity of finger tip surface - no clinical outcome data
Schull 2007	Describes the impact of SARS in a Toronto study
Seal 2010	Lab study
Seale 2009	Study looking at whether using respirators in A&E department is feasible

(Continued)

Sizun 1996	This is a review, with no original data presented
Stebbins 2009	Attitude survey
Stoner 2007	No study data available
Stukel 2008	Impact of the SARS disruption on care/mortality for other pathologies (for example, acute myocardial infarction). There are no interventions and outcomes are unrelated to acute respiratory infections
Svoboda 2004	Descriptive study with before and after data but shifting denominators
Tracht 2010	Model
Ueno 1990	Experimental study. No clinical intervention
van der Sande 2008	Laboratory study without any clinical outcomes
Viscusi 2009a	Lab study
Viscusi 2009b	Lab study
Wang 2003	Descriptive study
Wang 2005	Case-control study of susceptibility factors
Weber 2004	Editorial linked to Larson 2004
Wen 2010	Lab study
White 2005	Redundant publication of White 2003
Wilczynski 1997	Clinical trial of the effects of breast feeding
Wilder-Smith 2003	Description of risk factors in aircraft
Wilder-Smith 2005	Descriptive review
Wong 2005	Attitude survey
Yen 2010	Model
Yu 2004	Description of transmission
Zamora 2006	Head-to-head comparison of two sets of PPEs with no controls and no clinical outcomes
Zhai 2007	Non-comparative study

(Continued)

Zhao 2003	CCT of SARS treatment
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A&E: accident and emergency
ARI: acute respiratory infection
CCT: controlled clinical trial
MRSA: methicillin-resistant *Staphylococcus aureus*
RCT: randomized controlled trial
RSV: respiratory syncytial virus
PPE: personal protective equipment
PEP: post-exposure prophylaxis
SARS: severe acute respiratory syndrome
URTI: upper respiratory tract infection

DATA AND ANALYSES

Comparison 1. Case-control studies

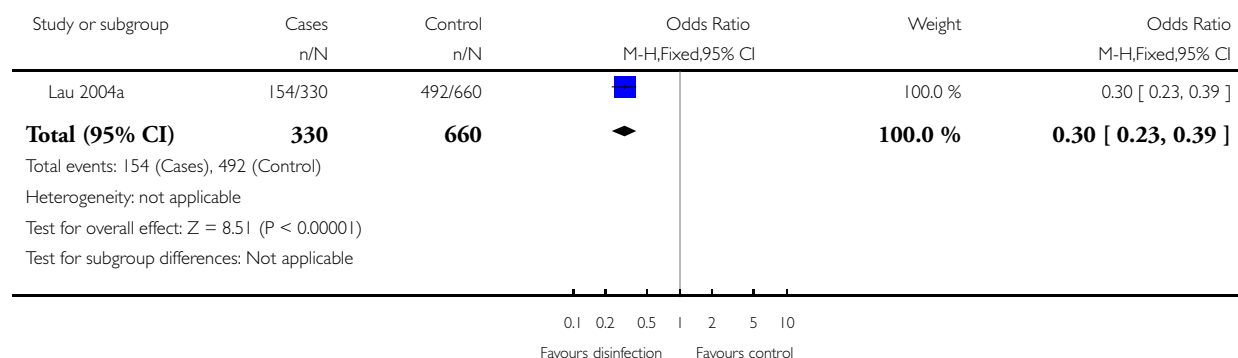
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Thorough disinfection of living quarters	1	990	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.23, 0.39]
2 Frequent handwashing	7	2825	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.44, 0.67]
3 Wearing mask	7	3216	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.26, 0.39]
4 Wearing N95 respirator	3	817	Odds Ratio (M-H, Fixed, 95% CI)	0.17 [0.07, 0.43]
5 Wearing gloves	6	1836	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.23, 0.45]
6 Wearing gowns	5	1460	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.24, 0.45]
7 All interventions	2	369	Odds Ratio (M-H, Fixed, 95% CI)	0.09 [0.02, 0.35]
8 Use of eye protection (mask/goggles)	3	1482	Odds Ratio (M-H, Fixed, 95% CI)	0.10 [0.05, 0.17]
9 Nose wash	2	1225	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.16, 0.57]

Analysis 1.1. Comparison 1 Case-control studies, Outcome 1 Thorough disinfection of living quarters.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 1 Thorough disinfection of living quarters

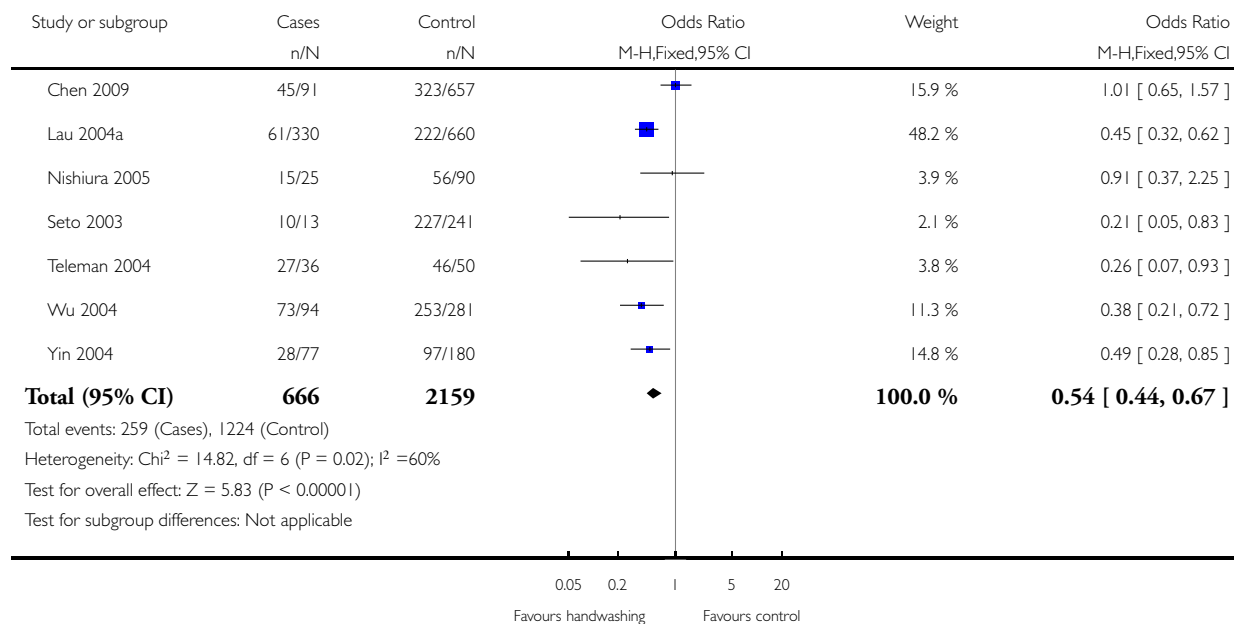


Analysis 1.2. Comparison 1 Case-control studies, Outcome 2 Frequent handwashing.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 2 Frequent handwashing

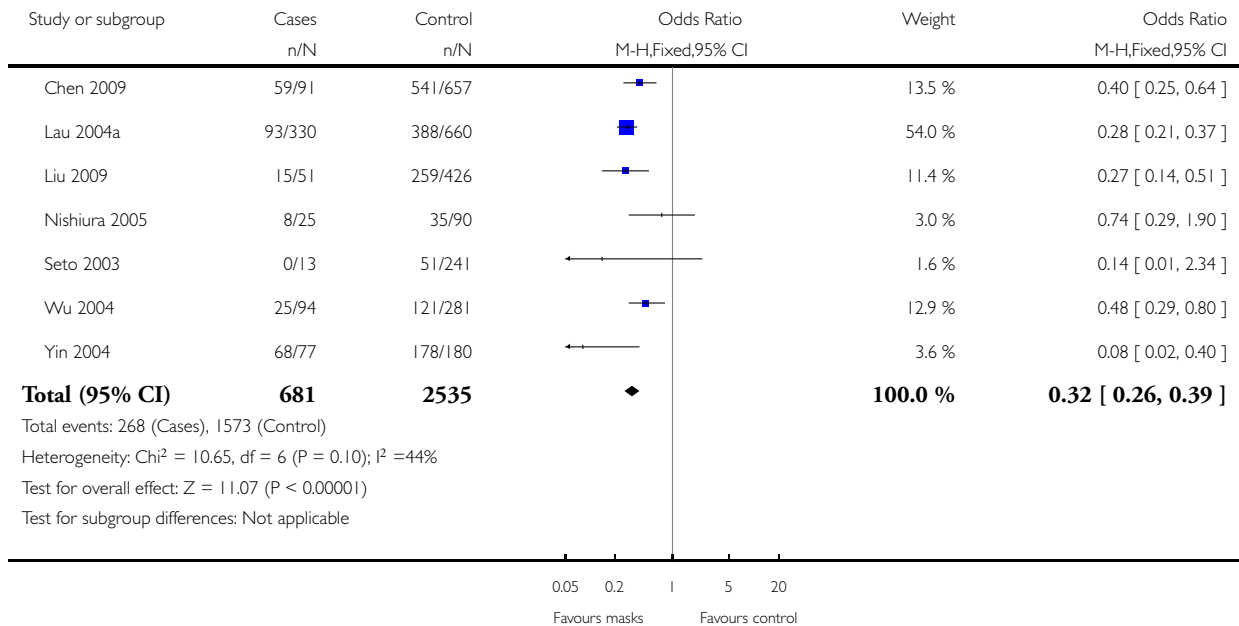


Analysis 1.3. Comparison 1 Case-control studies, Outcome 3 Wearing mask.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 3 Wearing mask

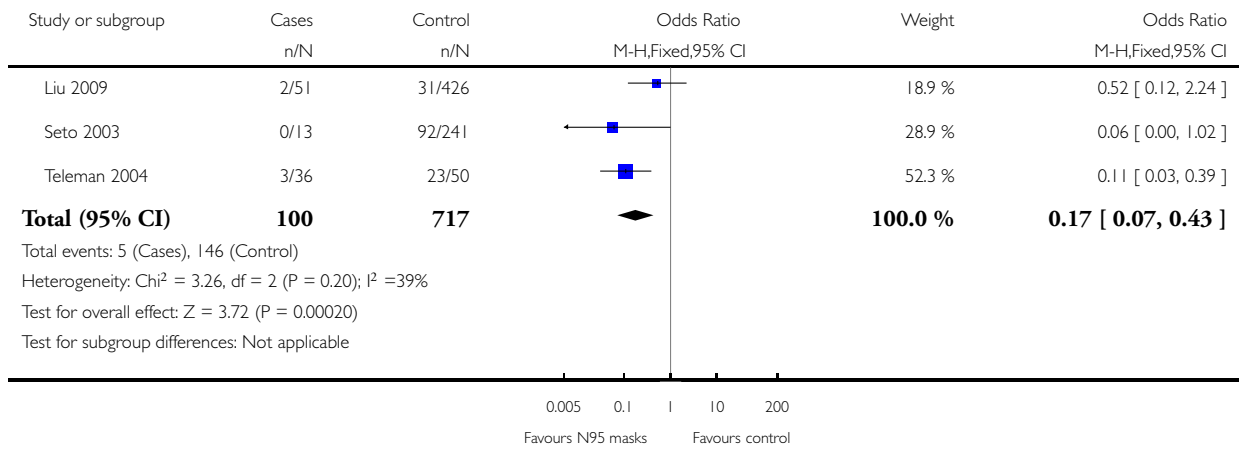


Analysis I.4. Comparison I Case-control studies, Outcome 4 Wearing N95 respirator.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: I Case-control studies

Outcome: 4 Wearing N95 respirator

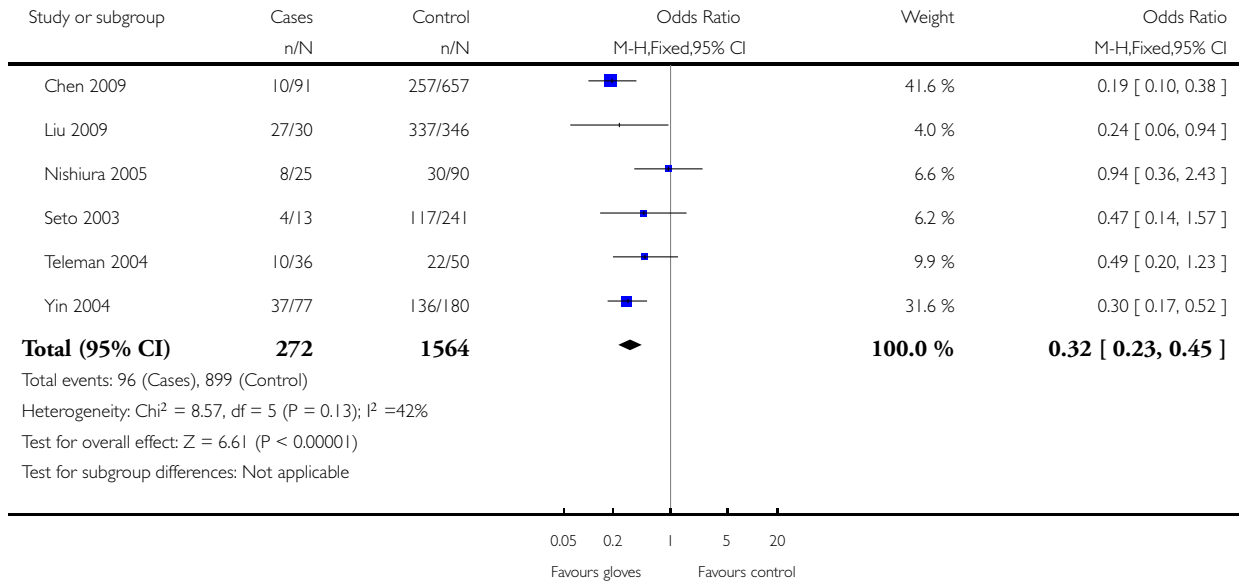


Analysis 1.5. Comparison 1 Case-control studies, Outcome 5 Wearing gloves.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 5 Wearing gloves

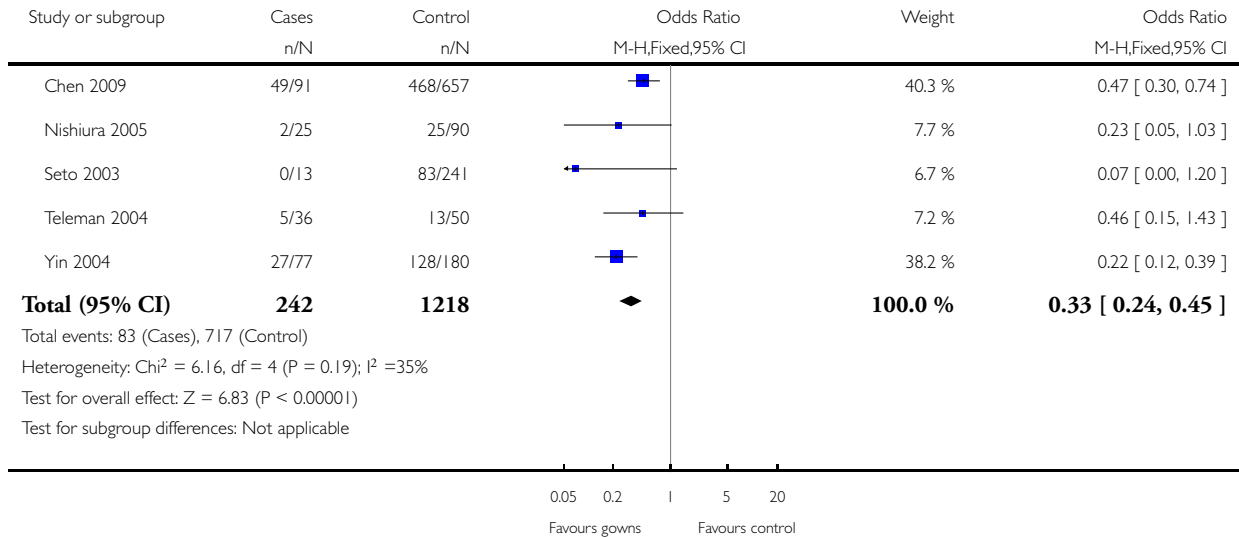


Analysis 1.6. Comparison 1 Case-control studies, Outcome 6 Wearing gowns.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 6 Wearing gowns

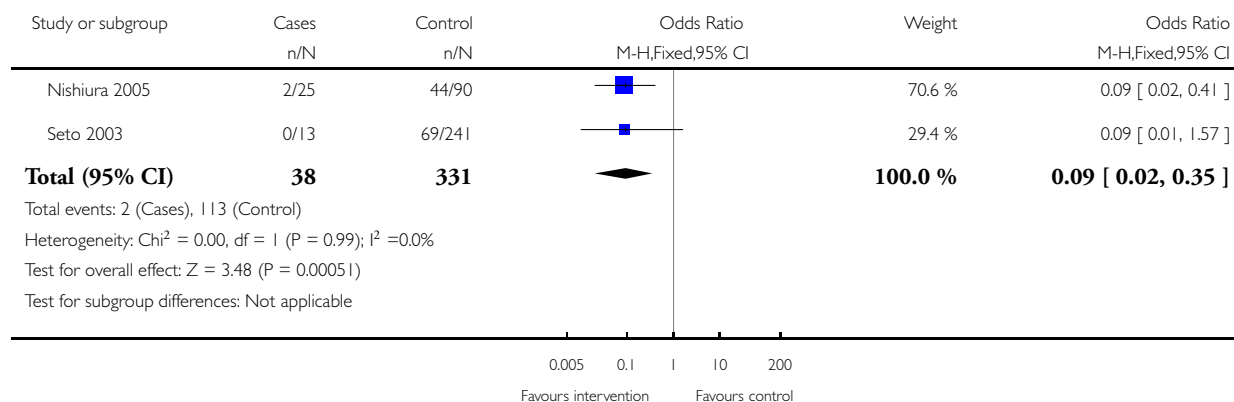


Analysis 1.7. Comparison 1 Case-control studies, Outcome 7 All interventions.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 7 All interventions

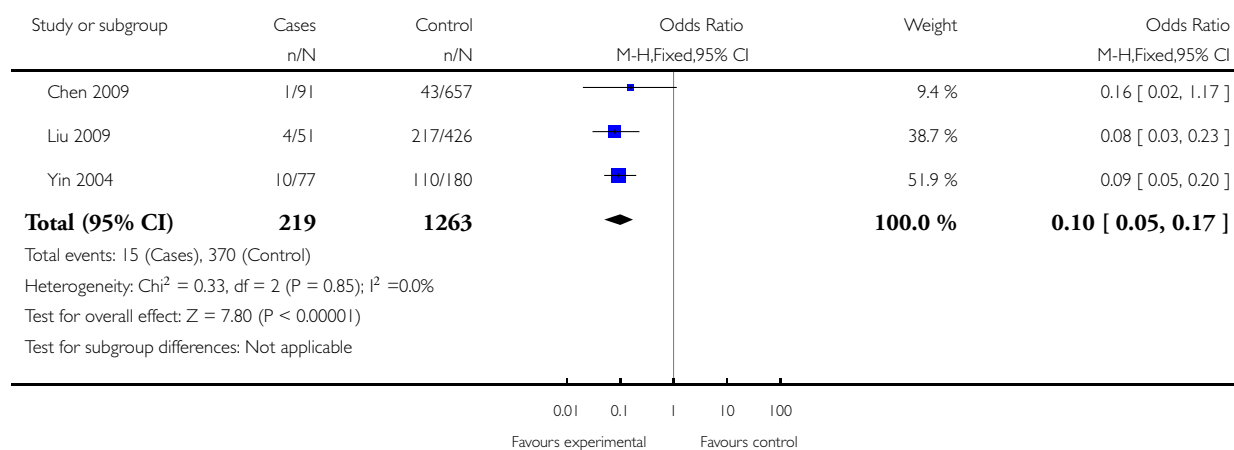


Analysis 1.8. Comparison 1 Case-control studies, Outcome 8 Use of eye protection (mask/goggles).

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 8 Use of eye protection (mask/goggles)

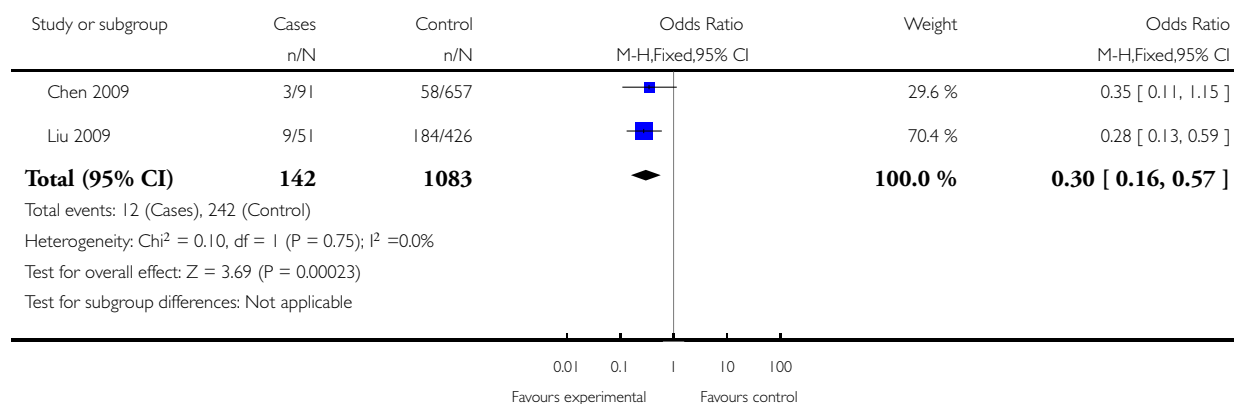


Analysis 1.9. Comparison 1 Case-control studies, Outcome 9 Nose wash.

Review: Physical interventions to interrupt or reduce the spread of respiratory viruses

Comparison: 1 Case-control studies

Outcome: 9 Nose wash



ADDITIONAL TABLES

Table 1. Significance in multivariable analysis of interventions to prevent SARS

Outcome or subgroup	Studies	How many statistically significant on multivariable analysis
1.1 Thorough disinfection of living quarters	1	1
1.2 Frequent handwashing	7	4
1.3 Wearing mask	7	6
1.4 Wearing N95 respirator	3	2
1.5 Wearing gloves	6	2

Table 1. Significance in multivariable analysis of interventions to prevent SARS (Continued)

1.6 Wearing gowns	5	2
1.7 All interventions	2	1
1.8 Use of eye protection (mask/goggles)	3	1
1.9 Nose wash	2	1

Table 2. Summary of main results

	RCT (N = 6)	C-RCT (N = 17)	Case-control (N = 9)	Prospective cohort (N = 16)	Retrospective cohort (N = 6)	Before-after (N = 13)
Handwashing	-	3 trials in children effective 1 trial in households effective if implemented < 36 hours after onset	7 studies OR 0.54 (95% CI 0.44 to 0.67)	2 studies found effect, 2 no effect on ARIs	-	1 study in military recruits: > 5 times per day effective
Handwashing with antiseptic	-	3 trials in children: 2 antiseptic more effective 1 antiseptic = soap	-	2 studies added effect of antiseptic 1 study: no difference	-	-
Handwashing and surface disinfection	-	4 trials in children and families: 2 studies effective	-	-	-	1 study in school effective
Hand disinfection	3 trials effective	-	-	-	-	-
Gargling with iodine	1 trial effective	-	-	-	-	-
Nose wash	-	-	2 studies OR 0.30 (95% CI 0.16 to 0.57)	-	-	-
Virucidal tissues	-	1 trial: small effect 2 trials: non-significant	-	1 study effective	-	-

Table 2. Summary of main results (Continued)

Disinfection of living quarters	-	-	1 study OR 0.30 (95% CI 0.23 to 0.39)	-	-	-
Use of eye protection			3 studies OR 0.10 (95% CI 0.05 to 0.17)			
Barriers (masks, gloves, gowns combined)	-	-	2 studies OR 0.09 (95% CI 0.02 to 0.35)	1 study: masks + gowns no added effect to hand-washing	-	3 studies: combined with isolation effective 1 study: mask and gown added to isolation not effective 1 study: gowns and gloves effective in paediatric ward
Mask	1 trial: surgical masks no effect	1 trial: no effect added to hand-washing 1 trial: no effect of P2 mask 1 trial: added to handwashing effective if implemented < 36 hours after onset of illness 1 trial: added to handwashing effective during weeks 4 to 6 1 trial: no effect added to hand-washing	7 studies OR 0.32 (95% CI 0.26 to 0.39)	3 studies: masks effective (with air filter safer)	1 study: harm related to mask wearing	1 study in children's hospital effective
N95 respirator	1 trial: surgical masks non-inferior to N95 respirators	-	3 studies OR 0.17 (95% CI 0.07 to 0.43)	-	1 study: harm related to N95 respirator wearing	-
Gloves	-	-	6 studies OR 0.32 (95% CI 0.23 to 0.45)	-	1 study: harm related to gloves	-

Table 2. Summary of main results (Continued)

Gowns	-	-	5 studies OR 0.33 (95% CI 0.24 to 0.45)	-	1 study: harm related to gown wearing	1 study: no added effect in neonatal ICU
Distancing	-	-	-	1 study: no effect in military recruits 2 studies: cohorting in hospitals effective	1 study: cohorting in paediatric wards effective 1 study in military hospital cohorting with handwashing and gowns effective	6 studies: early identification of cases and isolation effective
Quarantine	-	-	-	1 study: isolation of close contacts effective	1 study: isolation of close contacts effective 1 study: marginal non-significant benefit of border entry screening	-

ARI: acute respiratory infection

C-RCT: cluster-randomised controlled trial

ICU: intensive care unit

OR: odds ratio

RCT: randomised controlled trial

APPENDICES

Appendix I. Previous search strategy

(Details of the search strategy used in the original review and the 2009 search strategy updates for MEDLINE, CENTRAL, EMBASE and CINAHL)

In the first publication of this review we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2006, issue 4); MEDLINE (1966 to November 2006); OLDMEDLINE (1950 to 1965); EMBASE (1990 to November 2006) and CINAHL (1982 to November 2006). The MEDLINE search terms were modified for OLDMEDLINE, EMBASE and CINAHL. In this 2009 update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, issue 2); Ovid MEDLINE (2006 to May Week 1 2009); OLDMEDLINE (1950 to 1965); Ovid EMBASE (2006 to Week 18, 2009) and Ovid CINAHL (2006 to May Week 1 2009).

Ovid MEDLINE

1 exp Influenza/

2 influenza.tw.

3 flu.tw.
 4 exp Common Cold/
 5 common cold.tw.
 6 exp Rhinovirus/
 7 rhinovirus*.tw.
 8 exp Adenoviridae/
 9 adenovirus*.tw.
 10 exp Coronavirus/
 11 exp Coronavirus Infections/
 12 coronavirus*.tw.
 13 exp Respiratory Syncytial Viruses/
 14 exp Respiratory Syncytial Virus Infections/
 15 respiratory syncytial virus*.tw.
 16 respiratory syncytial virus.tw.
 17 exp Parainfluenza Virus 1, Human/
 18 exp Parainfluenza Virus 2, Human/
 19 exp Parainfluenza Virus 3, Human/
 20 exp Parainfluenza Virus 4, Human/
 21 (parainfluenza or para-influenza or para influenza).tw.
 22 exp Severe Acute Respiratory Syndrome/
 23 (severe acute respiratory syndrome or SARS).tw.
 24 acute respiratory infection*.tw.
 25 acute respiratory tract infection*.tw.
 26 or/1-25 (59810)
 27 exp Hand Washing/
 28 (handwashing or hand washing or hand-washing).tw.
 29 hand hygiene.tw.
 30 (sanitizer* or sanitiser*).tw.
 31 (cleanser* or disinfectant*).tw.
 32 exp Gloves, Protective/
 33 exp Gloves, Surgical/
 34 glov*.tw.
 35 exp Masks/
 36 mask*1.tw.
 37 exp Patient Isolators/
 38 exp Patient Isolation/
 39 patient isolat*.tw.
 40 (barrier* or curtain* or partition*).tw.
 41 negative pressure room*.tw.
 42 reverse barrier nursing.tw.
 43 Cross Infection/pc [Prevention]
 44 school closure*.tw.
 45 (clos* adj3 school*).tw.
 46 mass gathering*.tw.
 47 public gathering*.tw.
 48 (ban or bans or banned or banning).tw.
 49 (outbreak* adj3 control*).tw.
 50 distancing.tw.
 51 exp Quarantine/
 52 quarantine*.tw.
 53 or/27-49
 54 26 and 53
 55 (animals not (humans and animals)).sh.

CENTRAL search strategy

- #1 MeSH descriptor Influenza, Human explode all trees
- #2 influenza:ti,ab,kw
- #3 flu:ti,ab,kw
- #4 MeSH descriptor Common Cold explode all trees
- #5 "common cold":ti,ab,kw
- #6 MeSH descriptor Rhinovirus explode all trees
- #7 rhinovirus*:ti,ab,kw
- #8 MeSH descriptor Adenoviridae explode all trees
- #9 adenovirus*:ti,ab,kw
- #10 MeSH descriptor Coronavirus explode all trees
- #11 MeSH descriptor Coronavirus Infections explode all trees
- #12 coronavirus*:ti,ab,kw
- #13 MeSH descriptor Respiratory Syncytial Viruses explode all trees
- #14 MeSH descriptor Respiratory Syncytial Virus Infections explode all trees
- #15 respiratory syncytial virus*:ti,ab,kw
- #16 respiratory syncythial virus*:ti,ab,kw
- #17 MeSH descriptor Parainfluenza Virus 1, Human explode all trees
- #18 MeSH descriptor Parainfluenza Virus 2, Human explode all trees
- #19 MeSH descriptor Parainfluenza Virus 3, Human explode all trees
- #20 MeSH descriptor Parainfluenza Virus 4, Human explode all trees
- #21 (parainfluenza or para-influenza or para influenza):ti,ab,kw
- #22 MeSH descriptor Severe Acute Respiratory Syndrome explode all trees
- #23 (severe acute respiratory syndrome or SARS):ti,ab,kw
- #24 acute respiratory infection*:ti,ab,kw
- #25 acute respiratory tract infection*:ti,ab,kw
- #26 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25)
- #27 MeSH descriptor Handwashing explode all trees
- #28 (handwashing or hand washing or hand-washing):ti,ab,kw
- #29 hand hygiene:ti,ab,kw
- #30 (sanitizer* or sanitiser*):ti,ab,kw
- #31 (cleanser* or disinfectant*):ti,ab,kw
- #32 MeSH descriptor Gloves, Protective explode all trees
- #33 MeSH descriptor Gloves, Surgical explode all trees
- #34 glov*:ti,ab,kw
- #35 MeSH descriptor Masks explode all trees
- #36 mask*:ti,ab,kw
- #37 MeSH descriptor Patient Isolators explode all trees
- #38 MeSH descriptor Patient Isolation explode all trees
- #39 (barrier* or curtain* or partition*):ti,ab,kw
- #40 negative NEXT pressure NEXT room*:ti,ab,kw
- #41 "reverse barrier nursing":ti,ab,kw
- #42 MeSH descriptor Cross Infection explode all trees with qualifier: PC
- #43 school NEXT closure*:ti,ab,kw
- #44 (clos* NEAR/3 school*):ti,ab,kw
- #45 mass NEXT gathering*:ti,ab,kw
- #46 public NEXT gathering*:ti,ab,kw
- #47 ("ban" or "bans" or banned or banning):ti,ab,kw
- #48 (outbreak* NEAR/3 control*):ti,ab,kw

#49 distancing:ti,ab,kw
 #50 MeSH descriptor Quarantine explode all trees
 #51 quarantine*:ti,ab,kw
 #52 (#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51)
 #53 (#26 AND #52)

Ovid EMBASE search strategy

1 exp Influenza/
 2 influenza.tw.
 3 flu.tw.
 4 exp Common Cold/
 5 common cold.tw.
 6 exp Human Rhinovirus/
 7 rhinovirus*.tw.
 8 exp Adenovirus/
 9 adenovirus*.tw.
 10 exp Coronavirus/
 11 coronavirus*.tw.
 12 exp Respiratory Syncytial Pneumovirus/
 13 respiratory syncytial virus*.tw.
 14 respiratory syncythial virus.tw.
 15 (parainfluenza or para-influenza or para influenza).tw.
 16 exp Severe Acute Respiratory Syndrome/
 17 (severe acute respiratory syndrome or SARS).tw.
 18 acute respiratory infection*.tw.
 19 acute respiratory tract infection*.tw.
 20 or/1-19
 21 exp Hand Washing/
 22 (handwashing or hand washing or hand-washing).tw.
 23 hand hygiene.tw.
 24 (sanitizer\$ or sanitiser\$).tw.
 25 (cleanser\$ or disinfectant\$).tw.
 26 exp Glove/
 27 exp Surgical Glove/
 28 glov*.tw.
 29 exp Mask/
 30 mask*1.tw.
 31 patient isolat*.tw.
 32 (barrier* or curtain* or partition*).tw.
 33 negative pressure room*.tw.
 34 reverse barrier nursing.tw.
 35 Cross Infection/pc [Prevention]
 36 school closure*.tw.
 37 (clos* adj3 school*).tw.
 38 mass gathering*.tw.
 39 public gathering*.tw. (5)
 40 (ban or bans or banned or banning).tw.
 41 (outbreak* adj3 control*).tw.
 42 distancing.tw.
 43 quarantine*.tw.
 44 or/21-43

EBSCO CINAHL search strategy

S26 S10 and S24

S25 S10 and S24

S24 S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or 23 or S24

S23 TI outbreak* N3 control* or AB outbreak* N3 control*

S22 TI (school closure* or mass gathering* or public gathering* or ban or bans or banned or banning or distancing or quarantine*) or AB (school closure* or mass gathering* or public gathering* or ban or bans or banned or banning or distancing or quarantine*)

S21 TI (patient isolat* or barrier* or curtain* or partition* or negative pressure room* or reverse barrier nursing) or AB (patient isolat* or barrier* or curtain* or partition* or negative pressure room* or reverse barrier nursing)

S20 TI (glov* or mask*) or AB (glov* or mask*)

S19 TI (handwashing or hand washing or hand-washing or hand hygiene) or AB (handwashing or hand washing or hand-washing or hand hygiene)

S18 (MH "Quarantine")

S17 (MM "Cross Infection")

S16 (MH "Isolation, Reverse")

S15 (MH "Patient Isolation+")

S14 (MH "Respiratory Protective Devices")

S13 (MH "Masks")

S12 (MH "Gloves")

S11 (MH "Handwashing+")

S10 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9

S9 TI (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythal virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory syndrome or SARS or respiratory viral infection* or viral respiratory infection*) or AB (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythal virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory syndrome or SARS or respiratory viral infection* or viral respiratory

infection*)TI (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythal virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory (syndrome or SARS or respiratory viral infection* or viral respiratory infection*) or AB (influenza or flu or rhinovirus* or adenovirus* or coronavirus* or respiratory syncytial virus* or respiratory syncythal virus* or parainfluenza or para-influenza or para influenza or severe acute respiratory syndrome or SARS or respiratory viral infection* or viral respiratory infection*)

S8 (MH "SARS Virus")

S7 (MH "Severe Acute Respiratory Syndrome")

S6 (MH "Respiratory Syncytial Virus Infections")

S5 (MH "Respiratory Syncytial Viruses")

S4 (MH "Coronavirus+")

S3 (MH "Coronavirus Infections+")

S2 (MH "Common Cold")

S1 (MH "Influenza+")

Appendix 2. Embase.com search strategy, October 2010

The search strategy was broadened in 2010 to be more inclusive of new and emerging viruses.

'influenza'/exp AND [embase]/lim OR ('influenza virus a'/exp OR 'influenza virus b'/de OR 'influenza virus c'/de AND [embase]/lim) OR (influenza*:ab,ti OR flu:ab,ti AND [embase]/lim) OR ('common cold'/de AND [embase]/lim) OR ('common cold':ab,ti OR 'common colds':ab,ti AND [embase]/lim) OR ('human rhinovirus'/de AND [embase]/lim) OR (rhinovir*:ab,ti AND [embase]/lim) OR ('rhinovirus infection'/de AND [embase]/lim) OR ('adenovirus'/de OR 'human adenovirus'/exp AND [embase]/lim) OR ('human adenovirus infection'/exp AND [embase]/lim) OR (adenovir*:ab,ti AND [embase]/lim) OR ('coronavirus'/de OR 'sars coronavirus'/de AND [embase]/lim) OR (coronavir*:ab,ti AND [embase]/lim) OR ('coronavirus infection'/de AND [embase]/lim) OR ('severe acute respiratory syndrome'/de AND [embase]/lim) OR ('severe acute respiratory syndrome':ab,ti OR sars:ab,ti AND [embase]/lim) OR ('respiratory syncytial pneumovirus'/de AND [embase]/lim) OR ('respiratory syncytial virus infection'/de AND [embase]/lim) OR ('respiratory syncytial virus':ab,ti OR 'respiratory syncytial viruses':ab,ti OR rsv:ab,ti OR 'respiratory syncytial pneumovirus':ab,ti OR 'respiratory syncytial pneumoviruses':ab,ti AND [embase]/lim) OR ('parainfluenza virus'/exp AND [embase]/lim) OR (parainfluenza*:ab,ti OR 'para influenza':ab,ti OR 'para-influenza':ab,ti AND [embase]/lim) OR ('enterovirus'/de OR 'enterovirus infection'/de AND [embase]/lim) OR (enterovir*:ab,ti AND [embase]/lim) OR ('human parvovirus b19'/de OR 'bocavirus'/de AND [embase]/lim) OR (parvovirus*:ab,ti OR bocavirus*:ab,ti AND [embase]/lim) OR ('human metapneumovirus'/de AND [embase]/lim) OR (metapneumovir*:ab,ti AND [embase]/lim) OR ('parechovirus'/de AND [embase]/lim) OR (parechovirus*:ab,ti AND [embase]/lim) OR ('acute respiratory infection':ab,ti OR 'acute respiratory infections':ab,ti OR 'acute respiratory tract infection':ab,ti OR 'acute respiratory tract infections':ab,ti AND [embase]/lim) AND ('hand washing'/de AND [embase]/lim) OR (handwashing:ab,ti OR 'hand washing':ab,ti OR 'hand-washing':ab,ti AND [embase]/lim) OR ('hand hygiene':ab,ti AND [embase]/lim) OR (sanitiser*:ab,ti OR sanitizer*:ab,ti OR cleanser*:ab,ti OR disinfectant*:ab,ti AND [embase]/lim) OR ('glove'/de OR 'surgical glove'/de AND [embase]/lim) OR (glov*:ab,ti AND [embase]/lim) OR ('mask'/de OR 'face mask'/de OR 'surgical mask'/de AND [embase]/lim) OR (mask:ab,ti OR masks:ab,ti OR respirator:ab,ti OR respirators:ab,ti AND [embase]/lim) OR ('protective clothing'/de OR 'protective equipment'/de AND [embase]/lim) OR ('patient isolator':ab,ti OR 'patient isolators':ab,ti OR 'patient isolation':ab,ti AND [embase]/lim) OR (cohorting:ab,ti OR 'cohort isolation':ab,ti AND [embase]/lim) OR (barrier*:ab,ti OR curtain*:ab,ti OR partition*:ab,ti AND [embase]/lim) OR ('negative pressure room':ab,ti OR 'negative pressure rooms':ab,ti AND [embase]/lim) OR ('reverse barrier nursing':ab,ti OR 'reverse-barrier nursing':ab,ti OR 'reverse barrier unit':ab,ti OR 'reverse-barrier unit':ab,ti AND [embase]/lim) OR (('cross infection' NEAR/2 prevent*):ab,ti AND [embase]/lim) OR ('infection control'/de AND [embase]/lim) OR ((school* NEAR/3 clos* OR dismissal*)):ab,ti AND [embase]/lim) OR ('temporary closure':ab,ti OR 'temporary closures':ab,ti AND [embase]/lim) OR ('mass gathering':ab,ti OR 'mass gatherings':ab,ti AND [embase]/lim) OR ((public NEAR/2 (gathering* OR event*)):ab,ti AND [embase]/lim) OR (bans:ab,ti OR banning:ab,ti OR banned:ab,ti OR ban:ab,ti AND [embase]/lim) OR ((outbreak* NEAR/3 control*):ab,ti AND [embase]/lim) OR (distancing*:ab,ti AND [embase]/lim) OR (quarantine*:ab,ti AND [embase]/lim) OR ((protective NEAR/2 (cloth* OR garment* OR gown* OR device* OR equipment)):ab,ti AND [embase]/lim) OR (((protective OR preventive) NEAR/2 (procedure* OR behavior* OR behaviour*)):ab,ti AND [embase]/lim) OR ('personal protective':ab,ti OR 'personal protection':ab,ti AND [embase]/lim) OR ('isolation room':ab,ti OR 'isolation rooms':ab,ti OR 'isolation strategy':ab,ti OR 'isolation strategies':ab,ti AND [embase]/lim) OR ((distance NEAR/2 patient*):ab,ti AND [embase]/lim) OR (((spatial OR patient) NEAR/1 separation):ab,ti AND [embase]/lim)) AND ('randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp AND [embase]/lim) OR (random*:ab,ti OR placebo*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR 'cross over':ab,ti OR 'cross-over':ab,ti OR volunteer*:ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR ((singl* OR doubl*) NEAR/2 (blind* OR mask*)):ab,ti AND [embase]/lim) OR ('controlled study'/de OR 'treatment outcome'/de OR 'major clinical study'/de OR 'clinical trial'/de AND [embase]/lim) OR (chang*:ab,ti OR evaluat*:ab,ti OR reviewed:ab,ti OR baseline:ab,ti OR compare*:ab,ti OR compara*:ab,ti OR consecutive:ab,ti OR retrospective:ab,ti AND [embase]/lim))

Appendix 3. CINAHL (EBSCO) search strategy, October 2010

The search strategy was broadened in 2010 to be more inclusive of new and emerging viruses.

S54 S32 and S53

S53 S44 or S52

S52 S45 or S46 or S47 or S48 or S49 or S50 or S51

S51 TI observational stud* or AB observational stud*

S50 TI cohort stud* or AB cohort stud*

S49 (MH "Cross Sectional Studies")

S48 (MH "Nonconcurrent Prospective Studies")

S47 (MH "Correlational Studies")

S46 (MH "Case Control Studies+")

S45 (MH "Prospective Studies")

S44 S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43

S43 TI allocat* N1 random* or AB allocat* N1 random*

S42 (MH "Quantitative Studies")

S41 TI placebo* or AB placebo*

S40 (MH "Placebos")

S39 TI random* allocation* or AB random* allocation*

S38 (MH "Random Assignment")

S37 TI (randomised control* trial* or randomized control* trial*) or AB (randomised control* trial* or randomized control* trial*)

S36 TI ((singl* W1 blind*) or (singl* W1 mask*) or (doubl* W1 blind*) or (doubl* W1 mask*) or (trebl* W1 blind*) or (trebl* W1 mask*) or (tripl* W1 blind*) or (tripl* W1 mask*)) or AB ((singl* W1 blind*) or (singl* W1 mask*) or (doubl* W1 blind*) or (doubl* W1 mask*) or (trebl* W1 blind*) or (trebl* W1 mask*) or (tripl* W1 blind*) or (tripl* W1 mask*))

S35 TI clinic* W1 trial* or AB clinic* W1 trial*

S34 PT clinical trial

S33 (MH "Clinical Trials+")

S32 S15 and S31

S31 S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30

S30 TI (bans or banning or banned or ban or "outbreak control" or "outbreak controls" or distancing* or quarantine* or "protective clothing" or "protective garment" or "protective garments" or "protective gown" or "protective gowns" or "protective device" or "protective devices" or "protective equipment" or "protective behaviour" or "protective behavior" or "protective behaviours" or "protective behaviors" or "protective procedure" or "protective procedures" or "preventive behaviours" or "preventive behaviour" or "preventive behavior" or "preventive behaviors" or "preventive procedure" or "preventive procedures" or "personal protective" or "isolation room" or "isolation rooms" or "isolation strategy" or "isolation strategies" or "patient distance" or "patient distancing" or "patient separation" or "spatial separation") or AB (handwashing or "hand washing" or hand-washing or "hand hygiene" or sanitiser or sanitizer or cleanser* or disinfectant* or glove* or mask or masks or respirator or respirators or "patient isolation" or "patient isolators" or barrier* or curtain* or partition* or "negative pressure room" or "negative pressure rooms" or "reverse barrier nursing" or "reverse barrier unit" or "reverse barrier isolation" or "cross infection" or "infection control" or "disease control" or "school closure" or "school closures" or "school dismissal" or "school dismissals" or "temporary closure" or "temporary closures" or "mass gathering" or "mass gatherings" or "public gathering" or "public gatherings" or "public event" or "public events")

S29 TI (handwashing or "hand washing" or hand-washing or "hand hygiene" or sanitiser or sanitizer or cleanser* or disinfectant* or glove* or mask or masks or respirator or respirators or "patient isolation" or "patient isolators" or barrier* or curtain* or partition* or "negative pressure room" or "negative pressure rooms" or "reverse barrier nursing" or "reverse barrier unit" or "reverse barrier isolation" or "cross infection" or "infection control" or "disease control" or "school closure" or "school closures" or "school dismissal" or "school dismissals" or "temporary closure" or "temporary closures" or "mass gathering" or "mass gatherings" or "public gathering" or "public gatherings" or "public event" or "public events") or AB (handwashing or "hand washing" or hand-washing or "hand hygiene" or sanitiser or sanitizer or cleanser* or disinfectant* or glove* or mask or masks or respirator or respirators or "patient isolation" or "patient isolators" or barrier* or curtain* or partition* or "negative pressure room" or "negative pressure rooms" or "reverse barrier nursing" or "reverse barrier unit" or "reverse barrier isolation" or "cross infection" or "infection control" or "disease control" or "school closure" or "school closures" or "school dismissal" or "school dismissals" or "temporary closure" or "temporary closures" or "mass gathering" or "mass gatherings" or "public gathering" or "public gatherings" or "public event" or "public events")

S28 (MH "Sterilization and Disinfection")

S27 (MH "Quarantine")
 S26 (MH "Area Restriction (Iowa NIC)") OR (MH "Infection Protection (IowaNIC)")
 S25 (MH "Infection Control")
 S24 (MH "Cross Infection/PC")
 S23 (MH "Isolation, Reverse")
 S22 (MH "Patient Isolation")
 S21 (MH "Protective Devices")
 S20 (MH "Protective Clothing")
 S19 (MH "Respiratory Protective Devices")
 S18 (MH "Masks")
 S17 (MH "Gloves")
 S16 (MH "Handwashing+")
 S15 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14
 S14 TI ("acute respiratory tract infection" or "acute respiratory tract infections" or "acute respiratory infection" or "acute respiratory infections") or AB (influenza* or flu or "common cold" or "common colds" or rhinovir* or adenovir* or coronavir* or sars or "severe acute respiratory syndrome" or "respiratory syncytial virus" or "respiratory syncytial viruses" or rsv or pneumovir* or parainfluenza* or "para influenza" or para-influenza or enterovir* or bocavir* or metapneumovir* or parvovir* or parechovir*)
 S13 TI (influenza* or flu or "common cold" or "common colds" or rhinovir* or adenovir* or coronavir* or sars or "severe acute respiratory syndrome" or "respiratory syncytial virus" or "respiratory syncytial viruses" or rsv or pneumovir* or parainfluenza* or "para influenza" or para-influenza or enterovir* or bocavir* or metapneumovir* or parvovir* or parechovir*) or AB (influenza* or flu or "common cold" or "common colds" or rhinovir* or adenovir* or coronavir* or sars or "severe acute respiratory syndrome" or "respiratory syncytial virus" or "respiratory syncytial viruses" or rsv or pneumovir* or parainfluenza* or "para influenza" or para-influenza or enterovir* or bocavir* or metapneumovir* or parvovir* or parechovir*)
 S12 (MH "Respiratory Tract Infections+")
 S11 (MH "Parvovirus Infections+")
 S10 (MH "Enterovirus Infections+")
 S9 (MH "Enteroviruses+")
 S8 (MH "Respiratory Syncytial Virus Infections")
 S7 (MH "Respiratory Syncytial Viruses")
 S6 (MH "SARS Virus")
 S5 (MH "Severe Acute Respiratory Syndrome")
 S4 (MH "Coronavirus Infections+")
 S3 (MH "Coronavirus+") OR (MH "Coronavirus Infections")
 S2 (MH "Common Cold")
 S1 (MH "Influenza+") OR (MH "Influenza A H5N1") OR (MH "Influenza A

Appendix 4. LILACS (Latin America and Caribbean) search strategy

Tw acute respiratory tract infection\$ or Tw acute respiratory infection\$ or Mh human influenza or Mh influenza a virus or Mh influenza a virus, h1n1 subtype or Mh influenza a virus, h3n2 subtype or Mh influenza a virus, h3n8 subtype or Mh influenza a virus, h5n1 subtype or Mh influenza b virus or Mh influenza c virus or Mh influenza in humans or Mh influenza viruses type a or Mh influenza viruses type b or Mh influenza viruses type c or Mh influenza, human or Tw influenza\$ or Tw flu or Mh influenzavirus a or Mh influenzavirus b or Mh influenzavirus c or Mh adenoviridae or Mh adenoviridae infections or Mh adenovirus infections or Mh adenovirus infections, human or Mh adenoviruses, human or Tw rhinovir\$ or Tw adenovir\$ or Tw common cold\$ or Tw resfriado comum or Tw resfriado comun or Mh coronavirus or Mh sars-associated coronavirus or Mh human coronavirus 229e or Mh coronavirus 229e, human or Mh coronavirus infections or Tw coronavir\$ or Mh severe acute respiratory syndrome or Mh severe acute respiratory syndrome virus or Tw severe acute respiratory syndrome or Tw sars or Tw sindrome respirat\$ agudo grave or Mh human respiratory syncytial virus or Mh respiratory syncytial virus infections or Mh respiratory syncytial virus, human or Mh respiratory syncytial viruses or Tw respiratory syncytial virus\$ or Tw rsv or Tw virus sincitiales respiratorios or Tw virus sinciciais respiratorios or Mh pneumovirus or Tw pneumovir\$ or Mh human parainfluenza virus 1 or Mh parainfluenza virus 1, human or Mh human parainfluenza virus 2 or Mh parainfluenza virus 2, human or Mh human parainfluenza virus 3 or Mh parainfluenza virus 3, human or Mh parainfluenza virus infections Tw parainfluenza\$ or Tw para influenza or Tw para-influenza or Mh enterovirus or Mh human enterovirus b or Mh

enterovirus b, human or Mh enterovirus infections or Tw enterovir\$ or Mh bocavirus or Tw bocavir\$ or Mh metapneumovirus or Mh human metapneumovirus or Mh metapneumovirus, human or Tw metapneumovir\$ or Mh parvovirus or Mh human parvovirus b19 or Mh parvovirus b19, human or Mh parvovirus infections or Tw parvovir\$ or Mh parvoviridae or Mh parvoviridae infections or Tw parechovir\$ [Words]

and

Mh Handwashing or Tw handwashing or Tw hand washing or Tw hand-washing or Tw lavado de manos or Tw lavagem de maos or Tw hand hygiene or Tw higiene or Tw sanitiser\$ or Tw sanitizer or Tw cleanser\$ or Tw disinfectant\$ or Tw esteriliza\$ or Tw desinfectar\$ or Mh protective gloves or Mh surgical gloves or Mh gloves, protective or Mh gloves, surgical or Tw glov\$ or Tw guantes or Tw luvas or Mh masks or Mh facial masks or Tw mask or Tw masks or Tw mascarar or Mh respiratory protective devices or Tw respirator or Tw respirators or Mh protective clothing or Mh protective devices or Mh patient isolation or Tw patient isolat\$ or Tw aisladores de pacientes or Tw aislamiento de pacientes or Tw isoladores de pacientes or Tw isolamento de pacientes or Tw barrier\$ or Tw curtain\$ or Tw partition\$ or Tw barrera or Tw barreira or Tw cortina or Tw tabique or Tw protective clothing or Tw protective devices or Tw ropa de protec\$ or Tw equipos de seguridad or Tw roupa de prote\$ or Tw equipamentos de prote\$ or Mh cross infection or Tw cross infection\$ or Tw infec\$ hospital\$ or Tw infection control\$ or Tw control\$ de infec\$ or Mh communicable disease control or Tw communicable disease control or Tw control de enfermedades transmisibles or Tw controle de doen\$ transmiss\$ or Mh infection control or Mh quarantine Tw quarantine\$ or Tw cuarentena or Tw quarentena or Tw protective devices or Tw dispositivos de prtoccc\$ or Tw personal protect\$ or Tw equipamentos de protec\$ or Tw equipo de protecc\$ or Tw isolation room or Tw sala de aislamiento or Tw quarto de isolamento or Tw patient distance or Tw distancia del paciente or Tw spatial separation or Tw separa\$ especial or Tw cohort isolation or Tw cohort\$ or Tw ban or Tw bans or Tw banning or Tw banned or Tw prohibici\$ or Tw proibi\$ or Tw outbreak control or Tw distanc\$ or Tw school closure or Tw temporary closure or Tw cierre de la escuela or Tw fechamento da escola or Tw public gathering or Tw reunion publica or Tw reuni\$ publica or Tw reverse barrier nursing or Tw reverse barrier unit or Tw reverse barrier isolation or Tw negative pressure room\$ or Tw patient separation [Words]

Appendix 5. Indian MEDLARS search strategy

(influenza\$ or flu or common cold\$ or rhinovir\$ or coronavir\$ or adenovir\$ or severe acute respiratory syndrome\$ or sars or respiratory syncytial virus\$ or rsv or parainfluenza\$ or enterovir\$ or metapneumovir\$ or parvovir\$ or bocavir\$ or parechovir\$) and (handwashing or hand washing or mask\$ or glov\$ or protect\$ or isolat\$ or barrier\$ or curtain\$ or partition\$ or cross infection\$ or infection control\$ or disease control\$ or school\$ or quarantine\$ or ban\$ or cohort\$ or distanc\$ or spatial separation\$)

Appendix 6. IMSEAR (Index Medicus for the South East Asia Region) search strategy

(influenza or flu or common cold or rhinovirus or coronavirus or adenovirus or severe acute respiratory syndrome or sars or respiratory syncytial virus or rsv or parainfluenza or enterovirus or bocavirus or metapneumovirus or parvovirus or parechovirus) and (handwashing or hand washing or hand hygiene or sanitiser or sanitizer or cleanser or disinfectant or gloves or masks or mask or protective clothing or protective devices or patient isolation or barrier or curtain or partition or cross infection or disease control or infection control or school or schools or bans or banning or banned or ban or distancing or quarantine or isolation or spatial separation or cohorting or cohort isolation)

Appendix 7. GRADE evidence profiles physical barriers/handwashing and related interventions in hospital and community settings

Author(s): J Conly MD, Vijay K. Shukla Ph.D, R.Ph (Reviewer)

Date: 8 March 2011

Question: should standard procedure mask versus standard procedure mask plus alcohol gel for handwashing versus nothing be used for reducing influenza-like illness (ILI) and laboratory-confirmed influenza virus infection?

Settings: in a university residence setting

Bibliography: Aiello AE, Murray GF, Perez V, Coulborn RM, Davis BM, Uddin M, et al. Mask use, hand hygiene, and seasonal influenza-like illness among young adults: a randomized intervention trial. J Infect Dis. 2010 Feb 15;201(4):491-8

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Standard procedure mask versus standard procedure mask plus alcohol gel for hand-washing	Nothing	Relative (95% CI)	Absolute		
ILI (follow up 6 weeks; surveys ^{1,2)})												
1	Randomised trials	No serious limitations ³	No serious inconsistency	No serious indirectness	Serious ⁴	None	99/378 (26.2%)	177/552 (32.1%)	RR 0.82 (0.66 to 1) ⁵	58 fewer per 1000 (from 109 fewer to 0 more)	⊕⊕⊕⊖ MODERATE	CRITICAL
ILI (follow up 6 weeks; surveys ^{2,6)})												
1	Randomised trials	No serious limitations ³	No serious inconsistency	No serious indirectness	Serious ⁴	None	92/367 (25.1%)	177/522 (33.9%)	RR 0.78 (0.63 to 0.97) ⁵	75 fewer per 1000 (from 10 fewer to 125 fewer)	⊕⊕⊕⊖ MODERATE	CRITICAL

¹ Masks only ILI + 99/378; 5 with laboratory-confirmed influenza versus 2 in control group.

² Neither face mask use and hand hygiene nor face mask use alone was associated with a significant reduction in the rate of ILI cumulatively.

³ Students were away during spring break and did not carry on the intervention.

⁴ Relatively wide confidence intervals (CIs).

⁵ Significant reductions in ILI occurred during weeks 4 to 6 in the mask and hand hygiene group, compared with the control group, ranging from 35% (confidence interval 9% to 53%) to 51% (CI 13% to 73%), after adjusting for vaccination and other covariates.

⁶ Masks plus sanitiser 92/367; 2 with laboratory-confirmed influenza versus 2 in control group.

Author(s): J Conly MD, Vijay K. Shukla Ph.D, R.Ph (Reviewer)

Date: 8 March 2011

Question: should standard surgical face masks be worn while on hospital property versus no face masks while on hospital property be used for reducing upper respiratory infection (URI) symptoms ?

Settings: hospital

Bibliography: Jacobs JL, Ohde S, Takahashi O, Tokuda Y, Omata F, Fukui T. Use of surgical face masks to reduce the incidence of the common cold among healthcare workers in Japan: a randomized controlled trial. Am J Infect Control. 2009 Jun;37(5):417-9. Epub 2009 Feb 12

Quality assessment							Summary of findings					Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect		Quality	
							Standard surgical face masks be worn while on hospital property	No face masks while on hospital property	Relative (95% CI)	Absolute		
URI symptoms using a modified Jackson score (MJS) criteria (follow up 77 days; 8 self-recorded URI symptoms with a 4-point severity rating scale)												
1	Ran-domised trials	Very se-rious ^{1,2}	Serious	Serious ³	Very se-rious ⁴	None	1/15 (6.7%) ⁵	2/ 17 (11.8%) ⁵	RR 1.13 (0.12 to 10.7)	15 more per 1000 (from 104 fewer to 1141 more)	⊕⊕⊕⊕ VERY LOW	IM-POR-TANT
								0%		0 more per 1000 (from 0 fewer to 0 more)		

(Continued)

								0%		0 more per 1000 (from 0 fewer to 0 more)		
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¹ Very low recruitment and no power calculation.

² Nurses made up the majority of the recruited hospital personnel.

³ No attempts to consider exposures outside of the hospital.

⁴ No CONSORT diagram is provided and use of Jackson criteria may be questioned for its precision.

⁵ A separate analysis demonstrated that having children in the household under 16 years of age was significantly ($P = 0.02$) associated with a mean MJS above the median of 28.5.

Author(s): J Conly MD, Vijay K. Shukla Ph.D, R.Ph (Reviewer)

Date: 8 March 2011

Question: should education with hand sanitiser versus education with hand sanitiser and face masks versus education alone be used for prevention of URI, ILI and laboratory-confirmed influenza?

Settings: community

Bibliography: Larson EL, Ferng YH, Wong-McLoughlin J, Wang S, Haber M, Morse SS. Impact of non-pharmaceutical interventions on URIs and influenza in crowded, urban households. Public Health Rep. 2010 Mar-Apr;125(2):178-91

Quality assessment							Summary of findings				Importance
							No of patients		Effect		
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Education with hand sanitiser versus education with hand sanitiser and face masks	Education alone	Relative (95% CI)	Absolute	
Self-reported URI, ILI and laboratory-confirmed influenza (follow up 19 months; self-reports, home visits, telephone calls, laboratory tests ¹)											

(Continued)

1	Ran- domised trials	Very se- rious ²	Serious ³	Serious ⁴	Serious ⁵	None	79/859 (9.2%)	105/ 889 (11. 8%)	RR 0. 80 (0.6 to 1.05)	24 fewer per 1000 (from 47 fewer to 6 more)	⊕⊕⊕⊕ VERY LOW	IM- POR- TANT
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Self-reported URI, ILI and laboratory-confirmed influenza (follow up 19 months; self-reports, home visits, telephone calls, laboratory tests⁶)

1	Ran- domised trials	Very se- rious ²	Serious ³	Serious ⁴	Serious ⁵	None	94/946 (9.9%)	105/ 944 (11. 1%)	RR 0.94 (0. 72 to 1. 22)	7 fewer per 1000 (from 31 fewer to 24 more)	⊕⊕⊕⊕ VERY LOW	IM- POR- TANT
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¹ ILI in mask plus sanitiser plus education versus education; only ILI reported; no significant differences in URI rates or laboratory-confirmed cases.

² Difficult to follow flow of consented and non-consented patients throughout the trial to assess all outcomes ; major intervention bias which may have contaminated the entire study as the "control" since it was reported that 56.95% of households (number of persons not stated) and 44.2% of households (number of persons not stated) used hand sanitiser within the previous 24 hours or at some point during the course of the study.

³ Appear to have analysed only those who were randomised and had complete home visits and unclear if intention-to-treat (ITT) completed.

⁴ Very difficult community environment setting in which to conduct the trial.

⁵ Cannot distinguish if the "dropped" category represents individual participants or households.

⁶ ILI in mask plus education versus education group; no significant differences in the URI rates or laboratory-confirmed cases.

Author(s): J Conly MD, V Shukla PhD (Reviewer)

Date: 8 March 2011

Question: should N95 respirators versus surgical masks be used for prevention of influenza?

Settings: healthcare workers

Bibliography: Loeb M, Dafoe N, Mahony J, John M, Sarabia A, Glavin V, et al. Surgical mask versus N95 respirator for preventing influenza among health care workers: a randomized trial. JAMA. 2009 Nov 4;302(17):1865-71

Quality assessment							Summary of findings				Qual- ity	Importance
							No of patients		Effect			
No of studies	Design	Limitations	Incon- sis-	Indi- rect-	Impre- cision	Other consid-	N95 respi-	Surgi- cal	Rela- tive	Abso-		

(Continued)

			tency	ness		era- tions	rators	masks	(95% CI)	lute		
Laboratory-confirmed influenza (follow up 7 months; reverse transcription polymerase chain reaction (RT-PCR) or serology)												
1	Ran- domised trials	No seri- ous lim- itations ¹	No seri- ous in- consis- tency	No seri- ous in- direct- ness	No seri- ous im- preci- sion ^{2,3,4}	Report- ing bias ⁵	48/210 (22.9%)	50/212 (23.6%)	RR 0.97 (0.73 to 1.46)	7 fewer per 1000 (from 64 fewer to 108 more)	⊕⊕⊕⊕ MOD- ERATE	CRITI- CAL

¹ Non-inferiority trial design but the established criteria for non-inferiority were met.

² Absolute risk difference -0.73% (95% CI -0.88 to 7.3).

³ Audits were done to assess compliance.

⁴ Results similar for per protocol (PP) and ITT analysis.

⁵ Authors may have been aware of other similar studies which were ongoing at the time of conduct of this trial.

Author(s): Vijay K. Shukla Ph.D, R.Ph. Reviewed by: John Conly, MD Karen Lee, MA

Date: 1 March 2011

Question: should physical barriers versus not using physical barriers be used in healthcare workers or the general public exposed to respiratory viruses (SARS CoV (SARS coronavirus) in these settings)?

Settings: hospital or community

Bibliography: Jefferson T et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database of Systematic Reviews March 2011. Search conducted 22 October 2010

Quality assessment				Summary of findings				No Im- of pa- por- tients tanc	Effect	Qua ity	No of stud ies	De- sign i- ta- tion	Lim sis- tenc	In- con- rect ness	Im- pre- ci- sion	Oth con- sid- er-	Phys- cal bar-
				Not us- ing phy- i- cal bar- ri- ers	Rel- a- tive (95% CI)	Ab- so- lute			Wearing gowns (follow up 10 to 58 days ¹ ; number of people wearing gowns)							Ob- ser- va- tion: stud ies ²	Very se- ri- ous stud ies ³
No se- ri-	No se- ri-	N se- ri- ous	Very stro as-	242/ 0 (0%	0% 5	OR 0.33	0 fewe per 100	⊕ ⊕ ⊕	0 fewe per	Wearing gloves (follow up 10 to 90 days ^{1,6} ; number of people wearing gloves)							

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[illegible]

[illegible]

⁹ One study ([Chen 2009](#)) reported duration.

Bibliography: Jefferson T et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database of Systematic Reviews 2011. Literature search done up to 22 October 2010

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(Continued)

2	Observational studies ²	Very serious ³	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁷	142/0 (0%)	0% ⁶	OR 0.3 (0.16 to 0.57)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕⊖ LOW	
Thorough disinfection of living quarters (follow up 66 days⁸; number of people living in thoroughly disinfected houses)												
1	Observational studies ²	Very serious ³	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias ⁸ very strong association ⁷	330/0 (0%)	0% ⁶	OR 0.30 (0.23 to 0.39)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊖⊖⊖ VERY LOW	

¹ For one study (Yin 2004) duration of study or follow up is not reported.

² Case-control.

³ Case-control study which is a weak observational study design.

⁴ Variation patient population, duration of exposure not reported.

⁵ Effect size is relatively large (OR 0.54, 95% CI 0.44 to 0.67).

⁶ Baseline risks are not available from case control studies.

⁷ Effect size large (i.e. OR < 0.5).

⁸ Single study.

Author(s): Vijay K. Shukla Ph.D, R.Ph Reviewed by: John Conly, MD Karen Lee MA

Date: 8 March 2011

Question: should physical barriers versus not using physical barriers be used in healthcare workers in hospital setting?

Settings: hospital¹

Bibliography: Jefferson et al. Physical interventions to interrupt the spread of respiratory viruses. Cochrane Database of Systematic Reviews March 2011. Search conducted: 22 October 2010

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Physical barriers	Not using physical barriers	Relative (95% CI)	Absolute		
Wearing gowns (Copy) (follow up 10 to 58 days ² ; number of people wearing gowns)												
5	Observational	Very serious ⁴	No serious in-	No serious in-	No serious im-	Very strong	242/0 (0%)	0% ⁶	OR 0.33 (0.	0 fewer per	⊕⊕⊕⊖ LOW	

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	studies ³		consistency	directness	precision	association ⁵			24 to 0.45)	1000 (from 0 fewer to 0 fewer)		
								0% ⁶		0 fewer per 1000 (from 0 fewer to 0 fewer)		
Wearing gloves (Copy) (follow up 10 to 90 days^{2,7}; number of people wearing gloves)												
6	Observational studies ³	Very serious ⁴	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁵	272/0 (0%)	0%	OR 0.32 (0.23 to 0.45)	0 fewer per 1000 (from 0 fewer to 0 fewer) ⁶	⊕⊕⊕○ LOW	
Wearing masks (number of people wearing masks)												
5	Observational studies ³	Very serious ⁴	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁵	257/0 (0%)	0%	OR 0.34 (0.24 to 0.47)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕○ LOW	
Wearing N95 respirator (Copy) (follow-up 10 to 22 days^{2,8}; Number of people wearing N95 respirators)												
3	Observational studies ³	Very serious ⁴	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁵	100/0 (0%)	0% ⁶	OR 0.17 (0.07 to 0.43)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕○ LOW	
Use of eye protection (mask/goggles) (Copy) (follow up 90 days⁹; number of people wearing mask/goggles)												
3	Observational studies ³	Very serious ⁴	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁵	219/0 (0%)	0% ⁶	OR 0.10 (0.05 to 0.17)	0 fewer per 1,000 (from 0	⊕⊕⊕○ LOW	

(Continued)

										fewer to 0 fewer)		
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¹ Separate data analysis was done for hospital setting from Jefferson et al review.

² This is the period for which study was conducted. Exposure time is not reported.

³ Case-control.

⁴ Case-control study which is a weak observational study design.

⁵ Very large effect size.

⁶ These risks are not available from case-control studies.

⁷ For 2 studies (Yin 2004 and Liu 2009) duration of study and duration of follow up is not reported.

⁸ For one study (Liu 2009) duration of study or duration of follow up is not reported.

⁹ One study (Chen 2009) reported duration.

Author(s): Vijay K. Shukla Ph. D, R.Ph Reviewed by: John Conly MD Karen Lee MA

Date: 9 March 2011

Question: should physical barriers versus not using physical barriers be used in healthcare workers or the general public?

Settings: community

Bibliography: Jefferson T et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database of Systematic Reviews March 2011. Searches conducted 22 October 2010

Quality assessment							Summary of findings					Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect		Quality	
							Physical barriers	Not using physical barriers	Relative (95% CI)	Absolute		
Wearing masks (follow up 42 to 66 days ¹ ; number of people wearing masks)												
2	Observational studies ²	Very serious ³	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁴	424/0 (0%)	0%	OR 0.31 (0.25 to 0.4)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ LOW	

¹ This is the period for which study was conducted. Exposure time is not reported.

² Case-control.

³ Case-control studies which have a weak study design.

⁴ Very large effect size.

Author(s): Vijay K. Shukla Ph.D, R.Ph. Reviewed by: John Conly MD, Karen Lee MA

Date: 8 March 2011

Question: should washing or related interventions versus no handwashing and related interventions be used in healthcare workers in hospital setting?

Settings: hospital

Bibliography: Jefferson T et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database of Systematic Reviews 2011. Literature search done up to 22 October 2010

Quality assessment							Summary of findings				Importance	
							No of patients		Effect			Quality
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Washing or related interventions	No handwashing and related interventions	Relative (95% CI)	Absolute		
Frequent handwashing (follow up 22 to 90 days ¹ ; number of people frequently washing hands)												
5	Observational studies ²	Very serious ³	Serious ⁴	No serious indirectness	No serious imprecision	Strong association ⁵	242/0 (0%)	0%	OR 0.70 (0.52 to 0.94)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ VERY LOW	
Nose wash (Copy) (number of people washing nose)												
2	Observational studies ²	Very serious ⁶	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁷	142/0 (0%)	0% ⁸	OR 0.3 (0.16 to 0.57)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ LOW	

¹ One study (Yin 2004) has not reported duration or follow up.

² Case-control.

³ Case-control study which is a weak study design.

⁴ Wide variation in effect size (from no significant effect to significant effect).

⁵ Effect size is relatively large (OR 0.70, 95% CI 0.52 to 0.94).

⁶ Case-control study which is very weak observational study design.

⁷ Effect size large (i.e. OR < 0.5).

⁸ Baseline risks are not available from case-control studies.

Author(s): Vijay K. Shukla Ph.D, R.Ph. Reviewed by: John Conly MD Karen Lee MA

Date: 9 March 2011

Question: should handwashing or related interventions versus no handwashing and related interventions be used in healthcare workers or general public?

Settings: community setting

Bibliography: Jefferson T et al. Physical interventions to interrupt or reduce the spread of viruses. Cochrane Database of Systematic Reviews March 2011. Literature search conducted: 22 October 2010

Quality assessment							Summary of findings				Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients	Effect	Relative (95% CI)	Absolute		
							Handwashing or related interventions	No handwashing and related interventions				
Frequent handwashing (follow up 42 to 66 days¹; number of people frequently washing hands)												
2	Observational studies ²	Very serious ³	No serious inconsistency	No serious indirectness	No serious imprecision	Very strong association ⁴	424/0 (0%)	0%	OR 0.44 (0.33 to 0.58)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕○	LOW
Thorough disinfection of living quarters (Copy) (follow up 66 days⁵; number of people living in thoroughly disinfected houses)												
1	Observational studies ²	Very serious ⁶	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias ⁵ very strong association ⁷	330/0 (0%)	0% ⁸	OR 0.30 (0.23 to 0.39)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕○○	VERY LOW

¹ This is the period for which study was conducted. Exposure time is not reported.

² Case-control.

³ Case-control study which is a weak observational study design.

⁴ Very large effect size.

⁵ Single study.

⁶ Case-control study which is a weak observational study design.

⁷ Effect size large (i.e. OR < 0.5).

⁸ Baseline risks are not available from case-control studies.

WHAT'S NEW

Date	Event	Description
22 October 2010	New search has been performed	Searches conducted. We included seven new trials; four randomised controlled trials and three non-randomised comparative studies. We excluded 36 new trials
22 October 2010	New citation required but conclusions have not changed	We updated the review again at the behest of the World Health Organization (WHO). External sources of support amended. External support from the WHO. The WHO interim guidelines document on 'Infection Prevention and Control of Epidemic and Pandemic Prone Acute Respiratory Diseases in Health Care' was published in 2007 to provide infection control guidance to help prevent the transmission of acute respiratory diseases (ARD) in health care. The update of these guidelines will be evidence-based and an update of this review was requested to assist in informing the evidence base for the revision of the WHO guidelines. Dr John Conly, Dr Mark Jones and Sarah Thorning joined the review team

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 4, 2007

Date	Event	Description
7 May 2009	New search has been performed	For the 2009 update we included three cluster-randomised controlled trials (Sandora 2008 ; Cowling 2009 ; MacIntyre 2009) and one individual randomised controlled trial (Satomura 2005 , with its linked publication Kitamura 2007). We also included one retrospective cohort study (Foo 2006), one case-control study (Yu 2007) and two prospective cohort studies (Wang 2007 ; Broderick 2008). The content and conclusions of the 2007 review changed little, but the additional eight studies add more information and certainty. Our meta-analysis remains unchanged as there were no new studies for pooling
30 April 2009	New citation required but conclusions have not changed	New author joined the review team.
8 July 2008	Amended	Converted to new review format.

(Continued)

20 August 2007	Amended	Review first published Issue 4, 2007.
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CONTRIBUTIONS OF AUTHORS

Tom Jefferson (TOJ), Chris Del Mar (CDM) and Liz Dooley (LD) were responsible for drafting the protocol.

TOJ, Eliana Ferroni (EF), Bill Hewak (BH) and Adi Prabhala (AP) extracted study data and Sree Nair (SN) performed the analyses in the original review.

TOJ, EF, Lubna A Al-Ansary (LA), Ghada A Bawazeer (GB) and CDM adjudicated in data extraction in the 2009 update, and Mieke van Driel (MvD) assisted in the writing, construction of the summary of results table and updating with the most recent studies. All 2009 review authors contributed to the final report.

For the 2010 update TOJ and John Conly (JMC) extracted data and CDM checked extractions and arbitrated. All three checked the search strategy terms. Sarah Thorning designed and carried out the searches. All 2010 review authors contributed to the final report.

DECLARATIONS OF INTEREST

Chris Del Mar provided expert advice to GlaxoSmithKline about vaccination against acute otitis media in 2008-2009. He receives royalties from books published through Blackwell, BMJ Books and Elsevier.

SOURCES OF SUPPORT

Internal sources

- The Cochrane Collaboration Steering Group, UK.

External sources

- National Institute of Health Research (NIHR), UK.

Competitive grant awarded through the Cochrane Collaboration

- National Health and Medical Research Council (NHMRC), Australia.

Competitive grant to Chris Del Mar and Tom Jefferson, 2009

• Sabbatical year for John Conly while at the WHO in Geneva, Switzerland was supported by the University of Calgary, Calgary, Canada.

- World Health Organization, Geneva, Switzerland.

Requested and provided support to the Cochrane Collaboration for current update

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None, apart from the change in the title (see [Published notes](#), below).

NOTES

In Issue 1, 2010, the title was changed from *Interventions for the interruption or reduction of the spread of respiratory viruses* to *Physical interventions to interrupt or reduce the spread of respiratory viruses*.

The original review was subsequently published as Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, Hewak B, Prabhala A, Nair S, Rivetti A. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. *BMJ* 2008;336:77-80 and Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, van Driel ML, Foxlee R, Rivetti A. [Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review](#). *BMJ* 2009 Sep 21;339:b3675. doi: 10.1136/bmj.b3675.

INDEX TERMS

Medical Subject Headings (MeSH)

*Virus Shedding; Case-Control Studies; Influenza, Human [transmission; virology]; Randomized Controlled Trials as Topic; Respiratory Tract Infections [*prevention & control; transmission; virology]; Virus Diseases [*prevention & control; transmission]

MeSH check words

Humans

Achieving A Fair and Effective COVID-19 Response: An Open Letter to Vice-President Mike Pence, and Other Federal, State and Local Leaders from Public Health and Legal Experts in the United States

Sustained human-to-human transmission of the novel coronavirus in the United States (US) appears today inevitable. The extent and impact of the outbreak in the US is difficult to predict, and will depend crucially on how policymakers and leaders react. It will depend particularly on whether there is adequate funding and support for the response; fair and effective management of surging health care demand; careful and evidence-based mitigation of public fear, and necessary support and resources for fair and effective infection control.

A successful American response to the COVID-19 pandemic must protect the health and human rights of everyone in the US. One of the greatest challenges ahead is to make sure that the burdens of COVID-19, and our response measures, do not fall unfairly on people in society who are vulnerable because of their economic, social, or health status.

We write as experts in public health, law, and human rights, with experience in previous pandemic responses, to set forth principles and practices that should guide the efforts against COVID-19 in the US. It is essential that all institutions, public and private, address the following critical concerns through new legislation, institutional policies, leadership and spending.

ADEQUATE FUNDING AND SUPPORT FOR THE RESPONSE MUST BE PROVIDED

- **Federal, state and local governments should act immediately to allocate funds to ensure that necessary measures can be carried out and that basic human needs continue to be met as the epidemic unfolds.** Mitigating the impact of COVID-19 will be costly. Uneven distribution of resources will compromise collective control efforts and lead to unnecessary suffering and death. A major emergency congressional appropriation must be made for epidemic control and signed by the President, with quick disbursement to state and local actors on the frontlines of the response. In addition, these must be new funds that do not cannibalize existing health and safety net programs, nor social service programs, which are integral to protecting the public health in the long term.
- **The federal government and federal, local, and state agencies must minimize disruption to government activities throughout the epidemic to continue providing public services to those who need them.** Government must have a coordinated plan for keeping its operations running in the event of work absences. Priority should be given to essential services and support to the public, for example ensuring that Social Security, veterans' and other benefits are not disrupted.

SURGING HEALTHCARE DEMAND MUST BE MANAGED AND PATIENTS AND HEALTHCARE WORKERS PROTECTED

- **Our healthcare system will face severe burdens under all plausible scenarios. Hospitals must receive direct funding and adequate resources for enhanced surge capacity in order to handle the front-line response. Particular attention and funding must also be directed to primary care facilities and community health centers,** especially those that are currently under-resourced even under normal circumstances. These front-line sites of healthcare provision need to act as gatekeepers to prevent the

overburdening of tertiary hospitals and other acute care facilities and require support to allow them to fulfill this crucial role.

- **Healthcare workers and other first responders will be critical to the response. We must ensure their safety and give them fair working conditions.** Healthcare workers must, for example, be given adequate protective equipment, be afforded reasonable respite, and be protected from discrimination arising out of their work with infected patients.
- **Healthcare facilities must be immigration enforcement-free zones so that immigration status does not prevent a person from seeking care. The COVID-19 response should not be linked to immigration enforcement in any manner.** It will undermine individual and collective health if individuals do not feel safe to utilize care and respond to inquiries from public health officials, for example during contact tracing. Similar enforcement-free zones have been declared during hurricanes and other emergencies, including after the September 11 terrorist attacks. These policies should be clearly and unequivocally articulated to the public by the federal, state, and local governments.
- **Policymakers must work directly with insurance companies to allow all insured individuals to adhere to public health recommendations. It will be critical for policymakers to ensure comprehensive and affordable access to testing, including for the uninsured.** Control efforts will be less effective if some fail to seek appropriate diagnosis or care due to large out-of-pocket costs or copays. Out-of-network or other insurance provisions cannot be allowed to disrupt local triage and patient allocation plans.
- **If therapeutics or vaccines are developed, policymakers must assure that they are affordable and available to all.**
- **People residing in close living quarters are especially vulnerable to COVID-19 and will need special attention both to minimize transmission risk and address their healthcare needs in the context of an outbreak.** These populations include those living in nursing homes or other congregate facilities; incarcerated populations in prisons, jails, and other detention facilities along with corrections officers and other personnel; the homeless living on the streets or in homeless shelters.
- **Other critical healthcare programs must be maintained during this crisis.** People with chronic conditions depend on continuity of care to maintain their health. Whether it is dialysis for kidney disease, chemotherapy for cancer, or opioid agonist therapy for opioid use disorder, lapses in these programs can have disastrous implications for patients.

CLEAR, EVIDENCE-BASED COMMUNICATION IS CRITICAL TO MANAGE PUBLIC FEAR

- **Science needs to guide messaging to the public, and no government official should make misleading or unfounded statements, nor pressure others to do so.** Honest, transparent and timely reporting of developments will be crucial to maintaining public trust and cooperation. Suppression of information and attempts to manipulate it during the SARS epidemic in China exacerbated the crisis.¹ Clear, coherent, and uncontradictory messaging based on the best science will improve compliance and effectiveness of voluntary self-isolation, and other voluntary social distancing measures.²

¹ Jinqiu, Z. (2003). The SARS epidemic under China's media policy. *Media Asia*, 30(4), 191-196.

²Kavanagh, A.M., Bentley, R.J., Mason, K.E. et al. Sources, perceived usefulness and understanding of information disseminated to families who entered home quarantine during the H1N1 pandemic in Victoria, Australia: a cross-sectional study. *BMC Infect Dis* 11, 2 (2011).

- **Government and institutions must also actively prevent discrimination and scapegoating of individuals or groups.** In the context of COVID-19, Chinese-American and other Asian-American communities have already begun to face attacks on individuals linked to fears about the virus^{3,4}. The Centers for Disease Control and Prevention (CDC) has pointed out that such fears and misconceptions create “more fear or anger towards ordinary people instead of the disease that is causing the problem.”⁵ Local, state and federal officials should speak out against discrimination and stigma, and not use the outbreak to stoke xenophobia against Asian-Americans, other immigrant communities, and religious groups, for example.
- **Leaders should refrain from offering false assurances and should act aggressively to correct misinformation,** especially that which can incite panic and lead to hoarding of supplies and protective equipment. Governments must also provide comprehensive advice on best practices during epidemics, including proper personal hygiene and stocking up on, but not hoarding, needed supplies such as personal medications.

SUPPORT AND RESOURCES MUST BE PROVIDED FOR FAIR AND EFFECTIVE INFECTION CONTROL

- **The highest priority needs to be placed on allowing people to voluntarily cooperate with public health advice about prevention, by providing robust social and economic support and clear education.** Where social distancing measures are recommended, the government and relevant institutions should help ensure that people are in a position to comply, without excessive or unfairly distributed hardship. For example:
 - To enable people to cooperate with social distancing and other measures, policymakers must ensure that people are protected from job loss, economic hardship, and undue burden. If people are asked to avoid public transport or work, policymakers and employers should give them an explicit incentive to stay home, either with payments or by compensation for lost wages, as has been done elsewhere.^{6,7,8} Individuals will not cooperate with self-isolation or other voluntary social distancing measures if they are unable to provide for themselves and their families. For low-wage, gig-economy, and non-salaried workers, staying home from work has especially critical implications for economic survival.
 - The elderly and disabled are at particular risk when their daily lives and support systems are disrupted. Many have limited resources and depend on others to assist with care. Policymakers must explicitly accommodate these populations when making self-isolation recommendations.

³ <https://www.cnn.com/2020/02/20/us/coronavirus-racist-attacks-against-asian-americans/index.html>

⁴ <https://www.latimes.com/california/story/2020-02-03/fear-panic-around-the-coronavirus-fuels-racist-sentiment>

⁵ <https://www.cdc.gov/coronavirus/2019-ncov/about/related-stigma.html>

⁶ For example, Britain’s Health Secretary Matt Hancock sent guidance to employers recommending that staff who have been asked to self-isolate be able to clock that time as sick leave. See *Coronavirus: inquiry opens into hospitals at centre of Italy outbreak*, Guardian (Feb. 26, 2020), <https://www.theguardian.com/world/2020/feb/26/coronavirus-inquiry-opens-into-hospitals-at-centre-of-italy-outbreak>.

⁷ See, e.g., *Hong Kong to give cash gift of \$1,200 to residents*, BBC News (Feb. 26, 2020), <https://www.bbc.com/news/world-asia-china-51640456>.

⁸ Pichler, Stefan, Katherine Wen, and Nicolas R. Ziebarth. “Positive Health Externalities of Mandating Paid Sick Leave.” (February 2020)

- **Policymakers should base decisions on social distancing measures and closures on the best available science.** Employers, institutions, and schools should proactively determine adaptations and accommodations for closures (e.g. tele-communication or virtual education). These measures have been effective in mitigating the transmission of influenza.⁹ The abundance of evidence about influenza can help inform control efforts, but it will be important to recognize differences in the epidemiology of the diseases.
- **Special attention must be paid to the needs of people in long-term care or confinement, who are particularly vulnerable.** People in nursing homes, long-term care, and the incarcerated and homeless are at special risk of infection, given their living situations. These individuals may also be less able to participate in proactive measures to keep themselves safe, and infection control is challenging in these settings. Arrest and short-term incarceration can help amplify epidemics, and broader criminal justice policies should take into account the impact that policing and arrest policies have on health.
- **Mandatory quarantine, regional lockdowns and travel bans have been used to address the risk of COVID-19 in the US and abroad. But they are difficult to implement, can undermine public trust, have large societal costs and, importantly, disproportionately affect the most vulnerable segments in our communities.** Such measures can be effective only under specific circumstances. All such measures must be guided by science, with appropriate protection of the rights of those impacted. Infringements on liberties need to be proportional to the risk presented by those affected, scientifically sound, transparent to the public, least restrictive means to protect public health, and regularly revisited to ensure that they are still needed as the epidemic evolves.¹⁰
- **Voluntary self-isolation measures are more likely to induce cooperation and protect public trust than coercive measures, and are less likely to prevent attempts to avoid contact with the healthcare system.**¹¹ For mandatory quarantines to be effective and therefore scientifically and legally justified, three main criteria must be satisfied:¹² 1) the disease has to be transmissible in its presymptomatic or early symptomatic stages; 2) those who may have been exposed to COVID-19 must be able to be efficiently and effectively identified; and 3) those people must comply with the conditions of quarantine. There is evidence that COVID-19 is transmitted in its pre-symptomatic or early symptomatic stages.¹³ However, the contribution of infected individuals in their pre-symptomatic or early symptomatic stages to overall transmission is unknown. Efficiently identifying those exposed will be increasingly difficult as community transmission of the virus becomes more widespread, making quarantine a less plausible measure as community spread proceeds. Whether individuals can comply will be determined by the degree of support provided, particularly for low-wage workers and other vulnerable communities. While quarantines are in effect in many places already, their continuing and new use by federal, state or local

⁹ See Community Mitigation Guidelines to Prevent Pandemic Influenza — United States, 2017. MMWR Recomm Rep 2017;66(No. RR-1):1–34.

¹⁰ Abdo, A., Batman, S., Bhandari, E., Boyko, R., Goldberg, R.C., Gonsalves, G., Gonzalez, D.J.X., Kalu, E., Kapczynski, A., Roth, E., Stanley, J. "Fear, Politics, and Ebola: How Quarantines Hurt the Fight Against Ebola and Violate the Constitution" ACLU, GHJP (2015) <https://law.yale.edu/sites/default/files/area/center/ghjp/documents/fearpoliticsebola.pdf>.

¹¹ Aledort, Julia E.; Lurie, Nicole; Wasserman, Jeffrey; Bozzette, Samuel A. BMC Public Health. 2007, Vol. 7 Issue 1, p208-9..

¹² Schabas, Richard. "Severe acute respiratory syndrome: Did quarantine help?." *Canadian Journal of Infectious Diseases and Medical Microbiology* 15, no. 4 (2004): 204-204.

¹³ Park, Sang Woo, David Champredon, David JD Earn, Michael Li, Joshua S. Weitz, Bryan T. Grenfell, and Jonathan Dushoff. "Reconciling early-outbreak preliminary estimates of the basic reproductive number and its uncertainty: a new framework and applications to the novel coronavirus (2019-nCoV) outbreak." *medRxiv* (2020).

officials requires real-time assessment and evaluation to justify them as the science and the outbreak evolve, through a transparent, open decision making process including external scientific and legal experts.

- **Public health officials must provide safe and humane conditions to individuals who are quarantined whether in homes, facilities or communities. Government must ensure that anyone isolated or quarantined has access to the basic necessities, including food, water, medicine, and sanitation supplies.** Assistance should be provided to individuals who are in need of support to maintain daily living, and attention must be given to religious and communication needs. The failure to do so will undermine trust, adherence to the intervention and the overall effectiveness of quarantine. It will also be imperative not to impose inhumane or discriminatory conditions, as occurred on the Diamond Princess cruise ship, where passengers were quarantined to protect the population on land but were isolated in a high transmission setting. Furthermore, safe and humane conditions need to be provided to *all* quarantined individuals and do not differentiate between social or economic strata, or in the case of the Princess Diamond, between passengers and workers.
- **Where mandatory measures are used, steps must be taken to ensure that people are protected from job loss, economic hardship, and undue burden.** Government and employers must recognize that low-wage, gig-economy, and non-salaried workers who are unable to work because of quarantine or movement restrictions or other disruptions to the economy and public life face extraordinary challenges. They may find it impossible to meet their basic needs, or those of their family.
- **Individuals must be empowered to understand and act upon their rights.** Information should be provided on the justification of any mandatory restrictions as well as how and where to appeal such decisions. They should be afforded procedural due process, including universal access to legal counsel, to ensure their claims of discrimination or of hazardous conditions associated with their confinement are adjudicated.
- **The effectiveness of regional lockdowns and travel bans depends on many variables, and also decreases in the later stages of an outbreak.** Though the evidence is preliminary, a recent modeling study suggests that in China these measures may have mitigated but not contained the spread of the COVID-19 epidemic, delaying it locally by a few days, while having a more marked, though still modest, effect at the international scale, particularly if not combined with measures that achieved at least 50% reduction of transmission in the community.¹⁴ Travel restrictions also cause known harms, such as the disruption of supply chains for essential commodities.¹⁵ The authors of a recent review of research on the subject concluded that “the effectiveness of travel bans is mostly unknown” and “when assessing the need for, and validity of, a travel ban, given the limited evidence, it’s important to ask if it is the least restrictive measure that still protects the public’s health, and even if it is, we should be asking that question repeatedly, and often.”¹⁶

The COVID-19 outbreak is unprecedented in modern American history and there is no playbook for an epidemiological event of this scope and magnitude. To mitigate its impact, you must act swiftly, fairly, and effectively. We urge you to take these recommendations seriously, and act urgently so that we are best protected

¹⁴ Chinazzi, Matteo, Jessica T. Davis, Marco Ajelli, Corrado Gioannini, Maria Litvinova, Stefano Merler, Ana Pastore y Piontti et al. “The effect of travel restrictions on the spread of the 2019 novel coronavirus (2019-nCoV) outbreak.” *medRxiv*(2020).

¹⁵ <https://www.vox.com/2020/1/23/21078325/wuhan-china-coronavirus-travel-ban>

¹⁶ <https://www.sciencedaily.com/releases/2020/02/200213175923.htm>

from the damage of this unprecedented microbial threat and the possible harms of an uninformed or poorly conceived response.

* * *

[We thank Hanna Ehrlich, Rita Gilles, Mary Petrone and Kayoko Shioda, students at Yale School of Public Health and Yale Law School, for their assistance in the research and writing of this document.]

The letter will be sent to federal officials midday on Monday, March 2nd, but it will remain open for sign-ons at covid19.openletter@gmail.com and the online version of the letter will be updated as those new endorsements come in.

(Last updated at 4:56 PM on March 1)

[writing group]*

Signed (affiliations for identification purposes only),

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156. Michael A. Rodriguez, Professor and Vice Chair, Department of Family Medicine, David Geffen School of Medicine at UCLA; Professor, Department of Community Health Sciences, UCLA Fielding School of Public Health; Chair, UCLA Global Health Minor; Director, Health Equity Network of the Americas

Organizational Signatures

1. Broken No More
2. The Public Health Advocacy Institute
3. Big Cities Health Coalition

From: [Bogan, Sharon](#)
To: [Kay, Meagan](#)
Cc: [Duchin, Jeff](#); [Kawakami, Vance](#)
Subject: RE: FOR APPROVAL_ KEY MESSAGES
Date: Sunday, March 1, 2020 3:44:51 PM

Hi Meagan,

I imagine you are saying this statement may not be accurate. *"We are not recommending self-quarantining asymptomatic people regardless of their contact with COVID 19- cases (with the potential exception of people who entered LifeCare Kirkland)."*

To help us understand, **Can you say yes or no to each of these specific groups regarding whether they should self-quarantine?**

1. Recent travels to countries with widespread or ongoing community spread of COVID-19
2. Asymptomatic close contacts of presumed positive COVID_19
3. Contacts of asymptomatic LIFECARE staff and residents

Thanks-
Sharon

From: Bogan, Sharon
Sent: Sunday, March 1, 2020 3:21 PM
To: Kay, Meagan <Meagan.Kay@kingcounty.gov>
Cc: Duchin, Jeff <Jeff.Duchin@kingcounty.gov>; Kawakami, Vance <Vance.Kawakami@kingcounty.gov>
Subject: RE: FOR APPROVAL_ KEY MESSAGES

Thanks Meagan. Can you highlight specifically what pieces are not accurate regarding quarantine?

From: Kay, Meagan <Meagan.Kay@kingcounty.gov>
Sent: Sunday, March 1, 2020 3:21 PM
To: Bogan, Sharon <Sharon.Bogan@kingcounty.gov>
Cc: Duchin, Jeff <Jeff.Duchin@kingcounty.gov>; Kawakami, Vance <Vance.Kawakami@kingcounty.gov>
Subject: Re: FOR APPROVAL_ KEY MESSAGES

Sharon- I don't think these are accurate around quarantine. We are still waiting for recommendations

From: Bogan, Sharon <Sharon.Bogan@kingcounty.gov>
Sent: Sunday, March 1, 2020 3:07:48 PM
To: Kay, Meagan <Meagan.Kay@kingcounty.gov>
Cc: Duchin, Jeff <Jeff.Duchin@kingcounty.gov>; Kawakami, Vance

<Vance.Kawakami@kingcounty.gov>

Subject: FOR APPROVAL_ KEY MESSAGES

Meagan, Jeff and Vance,

These are the most important responses we need approval on. This content will be used for multiple messaging purposes.

PLEASE REVIEW, MAKE EDITS, AND APPROVE.

Thank you-

Sharon

UPDATED CONTENT FOR KEY MESSAGES

3.1.20 3:00 pm

1. **Guidance for contacts of presumed cases including Lifecare employees and residents:**

- If someone has respiratory illness and is an employee or resident of LifeCare, we are assuming they have COVID-19.
- We are not quarantining asymptomatic people regardless of their contact with COVID 19- cases (with the potential exception of people who entered LifeCare Kirkland).

Category 1: Contacts of the *asymptomatic* contacts of: any of the following: 1. confirmed cases, 2. PUIs, or 3. other LifeCare employees/residents **are not considered exposed.**

If you fall into this category and do develop symptoms, you should self-quarantine and contact your healthcare provider.

Example: Joni is a nurse at Lifecare. She is not sick. Mike lives with Joni. Mike does not need to self quarantine, nor does he need evaluation or testing for COVID-19.

If Joni gets sick, then Mike takes his temperature every day and watches himself carefully for any symptoms, but continues his life normally otherwise.

Joni should self-quarantine and call her healthcare provider.

Category 2: People who have entered the LifeCare Kirkland facility or for close contacts of LifeCare employees/residents who are sick.

They need to be self-monitoring – temperature checks daily, but they do not need to self-quarantine. If they develop any symptoms, they should immediately self-isolate and call their healthcare provider and Public Health: 206-296-4774

Example:

- Casey, (fake name) is a Lake Washington Technical student who went into LifeCare to clean. She is not sick. We do not yet have guidance on whether she needs to self-quarantine.
- Bob visited his grandmother at LifeCare. Bob's grandmother isn't sick. We do not yet have guidance on whether Bob needs to self-quarantine.
- Frank goes to lunch with his friend who is a LifeCare employee. The LifeCare employee now has symptoms and is a PUI. Self-monitor for 14 days. Go to work.

2.Can we confirm that community transmission is occurring? (We have been saying that specific cases are community transmission, but are we saying community transmission in King County?)

We have multiple (3) confirmed COVID-19 cases that currently do not have known contact with LifeCare, anyone who's been at LifeCare, or known travel. We are intensively investigating to understand the spread of the disease.djdjh;

3. Should employers and school administrators require healthcare provider documentation or a COVID-19 negative test before letting people enter?

Employers, and school administrators should not require any letter or documentation from employees' health care providers about their COVID-19 status. This will overwhelm the healthcare system and is not recommended as a measure to protect public health at this time.

4. Who should be tested for COVID-19? If we're not recommending wide-spread testing, why not?

We're not currently recommending widespread testing.

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We anticipate testing guidance to change in the near term as more testing comes on-line

at commercial laboratories.

More detail not for the public:

There are 3 categories of people recommended for testing:

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2. People hospitalized with severe pneumonia with unknown cause.
3. People who have traveled in the last 14 days to a country with widespread or ongoing community spread of COVID-19, and have fever, cough or shortness of breath, contact your healthcare provider about potential testing. For more information, visit the CDC's webpage: <https://www.cdc.gov/coronavirus/2019-ncov/faq.html#symptoms>

If someone meets the first criteria, they should contact their healthcare provider (call, do not attend in-person) and call the Public Health Communicable Disease team: 206-296-4774

5. **Guidance on social distancing**

Should schools cancel assemblies, sporting events or gatherings? We do not have any formal CDC recommendations for avoiding gatherings or events, and we are not recommending cancelling events at this time. However, people who are at higher risk, such as those with underlying health conditions such as heart disease, lung disease or who are immune compromised, may want to consider ways to lower their risk such as limiting with large numbers of people. Talk to your doctor to make a plan based on your specific health conditions.

Social distancing clarification

People who are over 60 (**DO WE REALLY WANT TO SAY THAT PEOPLE OVER 60 should consider avoiding contact with large numbers of people?**)

People with underlying health conditions may want to consider ways to lower their risk, such as: avoiding close contacts with large numbers of people.

Sharon Bogan
Communications

(she/her pronouns)

Public Health – Seattle & King County

401 5th Avenue | Seattle, WA 98104

206.263.8770 | sharon.bogan@kingcounty.gov

[Facebook](#) | [Twitter](#) | [Public Health Insider](#) | [Newsletter](#)

From: [Bogan, Sharon](#)
To: [Kay, Meagan](#)
Cc: [Duchin, Jeff](#); [Kawakami, Vance](#)
Subject: RE: FOR APPROVAL_ KEY MESSAGES
Date: Sunday, March 1, 2020 3:21:29 PM

Thanks Meagan. Can you highlight specifically what pieces are not accurate regarding quarantine?

From: Kay, Meagan <Meagan.Kay@kingcounty.gov>
Sent: Sunday, March 1, 2020 3:21 PM
To: Bogan, Sharon <Sharon.Bogan@kingcounty.gov>
Cc: Duchin, Jeff <Jeff.Duchin@kingcounty.gov>; Kawakami, Vance <Vance.Kawakami@kingcounty.gov>
Subject: Re: FOR APPROVAL_ KEY MESSAGES

Sharon- I don't think these are accurate around quarantine. We are still waiting for recommendations

From: Bogan, Sharon <Sharon.Bogan@kingcounty.gov>
Sent: Sunday, March 1, 2020 3:07:48 PM
To: Kay, Meagan <Meagan.Kay@kingcounty.gov>
Cc: Duchin, Jeff <Jeff.Duchin@kingcounty.gov>; Kawakami, Vance <Vance.Kawakami@kingcounty.gov>
Subject: FOR APPROVAL_ KEY MESSAGES

Meagan, Jeff and Vance,

These are the most important responses we need approval on. This content will be used for multiple messaging purposes.

PLEASE REVIEW, MAKE EDITS, AND APPROVE.

Thank you-

Sharon

UPDATED CONTENT FOR KEY MESSAGES

3.1.20 3:00 pm

1. **Guidance for contacts of presumed cases including Lifecare employees and residents:**
 - If someone has respiratory illness and is an employee or resident of LifeCare, we are assuming they have COVID-19.
 - We are not quarantining asymptomatic people regardless of their contact with COVID 19- cases (with the potential exception of people who

entered LifeCare Kirkland).

Category 1: Contacts of the *asymptomatic* contacts of: any of the following: 1. confirmed cases, 2. PUIs, or 3. other LifeCare employees/residents **are not considered exposed.**

If you fall into this category and do develop symptoms, you should self-quarantine and contact your healthcare provider.

Example: Joni is a nurse at Lifecare. She is not sick. Mike lives with Joni. Mike does not need to self quarantine, nor does he need evaluation or testing for COVID-19.

If Joni gets sick, then Mike takes his temperature every day and watches himself carefully for any symptoms, but continues his life normally otherwise.

Joni should self-quarantine and call her healthcare provider.

Category 2: People who have entered the LifeCare Kirkland facility or for close contacts of LifeCare employees/residents who are sick.

They need to be self-monitoring – temperature checks daily, but they do not need to self-quarantine. If they develop any symptoms, they should immediately self-isolate and call their healthcare provider and Public Health: 206-296-4774

Example:

- Casey, (fake name) is a Lake Washington Technical student who went into LifeCare to clean. She is not sick. We do not yet have guidance on whether she needs to self-quarantine.
- Bob visited his grandmother at LifeCare. Bob's grandmother isn't sick. We do not yet have guidance on whether Bob needs to self-quarantine.
- Frank goes to lunch with his friend who is a LifeCare employee. The LifeCare employee now has symptoms and is a PUI. Self-monitor for 14 days. Go to work.

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Social distancing clarification

People who are over 60 (**DO WE REALLY WANT TO SAY THAT PEOPLE OVER 60 should consider avoiding contact with large numbers of people?**)

People with underlying health conditions may want to consider ways to lower their risk, such as: avoiding close contacts with large numbers of people.

Sharon Bogan
Communications
(she/her pronouns)
Public Health – Seattle & King County
401 5th Avenue | Seattle, WA 98104
206.263.8770 | sharon.bogan@kingcounty.gov
[Facebook](#) | [Twitter](#) | [Public Health Insider](#) | [Newsletter](#)

From: [Kay, Meagan](#)
To: [Bogan, Sharon](#)
Cc: [Duchin, Jeff](#); [Kawakami, Vance](#)
Subject: Re: FOR APPROVAL_ KEY MESSAGES
Date: Sunday, March 1, 2020 3:20:32 PM

Sharon- I don't think these are accurate around quarantine. We are still waiting for recommendations

From: Bogan, Sharon <Sharon.Bogan@kingcounty.gov>
Sent: Sunday, March 1, 2020 3:07:48 PM
To: Kay, Meagan <Meagan.Kay@kingcounty.gov>
Cc: Duchin, Jeff <Jeff.Duchin@kingcounty.gov>; Kawakami, Vance <Vance.Kawakami@kingcounty.gov>
Subject: FOR APPROVAL_ KEY MESSAGES

Meagan, Jeff and Vance,

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PLEASE REVIEW, MAKE EDITS, AND APPROVE.

Thank you-

Sharon

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3.1.20 3:00 pm

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206.263.8770 | sharon.bogan@kingcounty.gov
[Facebook](#) | [Twitter](#) | [Public Health Insider](#) | [Newsletter](#)

From: [McKeirnan, Shelly](#)
To: [Morrison, Amy](#)
Cc: [Kay, Meagan](#); [Brostrom-Smith, Claire](#); [Clark, Shauna](#); [Valenzuela, Matias](#)
Subject: RE: Follow-up to our call earlier this evening
Date: Monday, March 2, 2020 10:00:01 AM

Thanks Amy, yes, the recommendation from Public Health (based on CDC recommendations) is for these students and faculty who were at LifeCare SNF to quarantine themselves at home for 14 days from their last exposure at SNF and they should be doing self-monitoring (more details on how to do this in the document I sent to you). All the faculty and staff who spent time at LifeCare recently are considered exposed. As of yesterday, there are 6 confirmed cases of COVID-19 infection in residents/staff of LifeCare with more testing in process.

Thanks, Shelly

Shelly McKeirnan (she/her), BSN MPH | Public Health Services Supervisor | Communicable Disease Epidemiology & Immunization Section | 401 5th Ave., Suite 1250 | Seattle WA 98104 | P: 206.296.4774 (Main) | P: 206.263.8195 (Direct) | F: 206.296.4803 | <http://www.kingcounty.gov/health/cd>
My normal work week is M-F (off work every other Wednesday)

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From: Morrison, Amy <Amy.Morrison@lwtech.edu>
Sent: Monday, March 2, 2020 8:26 AM
To: McKeirnan, Shelly <Shelly.McKeirnan@kingcounty.gov>
Cc: Kay, Meagan <Meagan.Kay@kingcounty.gov>; Brostrom-Smith, Claire <Claire.Brostrom-Smith@kingcounty.gov>; Clark, Shauna <shclark@kingcounty.gov>; Valenzuela, Matias <Matias.Valenzuela@kingcounty.gov>
Subject: RE: Follow-up to our call earlier this evening

[EXTERNAL Email Notice!] External communication is important to us. Be cautious of phishing attempts. Do not click or open suspicious links or attachments.

Thank you Shelly,

I have communicated your request for self-monitoring with the anticipated final plan to self-quarantine to students and faculty at LifeCare. We are assessing what they need to do in order to be better prepared.

Please call me today any time at 425-256-1981.

Thanks.

Amy

From: McKeirnan, Shelly [<mailto:Shelly.McKeirnan@kingcounty.gov>]

Sent: Sunday, March 1, 2020 11:00 PM

To: Morrison, Amy <Amy.Morrison@lwtech.edu>

Cc: Kay, Meagan <Meagan.Kay@kingcounty.gov>; Brostrom-Smith, Claire <Claire.Brostrom-Smith@kingcounty.gov>; Clark, Shauna <shclark@kingcounty.gov>; Valenzuela, Matias <Matias.Valenzuela@kingcounty.gov>

Subject: Follow-up to our call earlier this evening

EXTERNAL SENDER: Use caution with links and attachments

Hi Amy, thanks so much for speaking with me earlier. I appreciate your concern for your students and faculty and I am sure this has been a challenging situation for you and the school. As I mentioned when we spoke, I am emailing you information on self-monitoring and quarantine (the self-monitoring information and chart for documentation are at the end of this document) for you to review. As I mentioned, based on the information we have about the risk assessment, we are recommending home quarantine and self-monitoring for the nursing and physical therapy students and staff who were at the Lifecare SNF in the last 14 days. The period of monitoring/quarantine is for 14 days after last exposure at LifeCare. This is based on the information that the students/faculty were providing clinical care to residents of LifeCare SNF at the SNF.

As of earlier this afternoon, we have 10 confirmed cases of COVID-19 in King County residents, 6 of the 10 are residents/staff of LifeCare SNF, status update online at:

<https://www.kingcounty.gov/depts/health/news/2020/March/1-covid19-4-cases.aspx>

I understand you have concerns about the quarantine recommendation and the hardships for some of the students/staff, and we can discuss this further tomorrow. I will have one of our staff cc'ed on this email contact you tomorrow by email or call. I understand you want a final plan for management of the exposed students/faculty by the end of the day tomorrow. We will also reach out to the faculty member who is ill (thanks for her contact information and for letting her know we will be contacting her). If you get more information on the student who is not feeling well, we can follow-up with that person also.

Thanks, Shelly

Shelly McKeirnan (she/her), BSN MPH | Public Health Services Supervisor | Communicable Disease Epidemiology & Immunization Section | 401 5th Ave., Suite 1250 | Seattle WA 98104 | P: 206.296.4774 (Main) | P: 206.263.8195 (Direct) | F: 206.296.4803 | <http://www.kingcounty.gov/health/cd>
My normal work week is M-F (off work every other Wednesday)

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NOTICE OF PUBLIC DISCLOSURE: RCW 42.56 says that this e-mail account is public domain. What you write is a public record.

From: [Ulrey, Ingrid](#)
To: [Smith, Rachel](#)
Cc: [Hayes, Patty](#); [Schaeffer, Cyndi](#); [Bauer, Brenda](#); [Worsham, Dennis](#); [Wysen, Kirsten](#); [Burkland, Anne](#); [Braddock, Shannon](#)
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow
Date: Sunday, March 1, 2020 11:59:02 AM
Attachments: [PH Update Challenge Seattle 3.1.2020.docx](#)

Hi everyone,

Attached please find the TPs for our 1:30pm phone call today with Challenge Seattle.

Please send me any suggested additions or edits by 1pm.

I did not include any specific information in her about emergency proclamation or specifics on structure of our Business sector outreach. I am using already vetted info from TPs from our press advisory today and TPs from yesterday.

Thank you,

Ingrid Ulrey

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Sent: Sunday, March 1, 2020 11:56 AM
To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Thanks Ingrid, look forward to your notes.

Rachel Smith
Deputy County Executive | Chief of Staff
King County Executive Dow Constantine
D: 206.263.9628 | C: 206.790.9168 | rachel.smith@kingcounty.gov

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>

Sent: Sunday, March 1, 2020 11:04 AM

To: Smith, Rachel <Rachel.Smith@kingcounty.gov>

Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>

Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi Rachel

I will be joining the 1:30pm call today to provide the PH update.

I will send the talking points for you and others on this chain to review in advance within 30 minutes.

Patty, Jeff and Dennis are unavailable.

Kirsten Wysen on my team will also dial in, she will be on point for us ongoing for business sector outreach.

Will you be on the call?

Do you want me to RSVP with this info to Colleen or would you prefer to?

Thank you

Ingrid

Ingrid Ulrey, MPP (she/her)

Policy Director

Public Health – Seattle & King County

Phone: 206.477.7019

Ingrid.Ulrey@kingcounty.gov

From: Smith, Rachel <Rachel.Smith@kingcounty.gov>

Sent: Sunday, March 1, 2020 9:09 AM

To: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>

Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>

Subject: Re: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Thanks all.

Rachel Smith
Deputy County Executive | Chief of Staff
King County Executive Dow Constantine
D: 206.263.9628 | C: 206.790.9168
rachel.smith@kingcounty.gov

From: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>
Sent: Sunday, March 1, 2020 9:02:07 AM
To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>; Smith, Rachel <Rachel.Smith@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Wyses, Kirsten <Kirsten.Wyses@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

I am happy to review the talking points – Ingrid – thank you for covering.

I am trying to stay closely linked to CDC and our Infectious Disease team as we develop and implement strategies in this rapid response.

Dennis E. Worsham (he/him)

Prevention Division Director
Public Health – Seattle & King County
P - (206) 263-8158

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Sent: Sunday, March 1, 2020 8:56 AM
To: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wyses, Kirsten <Kirsten.Wyses@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi Rachel -

Patty, Dennis are not available and Jeff is maxed.

I will cover this – will send key TPs to all before the call.

Ingrid

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019

Ingrid.Ulrey@kingcounty.gov

From: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Sent: Sunday, March 1, 2020 8:49 AM
To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>; Colleen Daly <codaly@microsoft.com>
Cc: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wyses, Kirsten <Kirsten.Wyses@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>
Subject: Re: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi Ingrid - I already forward call in info to your inbox. Thanks!

Rachel Smith
Deputy County Executive | Chief of Staff
King County Executive Dow Constantine
D: 206.263.9628 | C: 206.790.9168
rachel.smith@kingcounty.gov

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Sent: Sunday, March 1, 2020 8:43:12 AM
To: Colleen Daly <codaly@microsoft.com>
Cc: Smith, Rachel <Rachel.Smith@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wyses, Kirsten <Kirsten.Wyses@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Thank you Colleen

Helpful to understand, I am coordinating with Rachel and identifying who from our team will be on the call.

Can you kindly send dial in information for the call? Correct that it is one hour total and you want the PH update at the beginning?

Ingrid

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Colleen Daly <codaly@microsoft.com>
Sent: Sunday, March 1, 2020 8:38 AM

To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>

Cc: Smith, Rachel <Rachel.Smith@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>

Subject: Re: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

These are the items businesses are spinning on.

- Should they cancel events and conferences?
- Should they implement travel restrictions beyond what the CDC has issued?
- When should they tell employees to work from home?

I have maintained with my leadership that we don't need to take action on above unless you or the CDC issues guidance. Following the current interim guidance from the CDC is sufficient. But since this an emotional situation we are seeing businesses struggle to stay grounded. A reminder/reinforcement from your office to this group would be helpful.

Colleen

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>

Sent: Sunday, March 1, 2020 7:39:27 AM

To: Colleen Daly <codaly@microsoft.com>

Cc: Smith, Rachel <Rachel.Smith@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <anne.burkland@kingcounty.gov>

Subject: [EXTERNAL] FW: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Dear Colleen,

Thank you for contacting our team with this request.

We are coordinating with Executive Constantine's office to respond.

I understand from Kirsten Wysen that you need to know by 10am.

Thank you,

Ingrid Ulrey
Cell 206-330-6531

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019

Ingrid.Ulrey@kingcounty.gov

From: Colleen Daly <codaly@microsoft.com>

Sent: Saturday, February 29, 2020 5:49 PM

To: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Kay, Meagan <Meagan.Kay@kingcounty.gov>

Subject: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hello,

First my leadership team was extremely appreciative of your assistance today around the cases. Tomorrow, members of Challenge Seattle, which has the 17 largest private-sector employers in the region are meeting at 1:30pm. Brad Smith our head of Corporate and Legal Affairs just spoke with Christine Gregoire. She said the meeting has a representative from Kaiser, but thought it would be very valuable to have a representative from your team. They would like someone that can best speak to what businesses should do. Specifically help the businesses to stay grounded in science and the current guidance. We are seeing an increasing trend business making reactive decisions versus informed decision. Can you please make a recommendation of who from your team can attend and I will make an introduction to Brad Smith to coordinate?

Colleen M Daly, PhD, MPH

Global Benefits Manager, Healthcare Transformation

COVID-19 Talking Points for Seattle Challenge

Prepared on 3/1/2020

Public Health Update

Intro

Thank you for the opportunity to join your call today. My name is Ingrid Ulrey, I am the Policy Director at Public Health – Seattle King County. Our Director, Patty Hayes and Health Officer Dr. Jeff Duchin are unable to be with you today because they are leading our outbreak response, in coordination with the State Department of Health, and as of last night a specialized team from the CDC.

I am here to offer their deep appreciation to you for your leadership in protecting the health of your employees and the broader community. I will provide the latest updates on the outbreak in King County, describe our overall response work and share guidance for employers.

As the largest employers in our region you are critical partners. We have already been in close contact with several of you and have established a Health and Medical Area Command (HMAC) Business Sector outreach group, which will be staffed by Kirsten Wysen from Public Health, in conjunction with leaders from Executive Dow Constantine's office. We will follow up with Colleen following this meeting to discuss our process for maintaining close coordination with you all.

Latest

COVID-19 test results have come back from the State Public Health Laboratory confirming two additional cases of COVID-19 in King County residents. With these two new results, the total number of cases in King County is six. This number is expected to rise as more people are tested and results confirmed.

The two new cases are in:

- A male in his 60s, hospitalized at Valley Medical Center in Renton. The man has underlying health conditions, and is in critical but stable condition.
- A male in 60s, hospitalized at Virginia Mason Medical Center. The man has underlying health conditions, and his status is critical.

Four other cases, already reported earlier by Public Health, include:

- A woman in her 50s, who had traveled to South Korea; recovering at home
- A woman in her 70s, who was a resident of LifeCare in Kirkland, hospitalized at EvergreenHealth
- A woman in her 40s, employed by LifeCare, who is hospitalized at Overlake Medical Center

- A man in his 50s, who was hospitalized and died at EvergreenHealth

Public Health is aware that the U.S. Postal Service is reporting that one of its employees was diagnosed with COVID-19. This person was one of the four cases already reported, and is included in the six total cases.

Public Health is leading the effort to as quickly as possible identify close contacts of these six confirmed cases. These close contacts may include family members, co-workers, emergency responders and other contacts. A team of CDC officials is on-the-ground working with Public Health, along with the Washington state Department of Health, our healthcare system partners and many others.

King County / Public Health – Seattle King County Response

- King County government is coordinating together with Public Health to share information, deploy resources, and respond at the maximum capacity we are able.
- Public Health – Seattle & King County is fully activated through its Incident Command structure. We are conducting disease investigations, mitigation planning and coordinating communications.
- We are in close contact with CDC, State DOH, hospitals, the Emergency Medical Services system, as well as our state and federal delegation. CDC in particular is providing close assistance, and sent a high level team to King County to help with the response.
- This is a troubling situation that health officials have been warning could happen. We have experience in responding to pandemics and our health officials have tremendous expertise and skills, but this is a very quickly-moving situation and information is changing daily.

Business Sector Guidance

First, everyone should adhere public health guidance to the general public is as follows:

- 1) **Do not go to the emergency room unless essential.** Emergency rooms need to be able to serve those with the most critical needs. If you have symptoms like cough, fever, or other respiratory problems, contact your regular doctor first.
- 2) Stay home when sick
- 3) Practice excellent personal hygiene habits, including handwashing, coughing into tissue or elbow, avoid touching eyes, nose, or mouth.

- 4) Stay informed. Information is changing frequently. Check and subscribe to Public Health's website (www.kingcounty.gov/COVID) or blog (www.kingcounty.gov)

In addition, the CDC has issues interim guidance specifically for businesses and employers to plan and respond to the COVID-19. (see 2-page handout attached)

This guidance includes -

1. Personal Preparedness/Readiness
2. Communication
3. Performing Critical Functions
4. Continuity of Business Operations
5. Participate robustly in implementing 13 strategies to reduce the spread of the virus

The 13 strategies will be rolled out in in the next weeks and months, depending on how the crisis unfolds. They start with the least intensive and move to the more restrictive one based on how the spread takes place:

1. Increase hand washing and use of alcohol-based sanitizer
2. Respiratory hygiene and cough etiquette
3. Keep distance from others (> 6 feet) avoid,
4. Frequently clean and disinfect surfaces
5. Remain home during a respiratory illness
6. Voluntary isolation of sick persons
7. Voluntary quarantine of contacts of sick persons
8. Involuntary isolation of sick persons
9. Involuntary quarantine of contacts of sick persons
10. Recommend or order cancellation of major public and large private gatherings
11. Recommend or order closure of schools, child care facilities, workplaces, and public buildings
12. Prevent non-emergency travel outside of the home
13. Establish cordon sanitaire (isolate a geographic area)

This framework / ramped up approach from CDC, DOH and PHSKC will guide the next phase of work.

We are all in this together, and we are in it for the long haul. The best public health scientists are working 24/7 on how to respond and they have practiced how to respond to an outbreak for years. We have substantial experience from H1N1, SARS, MERS, Zika and Ebola. Be ready for major changes in your thinking and emotions related to Covid-19. Be ready for major changes in our daily lives and our work together. Self-care and staying calm are important for the next few months.

Answers to Key Questions

- **Should you cancel events and conferences?**

Not yet but stay tuned, and monitor PHSKC, DOH and CDC websites.

Events and gatherings should use stepped up infection prevention practices, such as hand washing signs and hand washing/hand sanitizing stations)

We don't have enough data to recommend cancelling events. CDC, DOH, PHSKC are working now on establishing a clear trigger for this recommendation. per Duchin this AM.

- **Should they implement travel restrictions beyond what the CDC has issued?**

Some employers are voluntarily limiting non-essential travel. This is no required.

- **When should they tell employees to work from home?**

If employees are sick they should stay home stay home

At this point, interim guidance from CDC does not suggest asking others to work from home, but some employer may choose to do so as a precautionary measure.

For more information:

www.kingcounty.gov/COVID

<https://www.doh.wa.gov/Emergencies/Coronavirus>

<https://www.cdc.gov/coronavirus/2019-ncov/index.html>

From: [Ulrey, Ingrid](#)
To: [Smith, Rachel](#)
Cc: [Hayes, Patty](#); [Schaeffer, Cyndi](#); [Bauer, Brenda](#); [Worsham, Dennis](#); [Wysen, Kirsten](#); [Burkland, Anne](#); [Braddock, Shannon](#)
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow
Date: Sunday, March 1, 2020 12:17:12 PM
Attachments: [Businesses-CDC-COVID-19 Pandemic Planning Guide022720.pdf](#)
[PH Update Challenge Seattle 3.1.2020.docx](#)

Hi all –

Regarding the Seattle Challenge call today -

Attached FYI - is the 2-page summary of CDC guide for businesses and organizations referenced in the talking points. Also including TPs again for reference.

Shannon – will touch based with you on getting them this in advance of the call.

Ingrid

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Ulrey, Ingrid
Sent: Sunday, March 1, 2020 11:59 AM
To: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Cc: Hayes, Patty <Patty.Hayes@kingcounty.gov>; Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Bauer, Brenda <Brenda.Bauer@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Braddock, Shannon <Shannon.Braddock@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi everyone,

Attached please find the TPs for our 1:30pm phone call today with Challenge Seattle.

Please send me any suggested additions or edits by 1pm.

I did not include any specific information in her about emergency proclamation or specifics on structure of our Business sector outreach. I am using already vetted info from TPs from our press advisory today and TPs from yesterday.

Thank you,

Ingrid Ulrey

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Sent: Sunday, March 1, 2020 11:56 AM
To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; WYSEN, Kirsten <Kirsten.Wysen@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Thanks Ingrid, look forward to your notes.

Rachel Smith
Deputy County Executive | Chief of Staff
King County Executive Dow Constantine
D: 206.263.9628 | C: 206.790.9168 | rachel.smith@kingcounty.gov

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Sent: Sunday, March 1, 2020 11:04 AM
To: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; WYSEN, Kirsten <Kirsten.Wysen@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi Rachel

I will be joining the 1:30pm call today to provide the PH update.

I will send the talking points for you and others on this chain to review in advance within 30 minutes.

Patty, Jeff and Dennis are unavailable.

Kirsten WYSEN on my team will also dial in, she will be on point for us ongoing for business sector

outreach.

Will you be on the call?

Do you want me to RSVP with this info to Colleen or would you prefer to?

Thank you

Ingrid

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Smith, Rachel <Rachel.Smith@kingcounty.gov>
Sent: Sunday, March 1, 2020 9:09 AM
To: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Wyses, Kirsten <Kirsten.Wyses@kingcounty.gov>
Subject: Re: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Thanks all.

Rachel Smith
Deputy County Executive | Chief of Staff
King County Executive Dow Constantine
D: 206.263.9628 | C: 206.790.9168
rachel.smith@kingcounty.gov

From: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>
Sent: Sunday, March 1, 2020 9:02:07 AM
To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>; Smith, Rachel <Rachel.Smith@kingcounty.gov>
Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Wyses, Kirsten <Kirsten.Wyses@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

I am happy to review the talking points – Ingrid – thank you for covering.

I am trying to stay closely linked to CDC and our Infectious Disease team as we develop and

implement strategies in this rapid response.

Dennis E. Worsham (he/him)

Prevention Division Director

Public Health – Seattle & King County

P - (206) 263-8158

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>

Sent: Sunday, March 1, 2020 8:56 AM

To: Smith, Rachel <Rachel.Smith@kingcounty.gov>

Cc: Schaeffer, Cyndi <Cyndi.Schaeffer@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>

Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi Rachel -

Patty, Dennis are not available and Jeff is maxed.

I will cover this – will send key TPs to all before the call.

Ingrid

Ingrid Ulrey, MPP (she/her)

Policy Director

Public Health – Seattle & King County

Phone: 206.477.7019

Ingrid.Ulrey@kingcounty.gov

From: Smith, Rachel <Rachel.Smith@kingcounty.gov>

Sent: Sunday, March 1, 2020 8:49 AM

To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>; Colleen Daly <codaly@microsoft.com>

Cc: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>

Subject: Re: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hi Ingrid - I already forward call in info to your inbox. Thanks!

Rachel Smith

Deputy County Executive | Chief of Staff

King County Executive Dow Constantine

D: 206.263.9628 | C: 206.790.9168

rachel.smith@kingcounty.gov

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Sent: Sunday, March 1, 2020 8:43:12 AM
To: Colleen Daly <codaly@microsoft.com>
Cc: Smith, Rachel <Rachel.Smith@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>
Subject: RE: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Thank you Colleen

Helpful to understand, I am coordinating with Rachel and identifying who from our team will be on the call.

Can you kindly send dial in information for the call? Correct that it is one hour total and you want the PH update at the beginning?

Ingrid

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Colleen Daly <codaly@microsoft.com>
Sent: Sunday, March 1, 2020 8:38 AM
To: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Cc: Smith, Rachel <Rachel.Smith@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <Anne.Burkland@kingcounty.gov>
Subject: Re: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

These are the items businesses are spinning on.

- Should they cancel events and conferences?
- Should they implement travel restrictions beyond what the CDC has issued?
- When should they tell employees to work from home?

I have maintained with my leadership that we don't need to take action on above unless you or the CDC issues guidance. Following the current interim guidance from the CDC is sufficient. But since this an emotional situation we are seeing businesses struggle to stay grounded. A reminder/reinforcement from your office to this group would be helpful.

Colleen

From: Ulrey, Ingrid <Ingrid.Ulrey@kingcounty.gov>
Sent: Sunday, March 1, 2020 7:39:27 AM
To: Colleen Daly <codaly@microsoft.com>
Cc: Smith, Rachel <Rachel.Smith@kingcounty.gov>; Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Burkland, Anne <anne.burkland@kingcounty.gov>
Subject: [EXTERNAL] FW: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Dear Colleen,

Thank you for contacting our team with this request.

We are coordinating with Executive Constantine's office to respond.

I understand from Kirsten Wysen that you need to know by 10am.

Thank you,

Ingrid Ulrey
Cell 206-330-6531

Ingrid Ulrey, MPP (she/her)
Policy Director
Public Health – Seattle & King County
Phone: 206.477.7019
Ingrid.Ulrey@kingcounty.gov

From: Colleen Daly <codaly@microsoft.com>
Sent: Saturday, February 29, 2020 5:49 PM
To: Worsham, Dennis <Dennis.Worsham@kingcounty.gov>; Wysen, Kirsten <Kirsten.Wysen@kingcounty.gov>; Kay, Meagan <Meagan.Kay@kingcounty.gov>
Subject: Request from Brad Smith and Christine Gregoire to join Challenge Seattle Meeting tomorrow

Hello,

First my leadership team was extremely appreciative of your assistance today around the cases. Tomorrow, members of Challenge Seattle, which has the 17 largest private-sector employers in the region are meeting at 1:30pm. Brad Smith our head of Corporate and Legal Affairs just spoke with Christine Gregoire. She said the meeting has a representative from Kaiser, but thought it would be

very valuable to have a representative from your team. They would like someone that can best speak to what businesses should do. Specifically help the businesses to stay grounded in science and the current guidance. We are seeing an increasing trend business making reactive decisions versus informed decision. Can you please make a recommendation of who from your team can attend and I will make an introduction to Brad Smith to coordinate?

Colleen M Daly, PhD, MPH

Global Benefits Manager, Healthcare Transformation

PLANNING FOR A CORONAVIRUS PANDEMIC

A guide for businesses and organizations

If the novel coronavirus (COVID-19) continues to spread around the world, it could become a pandemic. Though global by definition, pandemics have local impacts. Pandemics can cause absenteeism, alter patterns of business and travel, interrupt supply chains, and affect the daily operations of your business. A pandemic isn't an isolated incident, but an event that unfolds over time, sometimes spanning many months. You can minimize the impact to your organization by creating a plan that clearly outlines roles, responsibilities, and policies.

INITIATE

IDENTIFY PLAN OBJECTIVES



A well-designed plan can protect your employees and keep your business functioning during a disease outbreak.

Objectives might include:

- Reduce the spread of disease among staff.
- Protect people at higher risk for complications.
- Maintain business operations.
- Minimize impact on your customers and business partners.

OUTLINE KEY BUSINESS FUNCTIONS



Determine what people and resources are required for your business to operate.

- What jobs are needed to carry on day-to-day activities?
- Who are your key partners, suppliers, and contractors?
- What raw materials does your business need to function?

Consider how your business will adjust if resources are constrained.

- How can you back fill positions if employees are absent?
- How can you accomplish critical tasks if key partners are unavailable?
- How can you adapt if your supply chain is interrupted?

ASSESS WORKPLACE EXPOSURE RISK



Identify health risks your employees may face.

In the course of their duties, are employees likely to:

- Have face-to-face contact with large numbers of people?
- Spend time in work sites, like health care settings, where they may come into contact with ill people?
- Handle materials that could be contaminated, like laboratory samples or healthcare waste?

Workers with increased risk include those involved in healthcare, deathcare, airline operations, waste management, and travel to areas where the virus is spreading. Visit the OSHA website for guidance on controlling exposures among workers at risk: [osha.gov/SLTC/covid-19/](https://www.osha-slc.gov/covid-19/)
WA-KINGCO-20-0492-D-000295

REVIEW WORKPLACE POLICIES



Ensure your policies are responsive and adaptable.

- Verify that your human resources policies align with state and federal workplace laws. Visit the Department of Labor's website (www.dol.gov/) and the Equal Employment Opportunity Commission's website (www.eeoc.gov) for more information
- Implement flexible workplace and leave policies. Providing protected sick leave can limit the spread of disease in your workplace.
- During an outbreak or pandemic, adjust workplace policies to reflect public health recommendations.

I M P L E M E N T

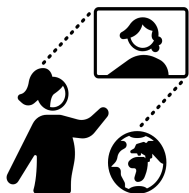
APPLY INFECTION CONTROL MEASURES



Before, during, and after an outbreak, create a culture of wellness.

- Place posters that encourage staying home when sick, cough and sneeze etiquette, and hand hygiene at the entrance to your workplace and in high visibility locations.
- Provide soap, water, and alcohol-based hand rubs in multiple locations and routinely refill.
- Instruct employees to clean hands often with an alcohol-based hand sanitizer or by washing for at least 20 seconds.
- Supply tissues and no-touch waste bins.
- Ask employees to stay home when sick. Ensure that sick leave policies are in place.
- Routinely clean commonly touched surfaces.

PREPARE FOR SOCIAL DISTANCING



Social distancing is an intervention to increase the physical distance between people and reduce the spread of disease.

If recommended by Public Health, consider what policies and procedures your business can implement to accomplish work remotely.

- Allow telecommuting where possible.
- Permit flexible work hours (e.g. staggered shifts).
- Ensure that you have the technology and infrastructure needed to support multiple employees working from home.
- Trial telecommuting and flexible hours during normal (non-pandemic) periods. Identify and remedy problems that arise.

PLAN TO SEPARATE SICK EMPLOYEES

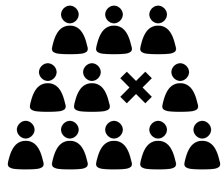


Employees who report having a fever or an acute respiratory illness upon arrival to work or who become sick during the work day should be separated from others and immediately sent home. Ensure that:

- All managers and employees are aware of your policies and the expectation that sick employees stay home.
- If possible, designate a separate area at your work site where sick employees can temporarily isolate. Use this space for employees who become ill during the work day and are awaiting transportation to their home or to medical care.

WA-KINGCO-20-0492-D-000296

ANTICIPATE ABSENTEEISM



Prepare for employee absences resulting from personal illness, caring for ill family members, and dismissal of early childhood programs and K-12 schools. Be ready to adapt your business practices to maintain critical operations.

- Cross-train employees to carry out essential functions so the workplace can operate when essential staff are out.
- Identify alternative suppliers to meet supply chain needs.
- Consider prioritizing customers with the greatest needs.
- Prepare to temporarily suspend operations if necessary.

PLAN FOR RESTRICTED TRAVEL



If there's evidence of an outbreak in the U.S. or to another business destination, you may need to cancel non-essential travel.

Consider:

- How can you accomplish work-related meetings or events remotely?
- How can you support employees who are abroad when travel restrictions are put into place, particularly those who become sick? Ensure you have clear policies for obtaining medical care during travel.

Prepare to consult travel guidance on the CDC website:

<https://wwwnc.cdc.gov/travel>

ENCOURAGE PERSONAL PREPAREDNESS



Your business is only as healthy as your employees. Encourage employees to take standard steps to prepare for staying at home if needed:

- Store a two-week supply of water and food.
- Make sure to have enough prescription drugs at home.
- Keep non-prescription drugs and other health supplies on hand. This includes pain relievers, stomach remedies, cough and cold aides, fluids with electrolytes, and vitamins.
- Get copies of electronic health records from the doctor, hospital, or pharmacy.
- Talk with family members and loved ones about how they would like to be cared for if they got sick, and what's needed to care for them at home.

I N V O L V E

ESTABLISH A COMMUNICATION PROTOCOL



Determine how you will relay information about the outbreak to employees and business partners.

- How will you keep your workforce and partners informed about the outbreak, latest public health recommendations, and your response?
- How can you support employees and partners experiencing anxiety and fear?
- How can you prevent rumors and misinformation from circulating, and respond effectively if they do?

DEVELOP A PROCESS FOR ACTIVATING YOUR PLAN



Decide when and how to activate and terminate your pandemic plan.

Consider:

- Which decision makers in your business should be involved?
- What event(s) should trigger action?
- What procedures should be used to activate or deactivate your plan?
- How can you efficiently and effectively transfer business knowledge to key employees?
- When you deactivate your plan, how can you most effectively reintegrate employees who have been absent?

Prepare to work with local health officials when answering these questions.

GET INPUT FROM YOUR WORKFORCE



Your plan is more likely to be successful if you get buy-in from employees and partners.

- Invite your employees to help develop and review the plan. If it's not possible to talk with every team member, try sampling a variety of departments in your organization.
- Test out your plan to help detect gaps or problems that need attention.
- Share your completed plan with employees. Explain what benefits are available to them, including paid time off, flexible scheduling, and health care coverage.
- Share your plan with other businesses in your community.

STAY INFORMED



Every disease outbreak is different, and the intensity of an outbreak can vary from one location to another. Stay alert to recommendations from federal, state, and local public health experts, and adapt your plan accordingly.

- Centers for Disease Control and Prevention (CDC):
<https://www.cdc.gov/coronavirus/2019-ncov/>
- Washington State Department of Health (DOH):
<https://www.doh.wa.gov/emergencies/coronavirus>
- Public Health - Seattle & King County (PHSKC):
kingcounty.gov/covid



COVID-19 Talking Points for Seattle Challenge

Prepared on 3/1/2020

Public Health Update

Intro

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I am here to offer their deep appreciation to you for your leadership in protecting the health of your employees and the broader community. I will provide the latest updates on the outbreak in King County, describe our overall response work and share guidance for employers.

As the largest employers in our region you are critical partners. We have already been in close contact with several of you and have established a Health and Medical Area Command (HMAC) Business Sector outreach group, which will be staffed by Kirsten Wysen from Public Health, in conjunction with leaders from Executive Dow Constantine's office. We will follow up with Colleen following this meeting to discuss our process for maintaining close coordination with you all.

Latest

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King County / Public Health – Seattle King County Response

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- Public Health – Seattle & King County is fully activated through its Incident Command structure. We are conducting disease investigations, mitigation planning and coordinating communications.
- We are in close contact with CDC, State DOH, hospitals, the Emergency Medical Services system, as well as our state and federal delegation. CDC in particular is providing close assistance, and sent a high level team to King County to help with the response.
- This is a troubling situation that health officials have been warning could happen. We have experience in responding to pandemics and our health officials have tremendous expertise and skills, but this is a very quickly-moving situation and information is changing daily.

Business Sector Guidance

First, everyone should adhere public health guidance to the general public is as follows:

- 1) **Do not go to the emergency room unless essential.** Emergency rooms need to be able to serve those with the most critical needs. If you have symptoms like cough, fever, or other respiratory problems, contact your regular doctor first.
- 2) Stay home when sick
- 3) Practice excellent personal hygiene habits, including handwashing, coughing into tissue or elbow, avoid touching eyes, nose, or mouth.

- 4) Stay informed. Information is changing frequently. Check and subscribe to Public Health's website (www.kingcounty.gov/COVID) or blog (www.kingcounty.gov)

In addition, the CDC has issues interim guidance specifically for businesses and employers to plan and respond to the COVID-19. (see 2-page handout attached)

This guidance includes -

1. Personal Preparedness/Readiness
2. Communication
3. Performing Critical Functions
4. Continuity of Business Operations
5. Participate robustly in implementing 13 strategies to reduce the spread of the virus

The 13 strategies will be rolled out in in the next weeks and months, depending on how the crisis unfolds. They start with the least intensive and move to the more restrictive one based on how the spread takes place:

1. Increase hand washing and use of alcohol-based sanitizer
2. Respiratory hygiene and cough etiquette
3. Keep distance from others (> 6 feet) avoid,
4. Frequently clean and disinfect surfaces
5. Remain home during a respiratory illness
6. Voluntary isolation of sick persons
7. Voluntary quarantine of contacts of sick persons
8. Involuntary isolation of sick persons
9. Involuntary quarantine of contacts of sick persons
10. Recommend or order cancellation of major public and large private gatherings
11. Recommend or order closure of schools, child care facilities, workplaces, and public buildings
12. Prevent non-emergency travel outside of the home
13. Establish cordon sanitaire (isolate a geographic area)

This framework / ramped up approach from CDC, DOH and PHSKC will guide the next phase of work.

We are all in this together, and we are in it for the long haul. The best public health scientists are working 24/7 on how to respond and they have practiced how to respond to an outbreak for years. We have substantial experience from H1N1, SARS, MERS, Zika and Ebola. Be ready for major changes in your thinking and emotions related to Covid-19. Be ready for major changes in our daily lives and our work together. Self-care and staying calm are important for the next few months.

Answers to Key Questions

- **Should you cancel events and conferences?**

Not yet but stay tuned, and monitor PHSKC, DOH and CDC websites.

Events and gatherings should use stepped up infection prevention practices, such as hand washing signs and hand washing/hand sanitizing stations)

We don't have enough data to recommend cancelling events. CDC, DOH, PHSKC are working now on establishing a clear trigger for this recommendation. per Duchin this AM.

- **Should they implement travel restrictions beyond what the CDC has issued?**

Some employers are voluntarily limiting non-essential travel. This is no required.

- **When should they tell employees to work from home?**

If employees are sick they should stay home stay home

At this point, interim guidance from CDC does not suggest asking others to work from home, but some employer may choose to do so as a precautionary measure.

For more information:

www.kingcounty.gov/COVID

<https://www.doh.wa.gov/Emergencies/Coronavirus>

<https://www.cdc.gov/coronavirus/2019-ncov/index.html>

From: [Berliner, Debra](#)
To: [Kay, Meagan](#)
Cc: [Duchin, Jeff](#); [Kawakami, Vance](#); [Bogan, Sharon](#)
Subject: School letter for review (sending tonight)
Date: Sunday, March 1, 2020 8:20:55 PM
Attachments: [Letter to Schools, 3-1-20.docx](#)

Hi Meagan, Jeff, and Vance,

Attached is an email draft for school nurses and administrators to update them on the latest situation. I'd like to send this out tonight so that they have this information before the school day begins. I'm sorry it comes so late – I didn't get to work on it until the evening.

If one of you is able to review and get back to me shortly, I'll make the recommended changes and send out. Sharon Bogan is also reviewing.

With thanks,

Debra

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March 1, 2020

Dear School Nurses and Administrators,

As you have likely heard, over the past three days, we have confirmed multiple local novel coronavirus (COVID-19) cases and two deaths. Many of these cases are associated with a nursing facility in Kirkland, WA. We understand that this news is worrisome to everyone, and we are working in close collaboration with the Centers for Disease Control (CDC) and the Washington Department of Health (DOH) to understand the connections between these cases and the implications for our community.

At this time, we do not have any cases in students or staff at any schools in King County, and we are not recommending school closures or cancellation of activities. This is a rapidly evolving situation, and we will be certain to update you should our recommendations change. To support you in your efforts to prepare for additional local cases, we are working with DOH and other state and regional bodies to update and develop resources to assist you in pandemic planning. Our partners at DOH anticipate having resources to share by the end of this week, if not sooner.

During this time of heightened anxiety, our community values are tested. We need to continue to demonstrate compassion and care as we navigate this global health situation. Please remind your students, their families, and your staff that COVID-19 infection is not connected with race, ethnicity, or nationality. Sharing accurate information is one of the best steps you can take to keep everyone healthy.

Below please find responses to frequently asked questions. We thank you for your continued partnership, and appreciate all that you are doing to keep our communities safe.

FREQUENTLY ASKED QUESTIONS

Where should I turn for accurate information or to ask specific questions?

Please continue to consult the CDC, DOH, and PHSKC webpages for the most up-to-date information:

- [Centers for Disease Control \(CDC\)](#), Coronavirus Disease 2019 (COVID-19)
- [Washington Department of Health \(DOH\)](#), Coronavirus School Resources and Recommendations
- [Public Health – Seattle and King County \(PHSKC\)](#), Coronavirus Disease 2019 (COVID-19)

If you have specific concerns about a possible exposure, please call (206) 296-4774. If you have other questions specific to King County, email coronavirus@kingcounty.gov. We aim to address urgent questions as quickly as possible and to respond to other inquiries within two days. For general questions about COVID-19 or Washington State's response, call the Washington State Call Center at 800-525-0127.

Given the increased number of cases, should our school take any additional precautions?

At this time, schools do not need to take any special precautions beyond what is normally recommended to prevent the spread of viruses. We strongly recommend that schools follow standard procedures for cleaning and encourage students and staff to stay home when sick, wash hands frequently, avoid touching one's face, and take other preventative steps outlined by DOH on their [School Nurse and Administrator Resources and Recommendations webpage](#). Please continue to use this time to develop and update your district's pandemic plans. As mentioned, DOH intends to share planning tools later this week.

Should we cancel assemblies, sporting events or other gatherings?

The CDC has not recommended that the general public avoid gatherings, and we are not recommending cancelling events at this time. However, people who are at higher risk of illness may want to consider ways to lower their risk of infection, such as limiting contact with crowds. This includes people with underlying health conditions such as heart disease and lung disease and those who are immune compromised. Individuals should talk to their healthcare provider to develop a plan based on their specific health conditions.

Who should be tested for COVID-19?

Students, staff and volunteers who are:

- Ill with a fever, cough, or difficulty breathing AND have recent recent travel (in the past 14 days) to countries with widespread or ongoing community spread (*hyperlink needed*).
- Ill with a fever, cough, or difficulty breathing AND have been identified by Public Health as a close contact of a confirmed COVID-19 case or had recent close contact with someone who is being evaluated for COVID-19 infection.
- Hospitalized with severe pneumonia with unknown cause (*include?*).

If someone meets the criteria, they should contact their healthcare provider by phone and call the Public Health Communicable Disease team at (206) 296-4774. Public Health is not currently recommending widespread testing for members of the general public. We anticipate testing guidance to change in the near term as more testing comes on-line at commercial laboratories.

Who should self-quarantine?

Individuals in the following categories should self-quarantine for 14 days:

- Recent travelers of areas to countries with widespread or ongoing community spread (*hyperlink needed*).
- Asymptomatic close contacts of confirmed COVID-19 cases. For example, Barry's wife, Shelly, works at a school in your district. Shelly was recently confirmed to have COVID-19. Barry should self-quarantine for 14 days, monitor symptom, and notify his healthcare provider and Public Health if he becomes ill.

Who does not need to self-quarantine?

Contacts of asymptomatic people who have had close contact with a confirmed case do not need to self-quarantine. For example, Joni is a nurse at Life Care nursing facility. She does not have any respiratory symptoms. Her son, Liam, does not need to self-quarantine and does not need evaluation or testing for COVID-19. However, if Joni becomes sick with COVID-19, Liam will need to self-quarantine.

Will Public Health notify our schools if we have a case?

Yes, Public Health will contact key school personnel, such as the school nurse or principal, if we have a positive case at your school. We will also contact you if we have concerns of any other COVID-19 exposures at your school.

A student or staff member in our district recently tested negative for COVID-19. Should the school require healthcare provider documentation for reentry?

School administrators should not require any letter or documentation from health care providers about their COVID-19 status. Requiring documentation may overwhelm the healthcare system and is not recommended as a measure to protect public health at this time.

How should we talk about coronavirus with our students and other children in our lives?

This situation can raise fear and anxiety for both adults and children. Check out this helpful article and comic strip from NPR, “Just for Kids: A Comic Exploring the New Coronavirus.”

Where can I find additional resources about stigma and discrimination?

Public Health – Seattle & King County has an [anti-stigma toolkit](#) with social media tools, a poster, infographic, and other information to help you prevent, interrupt, and respond to stigma.