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## Intervenciones para frenar o reducir la propagación de virus respiratorios

Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, Hewak B, Prabhala A, Nair S, Rivetti A

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## RESUMEN

### **Antecedentes**

Las epidemias o pandemias virales como la gripe o el síndrome respiratorio agudo grave (SRAG) representan una amenaza importante. Posiblemente los antivirales y la vacunación no sean adecuados para prevenir una catástrofe en dichas circunstancias.

### **Objetivos**

Investigar sistemáticamente las pruebas de la efectividad de las intervenciones para frenar o reducir la propagación de virus respiratorios (con exclusión de las vacunas y antivirales investigados anteriormente).

### **Estrategia de búsqueda**

Se hicieron búsquedas en el Registro Cochrane Central de Ensayos Controlados (Cochrane Central Register of Controlled Trials, CENTRAL) (*The Cochrane Library* 2006, número 4); MEDLINE (1966 hasta noviembre 2006); OLDMEDLINE (1950 hasta 1965); EMBASE (1990 hasta noviembre 2006); y CINAHL (1982 hasta noviembre 2006).

### **Criterios de selección**

Se analizaron 2300 títulos, se excluyeron 2162 y se recuperaron los artículos completos de 138 ensayos, incluidos 49 artículos de 51 estudios. La calidad de tres ensayos controlados aleatorios (ECA) era deficiente; al igual que la mayoría de los ECA por grupos. Los estudios observacionales eran de calidad mixta. Sólo se pudo realizar el metanálisis de los datos de casos y controles. Se buscaron todas las intervenciones para prevenir la transmisión de virus respiratorios (aislamiento, cuarentena, distanciamiento social, barreras, higiene y protección personal). El diseño de estudio incluía ECA, estudios de cohorte, estudios de casos y controles, estudios cruzados (cross-over), así como estudios de series de tiempo y de tipo antes y después.

### **Recopilación y análisis de datos**

Se analizaron los títulos, los resúmenes y los artículos de texto completo mediante un formulario estandarizado para evaluar la elegibilidad. Los ECA se evaluaron según el método de asignación al azar, la generación de las asignaciones, la ocultación, el cegamiento y el seguimiento. Se investigó la presencia de factores de confusión entre los ensayos controlados no aleatorios, y se los clasificó como de riesgo de sesgo bajo, medio y alto.

### **Resultados principales**

Los ECA agrupados de más alta calidad sugieren que la propagación de virus respiratorios puede prevenirse con medidas higiénicas entre los niños más pequeños. El beneficio adicional de una disminución en la transmisión de los niños a otros miembros de la familia es ampliamente apoyada por los resultados de otros diseños de estudio, con mayores probabilidades de factores de confusión. Los seis estudios de casos y controles indicaron que el empleo de barreras contra la transmisión, el aislamiento y las medidas higiénicas fueron eficaces para contener las epidemias de virus respiratorios. Las pruebas sobre la superioridad de las máscaras N95 (que son más incómodas y caras) sobre las máscaras quirúrgicas simples fueron limitadas. El efecto adicional del agregado de viricidas o antisépticos al lavado de manos normal para reducir las enfermedades respiratorias sigue siendo incierto.

La falta de una evaluación adecuada de medidas globales como la selección en los puertos de ingreso y el distanciamiento social impiden la formulación de conclusiones definitivas acerca de estas medidas.

### Conclusiones de los autores

Numerosas intervenciones simples y probablemente de bajo costo serían útiles para reducir la transmisión de los virus respiratorios epidémicos. La aplicación sistemática y a largo plazo de algunas de las medidas evaluadas quizá se vea dificultada ante la ausencia de una amenaza de epidemia inminente.

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## RESUMEN EN TÉRMINOS SENCILLOS

### Intervenciones para frenar o reducir la propagación de virus respiratorios

Si bien los virus respiratorios suelen restringirse a enfermedades leves, también pueden causar epidemias. Aproximadamente del 10% al 15% de las personas a nivel mundial contraen gripe anualmente, con tasas de brotes que alcanzan el 50% durante las epidemias graves. Las pandemias virales mundiales han sido devastadoras debido a su amplia propagación. En 2003, la epidemia de síndrome respiratorio agudo grave (SRAG) afectó a unas 8000 personas, mató a 780 y originó una gran crisis social y económica. Una nueva pandemia de gripe aviar causada por la cepa H5N1 probablemente sea aún más catastrófica. Medidas simples (en especial el uso de vacunas o antivirales) resultarían insuficientes para frenar la propagación.

Se hallaron 51 estudios incluidos los ensayos controlados aleatorios (ECA) y los estudios observacionales con un riesgo de sesgo mixto.

La propagación de virus respiratorios puede prevenirse con medidas higiénicas entre los niños más pequeños. Dichas medidas podrían, además, reducir la transmisión de los niños a otros miembros de la familia. El empleo de barreras contra la transmisión, el aislamiento y las medidas higiénicas podrían ser eficaces para contener las epidemias de virus respiratorios. Las pruebas sobre la superioridad de las máscaras N95 (que son más incómodas y caras) sobre las simples fueron limitadas. El beneficio de agregar viricidas o antisépticos al lavado de manos normal es incierto. Existe una escasa evaluación de las medidas globales como el cribado en los puertos de ingreso y el distanciamiento social.

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## ANTECEDENTES

Existe una creciente preocupación de una pandemia viral global que afecte seriamente a los seres humanos. Entre 2002 y 2003 una nueva epidemia de síndrome respiratorio agudo grave (SRAG), causado por un coronavirus, se extendió por el mundo. Unas 8000 personas resultaron afectadas y 780 murieron (incluido un elevado número de profesionales de la salud). Esta calamidad fue ensombrecida por una descomunal crisis social y económica, especialmente en Asia (Shute 2003). Actualmente hay una creciente preocupación sobre una amenaza de pandemia viral, originada por la gripe aviar, causada por la cepa H5N1 (WHO 2004). Si bien la mayoría de los casos de gripe logra una recuperación total, en EE.UU. la gripe provoca aproximadamente 36 000 muertes y 226 000 hospitalizaciones anuales (USDHHS 2005). Se estima que cada año, alrededor del 10% al 15% de las personas a nivel mundial contrae gripe. En las epidemias graves, la tasa de brotes de gripe puede ascender al 50%. Se asocia con mayores tasas de consulta de medicina general, de ingresos al hospital (Fleming 2000) y con un exceso de muertes (Fleming 2000; Simonsen 1997). También hay que tener en cuenta el aumento de los días perdidos por

ausentismo laboral y escolar, la planificación sanitaria y la planificación de la pandemia de gripe (Smith 2006)).

Una elevada carga viral y una elevada infectividad viral podrían ser los promotores de una pandemia de gripe (Jefferson 2006a) y de otras epidemias graves como el SRAG. Otros factores que colaboran con las pandemias de gripe incluyen las variaciones antigénicas mayores del virus. Una variación antigénica mayor es una modificación importante en la estructura genética del virus que origina un nuevo subtipo contra el cual se posee escasa inmunidad natural circulante (Smith 2006), debido a que la mayoría de las personas no estuvieron expuestas a este nuevo virus y, por lo tanto, son vulnerables a la infección. Siempre se creyó que estas pandemias provenían del sur de China donde los patos (el reservorio animal y el sitio de incubación de las cepas nuevas), los cerdos (que se creía que eran el huésped biológico intermediario o "recipiente de mezcla") y los seres humanos conviven muy próximos los unos de los otros (Bonn 1997). Los cerdos son considerados posibles huéspedes intermedios, debido a que las células del epitelio respiratorio poseen tanto receptores para la hemaglutinina viral aviar (como la de los patos) como la humana (Bonn 1997). Las variaciones

antigénicas menores en las estructuras antigénicas virales causan epidemias locales o más circunscritas. (Smith 2006)).

Cada vez hay más pruebas (Jefferson 2005a; Jefferson 2005b; Jefferson 2005c; Jefferson 2006a) de que las medidas individuales (como el uso de vacunas o antivirales) resultarían insuficientes para frenar la propagación de la gripe. Sin embargo un ensayo reciente halló que el lavado de manos puede ser eficaz en la disminución de la mortalidad por enfermedades respiratorias (Luby 2005). La posible efectividad de las medidas de salud pública durante la pandemia de 'gripe española' de 1918 a 1919 (Bootsma 2007) en ciudades estadounidenses llevó a plantear qué pruebas existen sobre la efectividad de las medidas de salud pública combinadas como el aislamiento, el distanciamiento y las barreras. También se tuvieron en cuenta las principales consecuencias sociales para la comunidad que las implemente (CDC 2005a; CDC 2005b; WHO 2006)). Dada la posible importancia global de frenar la transmisión viral, se necesitan estimaciones actualizadas y concisas sobre la efectividad para contribuir con la planificación y la toma de decisiones. No se pudo hallar revisiones sistemáticas anteriores sobre dichas pruebas.

## OBJETIVOS

Se analizaron sistemáticamente las pruebas sobre la efectividad de las intervenciones para frenar o reducir la propagación de virus respiratorios que causan enfermedades pseudogripales (con exclusión de las vacunas y antivirales ya tratados en revisiones Cochrane anteriores (Demicheli 2004; Jefferson 1999; Jefferson 2006b; Matheson 2003; Smith 2006; Swingler 2003))).

## CRITERIOS PARA LA VALORACIÓN DE LOS ESTUDIOS DE ESTA REVISIÓN

### Tipos de estudios

Se tuvieron en cuenta los ensayos (de asignación al azar individual o por grupos, o cuasialeatorios), los estudios observacionales (diseños de cohortes y de casos y controles) o cualquier otro diseño comparativo, con la condición de que se haya intentado controlar los factores de confusión, y que incluyeran a personas de todas las edades.

### Tipos de participantes

Personas de todas las edades.

### Tipos de intervención

Se incluyeron todas las intervenciones para prevenir la transmisión de virus respiratorios de animales a los seres humanos o de persona a persona (aislamiento, cuarentena, distanciamiento social, barreras, protección personal e higiene) comparadas con ninguna intervención o con otra intervención. Se excluyeron las vacunas y los antivirales.

## Tipos de medidas de resultado

Muertes

Número de casos de enfermedad viral

Gravedad de la enfermedad viral en las poblaciones comparadas.

Se estimó la carga de la gripe a través de las consecuencias en niños y adultos sanos, como las pérdidas en la productividad debidas al ausentismo de los padres. En cuanto a los ancianos en la comunidad, se estimó la carga teniendo en cuenta las repetidas consultas de asistencia sanitaria primaria, los ingresos al hospital y el riesgo de complicaciones

Todos los indicadores de estos resultados

## ESTRATEGIA DE BÚSQUEDA PARA LA IDENTIFICACIÓN DE LOS ESTUDIOS

Se hicieron búsquedas en el Registro Cochrane Central de Ensayos Controlados (Cochrane Central Register of Controlled Trials, CENTRAL) (*La Cochrane Library* 2006, número 4); MEDLINE (1966 hasta noviembre 2006); OLDMEDLINE (1950 hasta 1965); EMBASE (1990 hasta noviembre 2006); y CINAHL (1982 hasta noviembre 2006). Los términos de búsqueda para MEDLINE se modificaron para OLDMEDLINE, EMBASE y CINAHL.

### MEDLINE (OVID)

- 1 exp Influenza, Human/
- 2 influenza.mp.
- 3 flu.mp.
- 4 exp Common Cold/
- 5 common cold.mp.
- 6 exp Rhinovirus/
- 7 rhinovirus\$.mp.
- 8 exp Adenoviridae/
- 9 adenovirus\$.mp.
- 10 exp Coronavirus/
- 11 exp Coronavirus Infections/
- 12 coronavirus\$.mp.
- 13 exp Respiratory Syncytial Viruses/
- 14 exp Respiratory Syncytial Virus Infections/
- 15 respiratory syncytial virus\$.mp.
- 16 respiratory syncythial virus\$.mp.
- 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).mp.
- 22 exp Severe Acute Respiratory Syndrome/
- 23 (severe acute respiratory syndrome or SARS).mp.
- 24 acute respiratory infection\$.mp.
- 25 acute respiratory tract infection\$.mp.
- 26 or/1-25
- 27 exp Handwashing/
- 28 (handwashing or hand washing or hand-washing).mp.
- 29 hand hygiene.mp.
- 30 (sanitizer\$ or sanitiser\$).mp.

31 (cleanser\$ or disinfectant\$.mp.  
 32 exp Gloves, Protective/  
 33 exp Gloves, Surgical/  
 34 glov\$.mp.  
 35 exp Masks/  
 36 mask\$.mp.  
 37 exp Patient Isolators/  
 38 exp Patient Isolation/  
 39 barrier\$.mp.  
 40 curtain\$.mp.  
 41 partition\$.mp.  
 42 negative pressure room\$.mp.  
 43 reverse barrier nursing.mp.  
 44 Cross Infection/pc [Prevention & Control]  
 45 school closure\$.mp.  
 46 (clos\$ adj3 school\$.mp.  
 47 mass gathering\$.mp.  
 48 public gathering\$.mp.  
 49 (ban or bans or banned or banning).mp.  
 50 (outbreak\$ adj3 control\$.mp.  
 51 distancing.mp.  
 52 exp Quarantine/  
 53 quarantin\$.mp.  
 54 or/27-53  
 55 26 and 54  
 56 Animals/  
 57 Humans/  
 58 56 not 57  
 59 55 not 58

No hubo restricciones de idioma. Los filtros de diseño de estudio incluían los ensayos, los estudios de cohorte, de casos y controles y los estudios cruzados (cross-over), las series de tiempo y de tipo antes y después. Se examinaron las referencias de todos los estudios incluidos para detectar otros estudios potencialmente relevantes. También se tuvo acceso a los archivos de la antigua MRC Common Cold Unit (Jefferson 2005d) como una posible fuente de pruebas sobre el freno de la transmisión.

## MÉTODOS DE LA REVISIÓN

### *Evaluación de la calidad*

Los datos de los estudios aleatorios y no aleatorios se analizaron por separado. Los estudios aleatorios se evaluaron de acuerdo con: la asignación al azar; la generación de la secuencia de asignación; la ocultación de la asignación; cegamiento; y seguimiento. Los estudios no aleatorios se evaluaron en relación con la presencia de posibles factores de confusión mediante las escalas Newcastle-Ottawa Scales (NOS) apropiadas (Wells 2005) para los estudios de casos y controles y de cohorte; y una lista de verificación de tres puntos para los estudios controlados ecológicos y de tipo antes y después (Khan 2000)).

Utilizando la calidad como una forma de interpretar los resultados en la etapa de análisis, se asignaron las categorías

de riesgo de sesgo, para cada estudio, según el número de ítems calificados como inadecuados: 1) riesgo de sesgo bajo, hasta un ítem inadecuado; 2) riesgo de sesgo medio, hasta tres ítems inadecuados; y 3) riesgo de sesgo elevado, más de tres ítems inadecuados.

### *Elegibilidad de los estudios*

Después de realizar las búsquedas se analizaron los títulos y resúmenes. Si un estudio parecía satisfacer los criterios de elegibilidad (o si la información era insuficiente para excluirlo), se obtenían los artículos con el texto completo. Luego se utilizó un formulario estandarizado para evaluar la elegibilidad de cada estudio en base al artículo completo.

### *Extracción de los datos*

Dos autores de la revisión (TOJ, CDM) aplicaron de forma independiente los criterios de inclusión a todos los artículos identificados y recuperados. Cuatro revisores (TOJ, EF, BH, AP) extrajeron los datos de los estudios incluidos y verificaron la precisión con formularios Cochrane Vaccines Field estándar. El procedimiento fue supervisado y arbitrado por CDM.

El agrupamiento de los datos dependió del diseño del estudio, los tipos de comparaciones, la sensibilidad y la homogeneidad de las definiciones de exposición, las poblaciones y las medidas de resultado utilizadas. Se calculó la estadística  $I^2$  para cada estimación agrupada a fin de evaluar el efecto sobre la heterogeneidad estadística. (Higgins 2002; Higgins 2003)).

Cuando fue posible, se realizó un análisis cuantitativo y se resumió la efectividad como odds ratio (OR) con intervalos de confianza (IC) del 95%. La efectividad absoluta de la intervención se expresó en porcentajes mediante la fórmula de efectividad de la intervención =  $1 - OR$ , cuando era significativa. En los estudios que no pudieron agruparse, se utilizaron las medidas de efecto informadas por los revisores (como el riesgo relativo [RR] o el cociente de tasas de incidencia [CTI] con los IC del 95% o, cuando no estaban disponibles, los valores de P pertinentes).

No se estableció contacto con los autores.

### *Análisis de subgrupos*

Se programó un análisis de subgrupos a priori para:

- (a) los brotes de gripe pandémica;
- (b) la gripe estacional;
- (c) otras epidemias (como el SRAG).

Con los datos disponibles sólo se pudo realizar el último punto.

## DESCRIPCIÓN DE LOS ESTUDIOS

Ver tabla "Características de los estudios incluidos".

## CALIDAD METODOLÓGICA

Los tres ECA fueron inadecuadamente informados, sin detalles sobre la secuencia de asignación al azar, ni de la ocultación ni

de la asignación (Gwaltney 1980; Turner 2004a; Turner 2004b). El diseño de dos ensayos por un mismo autor significa que los resultados no pueden generalizarse a situaciones cotidianas. Esto se debe a artefactos en la administración de las intervenciones estudiadas (ver "Cuestiones de calidad" en la sección "Discusión") (Turner 2004a; Turner 2004b)).

La calidad de los ensayos con asignación al azar por grupos era variable. Sólo los ensayos de más alta calidad (Luby 2005; Roberts 2000; Sandora 2005) informaron coeficientes por grupos y realizaron análisis de datos por unidad de asignación (grupo) en lugar de hacerlo por individuo. Este problema frecuente es responsable de intervalos de confianza erróneamente estrechos sobre las estimaciones del efecto (Grimshaw 2004). Otros problemas frecuentes eran la ausencia de descripción del procedimiento de asignación al azar, el informe parcial de los resultados, numeradores o denominadores poco claros y las deserciones no justificadas (Carabin 1999; Kotch 1994; Morton 2004; White 2001), y, o bien el fracaso completo del doble cegamiento (Farr 1988a; Farr 1988b) o la elección inadecuada del placebo (Longini 1988)).

Cuatro de los seis estudios de casos y controles se clasificaron como de riesgo de sesgo medio (Lau 2004a; Seto 2003; Wu 2004; Yin 2004) y dos como de riesgo de sesgo bajo (Nishiura 2005; Teleman 2004), principalmente debido a incongruencias en el texto y a la ausencia de una adecuada descripción de los controles.

Seis de los 14 estudios de cohorte prospectivos se clasificaron como de riesgo de sesgo bajo (Agah 1987; Dick 1986; Falsey 1999; Leung 2004; Madge 1992; Somogyi 2004), cuatro como de riesgo medio (Dyer 2000; Kimel 1996; Murphy 1981; White 2003), y tres como de riesgo de sesgo elevado (Makris 2000; Master 1997; Niffenegger 1997). Uno era un informe muy breve de un estudio pequeño con escasos detalles como para permitir su evaluación (Derrick 2005)).

Los cuatro estudios de cohorte retrospectivos poseían un alto riesgo de sesgo (Doherty 1998; Isaacs 1991; Ou 2003; Yen 2006)).

Seis de los 13 estudios de tipo antes y después eran de riesgo de sesgo bajo (Hall 1981a; Leclair 1987; Macartney 2000; Pang 2003; Ryan 2001; Simon 2006), dos de riesgo medio (Krasinski 1990; Pelke 1994) y cinco de riesgo elevado (Gala 1986; Hall 1981b; Heymann 2004; Krilov 1996; Snyderman 1988)).

El problema más frecuente en todos estos estudios era la falta de información sobre la circulación viral en la población de referencia, esta situación provocó que la interpretación y generalizabilidad de sus conclusiones fuera cuestionable.

## RESULTADOS

Se identificaron y seleccionaron 2300 títulos de informes de estudios potencialmente relevantes; se excluyeron 2162. Se

recuperaron 138 artículos completos, incluidas 49 publicaciones de 51 estudios.

### *Resultados informados de estudios aleatorios*

Tres estudios evaluaron los efectos de la limpieza de manos para inactivar el virus y prevenir los resfriados experimentales por rinovirus. Como resultado se obtuvo ya sea una reducción de la incidencia de infección por rinovirus entre los voluntarios tratados con diferentes combinaciones de los ácidos usados para la limpieza ( $p = 0,025$ ) (Turner 2004a) o bien, no alcanzó significación estadística (13% versus 30% con un denominador combinado de sólo 60) (Turner 2004b). Al tratar con yodo los dedos, 1 de cada 10 voluntarios resultó infectado en comparación con 6 de cada 10 en el brazo del preparado de placebo ( $p = 0,06$  con la prueba exacta de Fisher) (Gwaltney 1980)).

Tres ensayos con asignación al azar por grupos evaluaron los efectos de la limpieza con un pañuelo viricida desechable en la incidencia y propagación de las infecciones respiratorias agudas (IRA). Uno informó una reducción de la incidencia de IRA en el grupo familiar después de 26 semanas, de 14% a 5% (Farr 1988a). Un estudio similar informó una pequeña disminución no significativa (5%) entre las familias (Farr 1988b). Sin embargo, como la disminución en la incidencia se restringió a la enfermedad primaria, no afectada por el uso de pañuelos de papel, podría concluirse que fueron ineficaces. Un ensayo comunitario también informó una reducción no significativa de las tasas de brotes secundarios de IRA (18,7% versus 11,8%) durante una época de gran circulación en la comunidad de gripe H3N2 y de rinovirus (Longini 1988)). Posiblemente este resultado sea un cálculo demasiado bajo ocasionado por un posible efecto de barrera del material inerte de los pañuelos utilizados por los controles.

Siete ensayos con asignación al azar por grupos evaluaron programas educacionales para promover el lavado de manos, con o sin agregado de agentes antisépticos, en la incidencia de IRA, ya sea en las escuelas o en las viviendas. Debido a diferencias en las definiciones, las comparaciones, la ausencia de informes de los coeficientes agrupados y (en dos casos) a la falta de datos de participantes (Carabin 1999; Kotch 1994), no se creyó apropiado realizar un metanálisis de los datos. Dos de estos ensayos informaron una falta de efecto: RR de prevención de la enfermedad respiratoria aguda de 0,94 (IC del 95%: -2,43 a 0,66) (Kotch 1994); y de 0,97 (IC del 95%: 0,72 a 1,30) (Sandora 2005). No obstante, los ensayos de mayor calidad informaron una disminución significativa en la enfermedad respiratoria en los niños de hasta 24 meses (RR 0,90; IC del 95%: 0,83 a 0,97), aunque la disminución no fue significativa en los niños mayores (RR 0,95; IC del 95%: 0,89 a 1,01) (Roberts 2000); y una disminución de la incidencia de neumonía del 50% (IC del 95%: -65% a -34%) en niños de menos de cinco años de edad en un país en desarrollo (Luby 2005). Otro estudio informó una disminución de 30% al 38% en las infecciones respiratorias con la incorporación de la limpieza de manos por frotado (RR de la incidencia de ausencia de enfermedad 0,69;

RR de la duración de la ausencia 0,71) (White 2001). Un estudio informó una reducción del ausentismo escolar del 43% con el uso adicional de geles de alcohol y de lavado de manos (Morton 2004). Dos ensayos informaron que el lavado de manos reiterado redujo significativamente la incidencia de resfriados en hasta un 20% (Carabin 1999; Ladegaard 1999)).

#### **Resultados informados de estudios de casos y controles**

Seis estudios de casos y controles evaluaron la repercusión de las medidas de salud pública para frenar la propagación de la epidemia de SRAG entre febrero y junio de 2003 en China, Singapur y Vietnam. La homogeneidad de la definición de casos, el agente, los contextos y los resultados permitieron el metanálisis. Se agruparon los datos binarios; ninguna de las comparaciones exhibió heterogeneidad significativa, por lo tanto se utilizó un modelo de efectos fijos. Si bien los datos continuos solían estar disponibles, las variables eran diferentes y se midieron en diferentes unidades, y las desviaciones estándar por lo general faltaban, lo cual impidió el metanálisis.

Los estudios informaron que la desinfección de viviendas fue sumamente efectiva para prevenir la propagación del SRAG (OR 0,30; IC del 95%: 0,23 a 0,39) (Lau 2004a); lavarse las manos al menos 11 veces al día previno la mayoría de los casos (OR 0,45; IC del 95%: 0,36 a 0,57), en base a los seis estudios (Lau 2004a; Nishiura 2005; Seto 2003; Teleman 2004; Wu 2004; Yin 2004); llevar una máscara simple fue sumamente eficaz (OR 0,32; IC del 95%: 0,25 a 0,40), en base a cinco estudios (Lau 2004a; Nishiura 2005; Seto 2003; Wu 2004; Yin 2004); dos estudios hallaron que usar una máscara N95 era aún más eficaz (OR 0,09; IC del 95%: 0,03 a 0,30) (Seto 2003; Teleman 2004); el uso de guantes fue eficaz (OR 0,43; IC del 95%: 0,29 a 0,65) (Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); llevar una bata también fue eficaz (OR 0,23; IC del 95%: 0,14 a 0,37) (Nishiura 2005; Seto 2003; Teleman 2004; Yin 2004); y la combinación de todos los métodos (lavado de manos, máscaras, guantes y batas) logró una efectividad muy elevada (OR 0,09; IC del 95%: 0,02 a 0,35) (Nishiura 2005; Seto 2003). Todos los estudios seleccionaron casos de hospitales, salvo uno (Lau 2004a) en el cual los casos eran personas con sospecha de SRAG informada al Departamento de Salud de Hong Kong.

#### **Estudios de cohorte prospectivos**

La limpieza con alcohol en las residencias comunales de estudiantes resultaron en un número significativamente inferior de síntomas (reducciones del 14,8% al 39,9%) y un menor ausentismo (reducción del 40%) (White 2003). En un estudio experimental pequeño muy citado, los pañuelos de papel viricidas que contenían ácido cítrico interrumpieron la transmisión de los resfriados por rinovirus transmitidos por jugar a los naipes: 42% de los usuarios de pañuelos de algodón reutilizables contrajeron resfriados comparados con ninguno en el grupo de pañuelos desechables con viricida (Dick 1986)).

Fueron pocos los estudios identificados que informaron intervenciones en el contexto ambulatorio, ya sea en el personal

o en pacientes. Tal vez, en lugar de incorporar la espuma para manos con viricida como un complemento del lavado de manos, un programa educativo del personal sobre el lavado de manos en un centro ambulatorio para adultos resultó efectivo durante los pasados cuatro años en la reducción de las tasas de infección respiratoria en pacientes ambulatorios de 14,5 a 10,4 por 100 personas al mes, a 5,7 ( $p < 0,001$ ), esto se acompañó de una disminución de las cepas virales (Falsey 1999). Este dato confirmó un informe anterior sobre la efectividad de un programa de lavado de manos para reducir el ausentismo por enfermedad pseudogripal en una escuela primaria (Kimmel 1996)).

Dos estudios con alto riesgo de sesgo informaron que la educación, el hábito del lavado de manos y enseñar a estornudar y toser correctamente a los niños del jardín de infancia, a los padres y al personal resultaron eficaces, aunque hubo fluctuaciones importantes en la incidencia de infecciones en los centros de control y de prueba (Niffenegger 1997); pero no fueron eficaces en reducir el ausentismo por infecciones respiratorias agudas (RR 0,79;  $p = 0,756$ ) (Master 1997)).

Dyer y cols. informaron un estudio de cohorte prospectivo, agrupado, cruzado y no enmascarado. El estudio evaluó la efectividad del desinfectante de manos acompañado de lavado de manos con agua y jabón a discreción en una escuela primaria privada de California. El empleo de desinfectante redujo el ausentismo por enfermedad en un 41,9% (49,7% de reducción de enfermedades respiratorias durante el período de estudio de diez semanas) (Dyer 2000)).

Curiosamente, un programa de educación sobre el control de la infección que reforzaba el lavado de manos y otras medidas higiénicas en el contexto nosocomial informó una reducción del número de microorganismos presentes en las manos y otras superficies y de infecciones respiratorias agudas, aunque los datos presentados sugirieron lo contrario (una tasa de incidencia de 4,15/1000 días de internación para los hogares de prueba versus 3,15/1000 para los hogares de control) (Makris 2000)).

Un estudio halló que el uso de máscaras protectoras por parte de los profesionales de la salud que visitan y cuidan a niños de hasta cinco años con virus sincitial respiratorio (VSR) y síntomas de enfermedad respiratoria fue eficaz (tasa de enfermedad del 5% para quienes utilizaron la máscara protectora contra el 61% en los controles sin máscaras) (Agah 1987)).

El diagnóstico de laboratorio rápido, una cohorte de enfermería y el uso de batas y guantes para todos los contactos con niños infectados por VSR, redujeron significativamente el riesgo de infección nosocomial por VSR (OR 0,013 a 0,76) (Madge 1992), si bien otro estudio similar no informó efectos relacionados con la incorporación del uso de batas ni de máscaras, a la práctica habitual de lavado de manos en el desarrollo de enfermedad en el personal a cargo de neonatos con enfermedad respiratoria (cuatro de 30 en el grupo de lavado de manos solo, comparado con cinco de 28 en el grupo de lavado de manos y uso de bata y máscara,  $p > 0,20$ ); aunque

los autores describieron un cumplimiento deficiente del protocolo de la barrera (Murphy 1981)).

Se informó que los estrictos procedimientos de triage y control de infecciones para detener la transmisión del SRAG de los niños infectados a las cuidadoras y las visitas de un gran hospital, en el punto álgido de la epidemia de 2003 en Hong Kong, resultaron eficaces para frenar la transmisión ya que ningún profesional de la salud se enfermó, en contraposición a las experiencias en otras instituciones (Leung 2004)).

Un estudio muy pequeño que comparó la máscara N95 con máscaras quirúrgicas de papel en voluntarios halló que las máscaras quirúrgicas, aun usadas superpuestas (hasta cinco máscaras), filtraban las partículas ambientales de manera deficiente (Derrick 2005); esta suposición fue confirmada por otro estudio pequeño sobre filtración de aire para prevenir la propagación de gotículas (Somogyi 2004).

#### ***Estudios de cohorte retrospectivos***

Dos estudios investigaron el aislamiento de niños menores de tres años de edad con sospecha de VSR. En uno, la transmisión se disminuyó en "hasta el 60%" (Isaacs 1991), mientras que en el otro estudio la afirmación de que la transmisión nosocomial "se redujo al mínimo" no fue apoyada por los datos (Doherty 1998)).

EL aislamiento de casos durante la epidemia de SRAG de 2003 en China informó una restricción en la transmisión sólo para los contactos que efectivamente tuvieron contacto en el hogar o el hospital con un paciente con SRAG sintomático (tasa de brotes de 31,1%, IC del 95%: 20,2 a 44,4 para los cuidadores; 8,9%, IC del 95%: 2,9 a 22,1 para los visitantes; 4,6%, IC del 95%: 2,3 a 8,9 para los que conviven con un caso de SRAG) pero no para los contactos que conviven en la misma vivienda, que trabajan con casos, o sin contacto con casos de SRAG durante el período de incubación. Esto pone en consideración extender la cuarentena sólo para los contactos con casos de SRAG sintomático (Ou 2003)).

Otro informe breve de 2003 durante la epidemia de SRAG, en un hospital militar de Taiwán, China, y 86 hospitales de control, comparó una política integrada de control de la infección para proteger a los profesionales de la salud contra la infección; sólo dos en el hospital militar estaban infectados por SRAG comparados con 43 casos presuntos y 50 casos probables en los hospitales de control (Yen 2006)).

#### ***Estudios controlados de tipo antes y después***

Dos estudios pequeños del mismo revisor principal evaluaron los medios de transmisión nosocomial del VSR en niños pequeños y los efectos de la incorporación del distanciamiento y las barreras: uno con riesgo del sesgo bajo informó la eficacia del distanciamiento físico y la separación de cuartos (0 infectado de 14 individuos que se sentaron lejos de los niños infectados por VSR comparado con 5 de 7 que tomaron en brazos a los niños y 4 de 10 que tocaron a los neonatos infectados) (Hall 1981a). El segundo estudio con riesgo de sesgo elevado no

informó beneficios adicionales con las batas y máscaras (infección del 32% versus el 41%) (Hall 1981b). La incorporación de protectores plásticos descartables para ojos y nariz a los demás procedimientos para el control de infecciones respiratorias (separar a los infectados de los no infectados, lavado de manos) también redujo la transmisión del VSR (6% versus 42% de los controles) (Gala 1986). El cribado y posterior aislamiento de las personas infectadas de las no infectadas (?formación de cohortes?) también redujo la transmisión nosocomial del VSR en niños mayores (de 5,33 infecciones por 1000 días de internación con atención a 1,23 infecciones por 1000 días de internación, después de la introducción del método de detección) (Krasinski 1990). Un estudio similar informó que el mayor cumplimiento de las medidas preventivas de aislamiento con empleo de guantes y batas redujo la elevada tasa de transmisión de VSR nosocomial en una sala para lactantes y niños pequeños (RR de las tasas de infección durante los períodos pre y posintervención 2,9; IC del 95%: 1,5 a 5,7) (Leclair 1987)).

Un estudio de protección con batas no protegió a los neonatos de la unidad de cuidados intensivos neonatales contra el VSR ni contra otros tipos de infección, tampoco afectó la mortalidad (1,21 por 100 días de internación con batas en comparación con 1,38 sin batas), aunque probablemente haya habido sesgo de selección ya que el 17% de los niños incluidos se perdieron durante el seguimiento (Pelke 1994)).

Un estudio alemán realizado a lo largo de tres estaciones informó una gran disminución de las infecciones nosocomiales por VSR, de 1,67/1000 días de internación en la primera estación a 0,18/1000 días de internación en la última estación, tras la implementación de una mejor vigilancia y retroalimentación (feedback), un diagnóstico rápido, barreras y aislamiento, así como la desinfección de superficies (Simon 2006). Un estudio similar pero con un elevado riesgo de sesgo informó una disminución de ocho casos confirmados de VSR por 1000 días de internación a ninguno (Snydman 1988). Un estudio de mejor calidad con una duración de ocho años que implementó una combinación de educación con un alto índice de sospecha para la detección de casos (precauciones de contacto), con barreras (pero sin protectores ni máscaras) y lavado de manos para los pacientes y el personal, redujo las infecciones por VSR en un hospital de Filadelfia (EE.UU.): RR 0,61; IC del 95%: 0,53 a 0,69 (Macartney 2000)).

Un estudio pequeño con sesgos potenciales graves evaluó el entrenamiento y un programa sanitario (lavado de manos, desinfección de autobuses escolares, útiles y juguetes) en un servicio de guardería de necesidades especiales para niños con síndrome de Down, con una relación alumno-personal de 5 ó 6 a 1 e informó reducciones en: enfermedades respiratorias de una media de 0,67 a 0,42 por niño por mes ( $p < 0,07$ ); visitas médicas de 0,50 a 0,33 ( $p < 0,05$ ); media de ciclos antibióticos prescritos de 0,33 a 0,28 ( $p < 0,05$ ); y días de escolaridad perdidos por infecciones respiratorias de 0,75 a 0,40 ( $p < 0,05$ ) (Krilov 1996)).

Un estudio muy amplio de reclutas militares informó que un programa verticalista y estructurado de lavado de manos al menos cinco veces al día redujo casi a la mitad la incidencia de infecciones respiratorias agudas. Los reclutas que se lavaban las manos con una frecuencia menor informaron más episodios de infecciones respiratorias agudas (OR 1,5; IC del 95%: 1,2 a 1,8), lo que representa una diferencia de 4,7 versus 3,2 infecciones medias por recluta, por año así como una mayor cantidad de hospitalizaciones (OR 10,9; IC del 95%: 2,7 a 46,2). Sin embargo, la implementación fue difícil (Ryan 2001).

Un estudio ecológico analizó los efectos de la cuarentena y el cribado en el puerto de ingreso sobre la epidemia de SRAG a principios de 2003 en Pekín, China, a partir de los datos obtenidos centralmente. Los hospitales eran las fuentes de inicio de la transmisión del virus del SRAG. El perfil de la epidemia sugiere que estas medidas posiblemente hayan reducido la transmisión del SRAG, aunque el hecho de haber identificado solamente 12 casos en más de 13 millones de personas cribadas (screened) pone en duda la efectividad directa de los controles en los puertos de entrada de aeropuertos y estaciones de ferrocarril, y probablemente el cribado haya sido más importante (Pang 2003)).

Un estudio israelí de 186 094 niños de 6 a 12 años de edad informó que el cierre de escuelas se asoció temporalmente con una reducción del 42% en la morbilidad de las infecciones de las vías respiratorias, la consiguiente disminución del 28% en las visitas al médico y a los departamentos de urgencias, así como una reducción del 35% en las compras de medicamentos (Heymann 2004)).

## DISCUSIÓN

### *Temas relativos a la calidad*

Deben analizarse varias características antes de establecer generalizaciones a partir de estos estudios.

Los contextos de los estudios, realizados durante cuatro décadas, fueron heterogéneos, e incluyeron desde escuelas de los suburbios (Carabin 1999; Dyer 2000; Heymann 2004; Niffenegger 1997) hasta cuarteles militares (Ryan 2001), unidades de cuidados intensivos, y salas pediátricas (Gala 1986; Leclair 1987) en países industrializados; barrios marginales de países de bajos ingresos (Luby 2005); y centros ambulatorios de necesidades especiales con una elevada relación de profesores por alumno (Krilov 1996). Se hicieron pocos intentos de obtener diversidad socioeconómica a través de (por ejemplo) incluir más escuelas en las evaluaciones del mismo programa (Dyer 2000). Se pudieron identificar pocos estudios de países de bajos ingresos donde reside gran parte de la carga y donde las intervenciones de bajo costo resultan críticas. Aun en los países occidentales, como Israel, la drástica caída en las infecciones respiratorias agudas (IRA) posterior al cierre de escuelas posiblemente se haya relacionado con la elevada población de niños de ese país (34%). Además, la limitada disponibilidad de fármacos sin prescripción y de seguros de

salud nacionales, integrales y universales que ofrezcan prescripciones médicas para el tratamiento sintomático podría restringir aún más la generalizabilidad de los hallazgos (Heymann 2004)).

La calidad variable de los métodos de estos estudios es sorprendente. Que el diseño sea improvisado durante las crisis de salud pública, en especial en los seis estudios de casos y controles, es comprensible, pero no así en los casos de ausencia de asignación al azar (ni siquiera por grupos) de varios estudios de cohorte y de tipo antes y después, realizados en circunstancias no apremiantes. La asignación al azar pudo haber provocado una mínima interrupción de la prestación del servicio. El informe inadecuado dificultó especialmente la interpretación de los estudios de tipo antes y después. Informe incompleto o inexistente: aleatorización (Turner 2004a); cegamiento (Farr 1988a; Farr 1988b); numeradores y denominadores (Carabin 1999; Kotch 1994); intervenciones; medidas de resultado (White 2003); deserción de participantes (Makris 2000); intervalos de confianza (Madge 1992); y coeficientes por grupos en los ensayos relevantes (Carabin 1999) ocasionó una considerable pérdida de información. Los sesgos potenciales (como los incentivos de dinero en efectivo para los participantes (White 2003)) no fueron tratados. Algunos revisores incluso confundieron los diseños de cohortes con los de tipo antes y después al establecer conclusiones no apoyadas por sus datos (Makris 2000). La calidad metodológica a veces fue debilitada por la necesidad de ofrecer intervenciones conductuales en medio de la prestación del servicio (Niffenegger 1997)).

No obstante, aun cuando se seleccionaron diseños subóptimos, muy pocas veces los revisores intentaron articular los posibles factores de confusión. Un factor de confusión generalmente ignorado, específico de esta área, es la enorme variabilidad en la incidencia viral (Heymann 2004; Isaacs 1991). En algunos casos este tema fue abordado en el diseño del estudio (Falsey 1999), incluso en los estudios controlados de tipo antes y después (uno intentó correlacionar los ingresos al hospital por VSR y el VSR circulante en la comunidad) (Krasinski 1990). Otro intentó relacionar las tasas de exposición (medida según la excreción nasal) y de infección en los períodos pre y posintervención (Leclair 1987)).

Los placebos inapropiados causaron problemas de diseño. En algunos estudios el placebo probablemente poseía el suficiente efecto de intervención como para diluir los efectos de la intervención (Longini 1988). Dos intentos valerosos probablemente hayan fracasado porque los pañuelos de placebo se impregnaron con un compuesto de diseño que irritaba los orificios nasales de los usuarios (Farr 1988a; Farr 1988b)).

Algunos estudios usaron intervenciones poco prácticas. Los voluntarios sometidos a la intervención de limpiador de manos (ácidos orgánicos) no tenían permitido usar las manos entre la limpieza y la exposición al virus, de manera que el efecto del uso habitual de las manos durante la intervención sigue siendo desconocido (Turner 2004a; Turner 2004b). Pintar las manos

con una solución acuosa de yodo al dos por ciento, si bien es una intervención antiviral exitosa, deja manchas estéticamente inadmisibles y, en general, es poco práctico salvo para quienes poseen un riesgo muy alto de contagio epidémico (Gwaltney 1980)).

El cumplimiento de las intervenciones, en especial los programas educacionales, representó un problema para varios estudios a pesar de la importancia de muchas de las intervenciones de bajo costo.

### **Las pruebas**

Los ensayos con asignación al azar por grupos de la más alta calidad sugieren que el mayor efecto en la prevención de la propagación del virus respiratorio se obtiene con medidas higiénicas en niños pequeños. Quizás esto se deba a que los niños pequeños son menos capaces de adoptar conductas de higiene por ellos mismos (Roberts 2000), y poseen infecciones más duraderas y un mayor contacto social, por consiguiente actúan como puertas de entrada de la infección al grupo familiar (Monto 1969)). El beneficio adicional de una disminución en la transmisión de este grupo a otros miembros de la familia es ampliamente apoyado por los resultados de otros diseños de estudio, con mayores probabilidades de factores de confusión.

Los seis estudios de casos y controles indican que la implementación de barreras contra la transmisión, el aislamiento y las medidas higiénicas son eficaces y se valen de intervenciones relativamente económicas para contener las epidemias de virus respiratorios. Se hallaron escasas pruebas sobre la superioridad de la efectividad de los dispositivos de barrera para las gotículas, como las máscaras N95 sobre las máscaras quirúrgicas simples. Las máscaras N95 son respiradores con una capacidad de filtración del 95% en comparación con los aerosoles de partículas no aceitosas (Teleman 2004)). Son más costosas e incómodas (especialmente si se las utiliza durante períodos prolongados) que las máscaras quirúrgicas simples, pero pueden resultar útiles en situaciones de muy alto riesgo.

No queda claro si el efecto gradual de agregar viricidas o antisépticos al lavado de manos normal efectivamente disminuyó la carga de enfermedad respiratoria más allá de los límites de los estudios bastante atípicos, sobre los cuales se informa. El beneficio adicional pudo haberse incrementado, al menos en parte, por el efecto de confusión de las rutinas adicionales.

Los estudios sobre prevención de la transmisión del VSR y otros virus similares parecían acercarse más a la vida real y sugerían una efectividad adecuada. Sin embargo, las cuestiones de calidad metodológica de los estudios controlados de tipo antes y después, anteriormente mencionados, sugieren que los beneficios posiblemente se deban a diferencias en la población, especialmente las tasas de infección viral. Estos se informaron inadecuadamente en la mayoría de los estudios.

La aplicación sistemática y a largo plazo de ciertas medidas evaluadas en la revisión resultaría problemática, en especial el mantenimiento de rutinas de barreras y de higiene estricta durante períodos prolongados. Probablemente esto sólo sería factible en contextos muy motivados, como los hospitales, sin una amenaza real de epidemia en camino. La mayoría de los revisores realizaron observaciones sobre la principal carga logística impuesta por las rutinas de barrera a nivel de la comunidad. Sin embargo, la amenaza de una epidemia inminente podría proporcionar el estímulo para su inicio.

Un hallazgo desalentador fue la falta de evaluaciones adecuadas de medidas mundiales y de grandes recursos como el cribado en los puertos de ingreso y el distanciamiento social. Los escasos estudios (principalmente realizados durante la epidemia de SRAG) no permiten establecer conclusiones definitivas.

## **CONCLUSIONES DE LOS AUTORES**

### **Implicaciones para la práctica**

Las siguientes intervenciones eficaces deben implementarse, preferentemente de manera combinada, para disminuir la transmisión de enfermedades respiratorias virales: lavado de manos asiduo con o sin agregado de antisépticos; medidas de barrera como guantes, batas, y máscaras con mecanismo de filtración; y diagnóstico de sospecha con aislamiento de los casos probables. El énfasis debe estar puesto en la reducción de la transmisión de los niños pequeños.

### **Implicaciones para la investigación**

Las medidas de salud pública pueden ser sumamente efectivas, sobre todo si forman parte de un programa estructurado que incluye instrucción y educación, y si se proporcionan de manera conjunta. Sin duda, es necesario realizar nuevos ensayos pragmáticos amplios para evaluar las combinaciones óptimas. De ser posible, deberían realizarse ensayos controlados aleatorios con un diseño pragmático, similar al ensayo Luby y cols. (Luby 2005). No obstante, esta revisión sistemática de la investigación disponible efectivamente proporciona ciertas apreciaciones importantes. Posiblemente el notable efecto de las medidas higiénicas centradas en los niños pequeños se deba a la escasa capacidad para mantener su propia higiene. La calidad variable y la pequeña escala de ciertos estudios se conoció a partir de los estudios descriptivos (Aiello 2002; Fung 2006; WHO 2006) y de las revisiones sistemáticas de las intervenciones seleccionadas (Meadows 2004)).

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## POTENCIAL CONFLICTO DE INTERÉS

Ninguno conocido.

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\* El asterisco señala los documentos más importantes para este estudio

## TABLAS

## Characteristics of included studies

Study	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 HCWs 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 healthcare workers (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
Allocation concealment	D - Not used
Study	Carabin 1999
Methods	Cluster randomised controlled trial carried out in day care 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 URTIs. 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 URTI 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). 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
Interventions	Training session (1 day) with washing of hands, toy cleaning, window opening, sand pit cleaning and repeated exhortations to hand wash
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

**Characteristics of included studies**

Notes	Risk of bias: high (no description of randomization; 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 two 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Derrick 2005</b>
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	Six volunteers who wore the masks and had their droplet count taken
Interventions	Pleated rectangular three-ply surgical mask
Outcomes	Laboratory
Notes	Risk of bias: high (report too brief to allow assessment) Notes: The authors conclude that the best combination of five 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 masks unless there is no alternative. Cautiously the authors state that they cannot comment on the capacity of five 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Dick 1986</b>
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. Twenty 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. Eight 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 CMS tissues to prevent spreading of R16 colds. In the two 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
Outcomes	Laboratory: serological evidence (serum samples or viral isolation) Effectiveness: rhinovirus colds Safety: N/A

**Characteristics of included studies**

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)
Allocation concealment	D - Not used
<b>Study</b>	<b>Doherty 1998</b>
Methods	Retrospective cohort study carried out in North Staffordshire hospital (UK) during two 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 minimize 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 six bedded bays on the paediatric ward. All carers observed standard routines (handwashing and gown wearing)
Participants	Children less than three 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
Interventions	RSV diagnosis and cohorting versus normal care
Outcomes	Laboratory: aspirates for RSV diagnosis Effectiveness: RSV illness (developed at least five 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 controls arms were (.i.e. cohorting of RSV infected children to prevent infection in whom?)
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Dyer 2000
Methods	Prospective cluster open-label cross-over cohort study of programmed use of a hand sanitizer in conjunction with at-will soap-and-water hand washing conducted in a private elementary school in California. The aim of the study was to assess the effectiveness of the SAB sanitizer at reducing illness absenteeism in a school setting. Subjects were grouped by classroom without formal randomisation. Seven classes received the instant sanitizer, while the remaining seven classes were assigned to the control group. Male-to-female ratios and age distributions of the two groups did not differ significantly. Prior to study commencement all students participated in an educational program about germs and the importance of hand washing to prevent illnesses. Children in the hand sanitizer group received a spray to use under teacher supervision to supplement normal, at-will hand washing 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 sanitizer 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 crossover cohort study over 10 weeks
Interventions	Educational programme plus the SAB (surfactant, allantoin and benzal konium chloride) spray hand sanitizer in 1oz bottles fitted with a pump spray top and with at-will soap-and-water hand washing 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 sanitizer with at-will hand washing using soap and water significantly decreased absences due to acute communicable illness. Use of the sanitizer 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
Allocation concealment	D - Not used
Study	Falsey 1999
Methods	Prospective cohort study conducted at three adult day-care centers in Rochester, New York. The study assessed the value of a staff educational program combined with the use of a portable virucidal hand foam for the reduction of respiratory infections in day-care 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 center 1: 69 elderly and 36 staff members; center 2: 67 elderly and 45 staff members; center 3: 68 elderly and 16 staff members

**Characteristics of included studies**

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 program for staff was associated with an almost 50% decrease in the infection rate in day-care attendees. The programme was effective only in the last of the four years of the programme (rates of infection in day-care 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 day-care setting, both in staff and patients. The decline in influenza-like illness episodes across the four study years is reflected in the decline in viral isolates, suggesting that aspecific measures such as handwashing are effective against the main respiratory viruses
Allocation concealment	D - Not used
<b>Study</b>	<b>Farr 1988a</b>
Methods	The study was a six-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 sulfate, while placebo tissues contained saccharin
Outcomes	Laboratory: serological evidence: no Effectiveness: respiratory illness Safety: N/A

**Characteristics of included studies**

Notes	Risk of bias: high (failure of blinding) 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 two study group, 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Farr 1988b</b>
Methods	The study was a six-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. Two-hundred and thirty-one 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 sulfate, while placebo tissues contained succinin 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	Risk of bias: high (failure of blinding) 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 (succinin 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
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Gala 1986
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. 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: hand washing, isolation and cohorting. In reality although on report, Gala and colleagues are conducting two studies. The first is a non-concurrent cohort study, in which two different population of children are assessed separated by a 1 week "washout" 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 1 177 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 1 174 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 one nosocomial RSV infection was detected. During period 2 277 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, two of the ward staff were acquired RSV infection and were not considered susceptible
Interventions	Use of a disposable plastic eye-nose goggle and respiratory infection control procedures vs. 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?
Allocation concealment	D - Not used

## Characteristics of included studies

Study	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. Other two 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 three 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 sec. Donors and recipients wore masks during the exposure period
Participants	15 and 20 volunteers in two 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 randomization 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 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
Allocation concealment	D - Not used
Study	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 three groups: "cuddlers", exposed to an infected infant over two to four hours by caring 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 three 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

**Characteristics of included studies**

Participants	31 Volunteers: seven 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
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. Infections 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Hall 1981b</b>
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 two months. All patients and staff on the ward for children less than three years of age were included. During the first four 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 four week the wearing of gowns and masks was discontinued and handwashing alone was used for the final five weeks of the study. Throughout the study handwashing, cohorting and isolation were employed and emphasized. The number of nosocomial infections in patients and staff for period 1 were compared with the period 2 (last four weeks of the study). Infections 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

**Characteristics of included studies**

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 two 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 two 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?
Allocation concealment	D - Not used
<b>Study</b>	<b>Heymann 2004</b>
Methods	Controlled before and after study to evaluate the effect of school closure on the occurrence of respiratory infection among children ages 6-12 years and its impact on health care 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-weeks 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

**Characteristics of included studies**

Notes	<p>Risk of bias: high</p> <p>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 Western countries with lower per centage of children. In addition there may be a difference in parental attitudes toward respiratory illness symptoms in other cultures that affect health care utilization. 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 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 Dec 1999</p> <p>Observed effect may be due to school closure or they may be due to lower circulation of the viruses</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Isaacs 1991</b>
Methods	<p>Retrospective prospective cohort study was conducted to evaluate the effectiveness of cohorting and educational program (handwashing) in reducing the incidence of nosocomial respiratory syncytial virus infections.</p> <p>Data on all children with RSV infection on any of the paediatric wards in winter of 1986-7 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 two paediatric wards and the paediatric intensive care unit and the number they spent in hospital. For the next two 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</p>
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	<p>Laboratory: indirect immunofluorescence on nasopharyngeal secretions or by culture of secretions</p> <p>Effectiveness: RSV infection</p> <p>Safety: N/A</p>

**Characteristics of included studies**

Notes	<p>Risk of bias: high (poor descriptions)</p> <p>Notes: the authors concluded that hand washing and cohorting reduced at least 66% in the number of hospital acquired infections due to RSV in the two 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</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Kimel 1996</b>
Methods	<p>Prospective cohort study conducted in a school of Chicago, USA, to evaluate the effectiveness of a handwashing program in reducing the absenteeism caused by flu-like illness. The school was located in a predominantly white, middle to upper middle class suburb. All four kindergarten and five 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 program was planned for presentation just prior to this time. The effectiveness of the program was determined by comparing absentee rates among participants and non participating classes (the control group). Absentee rates were determined by reviewing the computerized 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</p>
Participants	199 children of kindergarten and first grade schools
Interventions	Handwashing and educational program versus no intervention
Outcomes	<p>Laboratory: no</p> <p>Effectiveness: flu-like illness</p> <p>Safety: N/A</p> <p>Absenteeism from influenza-like illness was approximately double in the control arm (P = 0.01)</p>
Notes	<p>Risk of bias: medium</p> <p>Notes: The authors concluded that hand washing 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 flu-like illness 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 flu season was later than usual (February), and this represented a confounding variable. The teacher surveys indicated problems with handwashing facilities</p>
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Kotch 1994
Methods	Pair-matched cluster randomised controlled trial conducted in the period 19 October 1988 to 23 May 1989 in 24 child care 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 day care 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 coefficient reported. Centre were matched in pairs and then randomly allocated to either intervention of control programmes
Participants	389 children aged 3 years or less in day care 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 randomization; 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
Allocation concealment	D - Not used
Study	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 four children shared a room. All paediatric patients hospitalised on or before Dec 31 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

**Characteristics of included studies**

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
Allocation concealment	D - Not used
<b>Study</b>	<b>Krilov 1996</b>
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 to November 1993. The before between Nov 1991 and Oct 1992, followed by a one month washout period during which the intervention was introduced, followed by 12 months of after period (Dec 1992 to Nov 1993)
Participants	Thirty three 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Ladegaard 1999</b>
Methods	RCT with cluster randomisation (they called it "lottery", the same as "clip the coin") to intervention or control. Out of 10 institutions they excluded two because they want institutions 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

**Characteristics of included studies**

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 hand washing, importance of clean and fresh air. The aims of the intervention were: <ul style="list-style-type: none"> <li>- to increase the hygiene education of the day care teachers</li> <li>- to motivate the children by practical learning to have a better hand hygiene</li> <li>- to inform the parents about better hand hygiene</li> </ul>
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
Allocation concealment	D - Not used
<b>Study</b>	<b>Lau 2004a</b>
Methods	Case-control study carried out in Hong Kong, SAR 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 one index case were considered as having two index cases. Of the 1690 identified cases, 1214 from 996 households were enrolled in the study. One hundred and forty cases could not be contacted as they had a wrong phone number, 163 were uncontactable after at least five attempts, 163 refused to take part and 10 did not speak either Chinese or English. Seventeen were further excluded because they were aged less than 16. Twenty two 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 RX 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)

**Characteristics of included studies**

Notes	<p>Risk of bias: medium (inconsistencies in the text: lack of description of controls)</p> <p>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):</p> <ul style="list-style-type: none"> <li>- Visit to mainland China 1.95 (1.11 to 3.42)</li> <li>- Visited Price of Wales Hospital 7.07 (1.62 to 30.75)</li> <li>- Visited other hospitals 3.70 (2.54 to 5.39)</li> <li>- Visited Amoy Gardens 7.63 (3.77 to 15.43)</li> </ul> <p>The following activities/interventions had a significant protective function:</p> <ul style="list-style-type: none"> <li>- Thorough disinfection of living quarters 0.41 (0.29 to 0.58)</li> <li>- Wore a mask in public places frequently 0.36 (0.25 to 0.52)</li> <li>- Washed hands 11 or more times a day 0.58 (0.38 to 0.87)</li> </ul> <p>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</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Leclair 1987</b>
Methods	<p>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 three 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 five 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</p>
Participants	695 patients aged from 5 days to 4 years and 11 months. The distribution of ages was similar in the two periods. Thirty-seven acquired nosocomial RSV infections
Interventions	Infection-control intervention to increase use of gloves and gowns versus no intervention
Outcomes	<p>Laboratory: yes</p> <p>Effectiveness: RSV infection</p> <p>Safety: N/A</p>

**Characteristics of included studies**

Notes	<p>Risk of bias: low</p> <p>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 publicized, the head nurse introduced an educational program 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 its 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</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Leung 2004</b>
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	<p>Triage and UHR-S isolation &amp; strict infection control procedures versus triage and UHR-S isolation and less strict infection control procedures.</p> <p>Healthcare workers were exposed to nine 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 vs triage and UHR-S isolation + less strict infection control procedures.</p> <p>Triage at admission aimed at identifying children aged less than 18 who:</p> <ul style="list-style-type: none"> <li>were febrile or afebrile with a known SARS contact who were admitted to the UHR-S area</li> <li>with a positive CXR and a SARS contact who were admitted to the UHR-S area</li> <li>with CXR changes but no SARS contact who were admitted to the UHR-I area</li> <li>were febrile or afebrile but no SARS contact who were admitted to the HR area</li> </ul> <p>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),</p> <p>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 theatre garments and mask of N95 face respirator for HCWs and handwashing and paper mask for visitors and patients).</p>

**Characteristics of included studies**

Outcomes	Enforcement was directed by a police nurse in the UHR areas 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 health care workers. All the more remarkable as the paediatric department had not been built as isolation facility and had to be rapidly reorganised.
Allocation concealment	D - Not used
<b>Study</b>	<b>Longini 1988</b>
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" five 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 three-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, 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 two 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
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Luby 2005
Methods	<p>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).</p> <p>Randomisation took place by computer generated random numbers in three phases:</p> <ul style="list-style-type: none"> <li>- 25 neighbourhoods were assigned to handwashing and 11 to standard practice</li> <li>- 300 households assigned to using antiseptic soap</li> <li>- 300 households assigned to using plain soap</li> <li>- 306 households assigned to standard practice</li> <li>- 1523 children younger than 15 years assigned to using antiseptic soap</li> <li>- 1640 children younger than 15 years assigned to using plain soap</li> <li>- 1528 children younger than 15 years assigned to standard practice</li> </ul> <p>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</p>
Participants	<p>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</p> <p>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</p> <p>1528 children younger than 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</p>
Interventions	<p>Instruction programme and antibacterial soap containing 1.2% triclocarban, or ordinary soap to be used throughout the day by householders or standard procedure</p>
Outcomes	<p>Laboratory: N/A</p> <p>Effectiveness:</p> <ul style="list-style-type: none"> <li>- Number of new respiratory illness per person per week</li> <li>- Pneumonia (cough or difficulty in breathing with a respiratory rate of &gt; 60 min in children less than 60 days old, &gt; 50 min in those less than 1 year old and &gt; 40 min for those aged 1 to 5 years)</li> </ul> <p>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</p> <p>Safety: N/A</p>
Notes	<p>Risk of bias: low (cluster coefficients and analysis by unit of randomization provided)</p> <p>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</p>
Allocation concealment	D - Not used

**Characteristics of included studies**

<b>Study</b>	<b>Macartney 2000</b>
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 two 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 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Madge 1992</b>
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 two 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

**Characteristics of included studies**

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, two 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Makris 2000</b>
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 program 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 don't 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
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Master 1997
Methods	Prospective cohort study conducted in an elementary school, Detroit, to evaluate the effect of a mandatory scheduled handwashing program 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 eight 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 eight classrooms (162 students) were the control group
Interventions	Handwashing program 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 (URI) - 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
Allocation concealment	D - Not used
Study	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 crossover 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 hand washing 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)

**Characteristics of included studies**

Interventions	Use of an alcohol gel as an adjunct to regular handwashing and educational program 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 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Murphy 1981</b>
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 two 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 virus spread which would not be blocked by the use of mask and gown
Allocation concealment	D - Not used
<b>Study</b>	<b>Niffenegger 1997</b>
Methods	Prospective two-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 two groups, but data are not shown. No attrition is mentioned

**Characteristics of included studies**

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.
Allocation concealment	D - Not used
<b>Study</b>	<b>Nishiura 2005</b>
Methods	Case-control study carried out during the SARS outbreak (26 Feb 03 to 28 Apr 03) 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 three phases. The first phase (26 Feb to 4 Mar 03) in which an index case and 9 suspected secondary cases were admitted/cared for. The second phase (8 Mar to 11 Mar 03) in which outpatients were closed and staff no longer returned home as the outbreak spread and the third phase (11 Mar 03 to 28 April 03) 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
Outcomes	SARS infection

**Characteristics of included studies**

Notes	Risk of bias: low Notes: the authors conclude that masks (OR 0.3, 95% 0.1 to 0.7) and gowns (OR 0.2, 95% 0.0 to 0.8) were significantly associated with protection (OR, 95% to) during phase 1 but in Phase 2 masks (OR 0.1, 95% 0.0 to 0.3) and all measures (OR 0.1, 95% 0.0 to 0.3) were associated with protection probably because of the increased awareness of the danger of the outbreak and increase us 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Ou 2003</b>
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 Severe Acute Respiratory Syndrome (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: <ul style="list-style-type: none"> <li>- Health care worker not using personal protective equipment (PPE) when caring for/assessing a SARS case;</li> <li>- other persons caring for a SARS case</li> <li>- persons sharing accommodation with a SARS case</li> <li>- persons visiting a SARS case</li> <li>- persons working with a SARS case</li> <li>- classmates or teachers of a SARS case</li> <li>- persons sharing the same means of public transport with a SARS case</li> </ul> All quarantines 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

**Characteristics of included studies**

Notes	<p>Risk of bias: high</p> <p>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 several limits 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.</p> <p>Overall, not enough denominator data, non exposed data are given to allow data extraction or calculate OR</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Pang 2003</b>
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	<p>SARS was made notifiable on 9th of 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.</p> <p>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</p>
Outcomes	<p>Laboratory: laboratory testing for the presence of SARS-CoV was not part of the case definition</p> <p>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).</p> <p>Safety: N/A</p>

**Characteristics of included studies**

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 25th of 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Pelke 1994</b>
Methods	Controlled before and after study conducted in a neonatal intensive care unit (NICU) of Kapiolani medical center, Honolulu, Hawaii, to assess the effect of gowning on RSV and other infections, on traffic and handwashing patterns. Alternate 2- months 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 hand wash 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 464-6195 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
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
Allocation concealment	D - Not used

**Characteristics of included studies**

<b>Study</b>	<b>Roberts 2000</b>
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
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 randomization) Notes: The authors conclude that although there was no overall decrease in respiratory illness (RR 0.95 95% CI 0.89 to 1.01), but 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 three compliance levels are also reported. A so-so reported and well conducted trial
Allocation concealment	D - Not used
<b>Study</b>	<b>Ryan 2001</b>
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 two 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 hand washing
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

**Characteristics of included studies**

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 three stratified samples of recruits infrequent hand washers 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Sandora 2005</b>
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 child care 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 (two 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 a 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Seto 2003</b>
Methods	Case-control study Hong Kong, China, conducted during the period 15 March to 24 March 2003 in five hospitals. The study aims were to assess the effectiveness of protective procedures for contracting SARS in HCWs exposed to 11 index cases in three of the five hospitals during the SARS epidemic

**Characteristics of included studies**

Participants	<p>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 two of either: new cough, malaise, signs of consolidation</p> <p>Description of controls: 241 staff from the five 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</p>
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
Notes	<p>Risk of bias: medium (inconsistencies in the text: lack of description of controls)</p> <p>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</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Simon 2006</b>
Methods	Controlled before and after study to assess the effects of a programme to prevent transmission of nosocomially acquired RSV (RSV) infections in hospitalized patients. The study describes "a specialized database for surveillance" in a university children's hospital in Bonn, Germany. The study took place between 1999 and 2002 (three seasons each starting November 1 and finishing April 30) and the incidence of RSV nosocomially acquired infections for the first season was compared to those of the second and third seasons
Participants	The denominator was all paediatric in-patients with a diagnosis of RSV admitted for at least 24 hours (283 RSV infections in the 278 general - i.e. with and without risk factors for RSV - hospitalised people in total). As these were reported broken down by season data were extracted only for admissions. The numerator was 39 cases (13.8%) which were nosocomial infections (24, 13 and 2 respectively in each of the seasons). Nearly forty-nine percent of all nosocomial infections were found in prematurely born infants. Mean age of participants was 12 months. Other important data are reported (e.g. birth weight, length of stay and duration of viral shedding but without before and after breakdown). In prematurely born infants however the text reports 19 infections: 12 in 99-00, 7 in 00-01 and 0 in 01-02 (this contradicts the data in table 1, where 19 term infants had nosocomial infections, meaning the remaining 20 were premature)
Interventions	Multifaceted barrier concept (enhanced surveillance and feedback, rapid diagnosis, barriers and isolation, disinfection of surfaces) based on the CDC recommendations introduced in September 2000

**Characteristics of included studies**

Outcomes	Laboratory: quick and full pathogen identification with antigen detection Effectiveness: RSV nosocomial infection (RSV positive patient becoming symptomatic on day 5 or later since admission). Illness severity also defined but the data were not extracted
Notes	Risk of bias: low Notes: Following the introduction of the surveillance and prevention policy, a 9-fold decrease (1.67 vs. 0.18/1000 patient-days) was found when comparing the first and the last season. Intensive care treatment was required in 18% of all documented RSV-infections, in 48.7% of all NI cases and in 43.5% of all RSV-infected prematurely born infants. Overall RSV-related mortality was 0.71%. The authors conclude that early diagnosis, a strict cohorting and contact isolation policy, and prospective surveillance contribute to the reduction of nosocomial RSV infection. A reasonably reported study with incidence data presented by sex, age group, birth weight etc in an attempt to minimise bias
Allocation concealment	D - Not used
<b>Study</b>	<b>Snydman 1988</b>
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 two 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 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Somogyi 2004</b>
Methods	Prospective cohort study of 9 observation (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

**Characteristics of included studies**

Interventions	Three masks, two without air filter and allowing external exhalation, one with manifold and air filter
Outcomes	Effectiveness: plume of droplets as observed and photographed: masks were poor at preventing droplet spread
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
Allocation concealment	D - Not used
<b>Study</b>	<b>Teleman 2004</b>
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 meter Duration of exposure 60 or more minutes Wearing N95 mask 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 Hand washing after each patient
Outcomes	SARS
Notes	Risk of bias: low Notes: The authors conclude that three factors were associated with significant risks or protection: Wearing N95 mask OR 0.1 (95% CI 0.02 to 0.86) Contact with respiratory secretions OR 21.8 (95% CI 1.7 to 274.8) Hand washing 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. I wonder how much of the non-significance for certain factors is due to lack of statistical power
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Turner 2004a
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: high (no description of randomization 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
Allocation concealment	D - Not used

## Characteristics of included studies

Study	Turner 2004b
Methods	<p>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.</p> <p>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</p>
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	<p>Laboratory: yes</p> <p>Effectiveness: rhinovirus type 39 infection</p> <p>Safety: N/A</p>
Notes	Risk of bias: high (no description of randomisation process, concealment, or allocation)
Allocation concealment	D - Not used
Study	White 2001
Methods	<p>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 &amp; 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</p>
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 four colour coded bottles containing both. School staff, parents and participants were blinded
Outcomes	<p>Laboratory: testing of virucidal and bactericidal activity of the active compound</p> <p>Effectiveness: ARI (cough, sneezing, sinus trouble, bronchitis, fever, red eye, headache, mononucleosis, acute exacerbations of asthma)</p> <p>Gastrointestinal and other illnesses (data not extracted)</p> <p>Follow up and observation was carried out by classroom staff and illnesses were described by parents</p> <p>Safety: 7 students dropped out because of mild sensitivity to the rub</p>

**Characteristics of included studies**

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
Allocation concealment	D - Not used
<b>Study</b>	<b>White 2003</b>
Methods	Prospective open cohort study carried out at the university of Colorado Boulder campus during eight 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
Allocation concealment	D - Not used
<b>Study</b>	<b>Wu 2004</b>
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

## Characteristics of included studies

	<p>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.</p> <p>Seven controls (two matched sets) were excluded because they were aged less than 14 and seven matched sets were excluded because the case was reclassified as a HCW</p> <p>Cases and controls were interviewed for the 2 weeks preceding symptoms</p>
Interventions	<p>Always wearing a mask</p> <p>Intermittently wearing a mask</p> <p>Washing hands</p> <p>Owning a pet</p> <p>Visiting a farmer's market</p> <p>Visited clinics, eaten out, or taken taxis</p>
Outcomes	SARS
Notes	<p>Risk of bias: medium (inconsistencies in the text: lack of description of controls)</p> <p>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</p>
Allocation concealment	D - Not used
<b>Study</b>	<b>Yen 2006</b>
Methods	Retrospective cohort study carried out during 27 April to 21 May 2003 in one military hospital in Taiwan, China (intervention hospital) and 86 control hospitals. The study aims were to assess the effectiveness of an integrated infection control policy introduced in the intervention hospital in protecting HCWs and patients from SARS infection
Participants	85 doctors, 203 nurses and 171 administrative staff and volunteers in the intervention hospital and an unknown number of their colleagues in the 86 control hospitals (746 high risk infectious disease beds)
Interventions	Integrated infection-control strategy with triage and barriered traffic flow into hospital, risk zoning, negative pressure areas of isolation, personal hygiene and barrier interventions versus normal isolation procedures
Outcomes	<p>Laboratory: for confirmation of SARS Co-V</p> <p>Effectiveness: SARS cases probable or suspect (WHO case definitions)</p> <p>Safety: N/A</p>

**Characteristics of included studies**

Notes	Risk of bias: high Notes: the authors conclude that during the study period only 2 HCWs were infected with SARS but there were 43 suspected and 50 probable cases in the control hospital. The difference was statistically significant. Sketchily reported study with missing denominators and data on exposure to SARS, as one would expect from a study carried out during an epidemic. I am not clear how the intervention differed from high risk isolation procedures
Allocation concealment	D - Not used
<b>Study</b>	<b>Yin 2004</b>
Methods	Case-control study carried out in ten hospitals of Gunandong province, China, comparing the rate of usage of protective measures in HCWs with SARS and without SARS. The rate of exposure to SARS between two 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 Hand washing 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 interventions 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
Allocation concealment	D - Not used

**Characteristics of included studies**

Notas:

HCW: health care worker  
 CXR: chest X-ray  
 RSV: respiratory syncytial virus  
 URTI: upper respiratory tract infection  
 OR: odds ratio  
 Hanoi French Hospital (HFH)  
 ITT: intention-to-treat  
 GI: gastro-intestinal  
 SCBU: special care baby unit  
 WBC: white blood cell  
 NICU: neonatal intensive care unit

**Characteristics of excluded studies**

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
Aragon 2005	Descriptive paper (non-comparative). Has no viral outcomes
Barros 1999	Correlational study between incidence of upper respiratory tract infection (URTI) and factors such as overcrowding
Bell 2004	Has unpublished entry exit screening data and extensive references but no comparative data
Ben-Abraham 2002	Exclude - bacterial illness only
Black 1981	Diarrhoea only outcome
Breugelmans 2004	Description of risk factors in aircraft
CDC 2003	Case reports
Carter 2002	News item
Castillo-Chavez 2003	Editorial
Cava 2005a	Survey of quarantinees' views
Cava 2005b	Personal experiences of quarantine
Chai 2005	Letter - about MRSA
Chaovavanich 2004	Case report
Chau 2003	No original retrievable data. Mathematical model fitting expected to observed cases with quarantine in the SAR of Hong Kong
Chia 2005	Knowledge survey
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

**Characteristics of excluded studies**

Doebbeling 1992	RCT respiratory data not present. Only 3 viruses isolated in total with no viral typing available
Dwosh 2003	Case series
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
Gaydos 2001	Editorial linked to Ryan
Gensini 2004	Interesting historical review
Giroud 2002	Non clinical outcomes
Glass 2006	Mathematical model - no original data presented
Gore 2001	Summary of Dyer 2000 (already included)
Gostin 2003	Not an analytical study
Guinan 2002	It would appear that nine classes took part and "acted as their own controls", but it is not clear if there was crossover 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 is 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 an RCT with laboratory induced colds, small numbers 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 et al (included)
Hendley 1988	Inappropriate intervention
Hilburn 2003	No ARI/viral outcomes (e.g. URTIs)
Ho 2003	Descriptive review
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
Jones 2005	Historical account
Kaydos-Daniels 2004	Not an analytical 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

**Characteristics of excluded studies**

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
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
Marin 1991	Viral resistance study
Monsma 1992	Non-comparative study
O'Callaghan 1993	Letter linked to Isaacs 1991
Olsen 2003	Description of transmission
Ooi 2005	Descriptive study but with interesting organisational chart
Pang 2004	Descriptive study of Beijing outbreak. Some duplicate data in common with Pang 2004
Pittet 2000	Analysis of relationship between handwashing compliance campaign and nosocomial bacterial infections (e.g. MRSA)
Prasad 2004	Letter of retrospective cohort - behavioural
Rabenau 2005	In vitro test of several disinfectants
Riley 2003	Mathematical model fit to evidence
Rosenthal 2005	Outcomes were generic (for example, pneumonia, URTIs). No laboratory data available for viral diagnosis
Safiulin 1972	Non-comparative set of studies with no clinical outcomes
Satter 2000	Experiment assessing virucidal activity of finger tip surface - no clinical outcome data
Sizun 1996	This is a review, with no original data presented
Svoboda 2004	Descriptive study with before and after data but shifting denominators
Ueno 1990	Experimental study. No clinical intervention
Wang 2003	Descriptive study
Wang 2005	Case-control study of susceptibility factors
Weber 2004	Editorial linked to Larson 2004
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

**Characteristics of excluded studies**

Yu 2004	Description of transmission
Zamora 2006	Head-to-head comparison of two sets of PPEs with no controls and no clinical outcomes
Zhao 2003	CCT of SARS treatment

**CARÁTULA**

Titulo	<b>Intervenciones para frenar o reducir la propagación de virus respiratorios</b>
Autor(es)	<b>Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, Hewak B, Prabhala A, Nair S, Rivetti A</b>
Contribución de los autores	Ruth Foxlee (RF) y Alex Rivetti (AR) fueron responsables de la elaboración de las estrategias de búsqueda. Tom Jefferson (TOJ), Chris Del Mar (CDM) y Liz Dooley (LD) fueron responsables de la redacción del protocolo. TOJ, Eliana Ferroni (FE), Bill Hewak (BH) y Adi Prabhala (AP) extrajeron los datos de los estudios. Sree Nair (SN) realizó los análisis. TOJ y CDM redactaron el informe final. Todos los autores colaboraron en el informe final.
Número de protocolo publicado inicialmente	2006/4
Número de revisión publicada inicialmente	2007/4
Fecha de la modificación más reciente"	20 agosto 2007
"Fecha de la modificación SIGNIFICATIVA más reciente	27 julio 2007
Cambios más recientes	<b>El autor no facilitó la información</b>
Fecha de búsqueda de nuevos estudios no localizados	<b>El autor no facilitó la información</b>
Fecha de localización de nuevos estudios aún no incluidos/excluidos	<b>El autor no facilitó la información</b>
Fecha de localización de nuevos estudios incluidos/excluidos	21 noviembre 2006
Fecha de modificación de la sección conclusiones de los autores	<b>El autor no facilitó la información</b>

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Número de la Cochrane Library	CD006207
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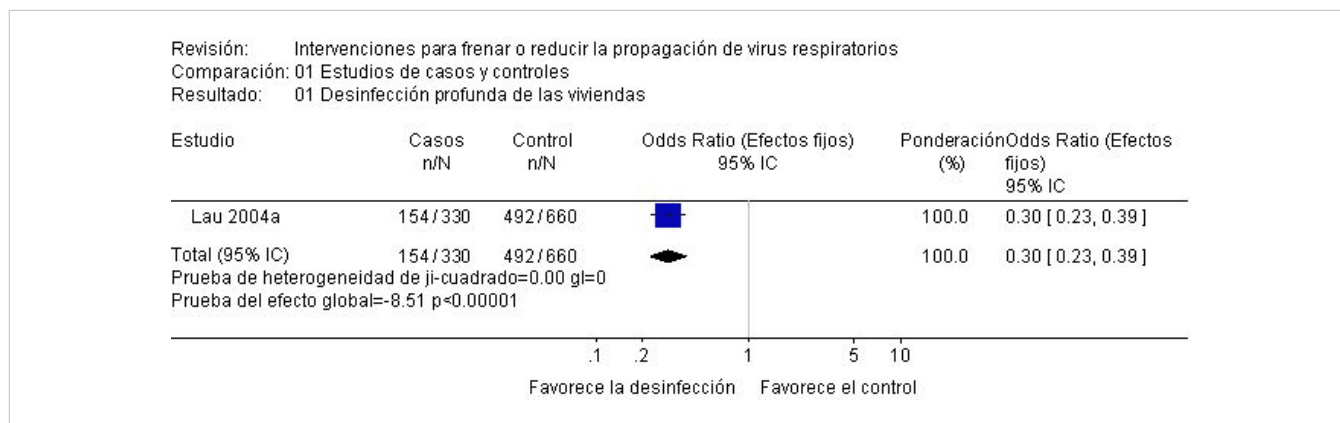
## RESUMEN DEL METANÁLISIS

01 Estudios de casos y controles				
Resultado	Nº de estudios	Nº de participantes	Método estadístico	Tamaño del efecto
01 Desinfección profunda de las viviendas	1	990	Odds ratio (efectos fijos) IC del 95%	0.30 [0.23, 0.39]
02 Lavado de manos asiduo	6	2077	Odds ratio (efectos fijos) IC del 95%	0.45 [0.36, 0.57]
03 Uso de máscaras	5	1991	Odds ratio (efectos fijos) IC del 95%	0.32 [0.25, 0.40]
04 Uso de máscaras N95	2	340	Odds ratio (efectos fijos) IC del 95%	0.09 [0.03, 0.30]
05 Uso de guantes	4	712	Odds ratio (efectos fijos) IC del 95%	0.43 [0.29, 0.65]
06 Uso de batas	4	712	Odds ratio (efectos fijos) IC del 95%	0.23 [0.14, 0.37]
07 Todas las intervenciones	2	369	Odds ratio (efectos fijos) IC del 95%	0.09 [0.02, 0.35]

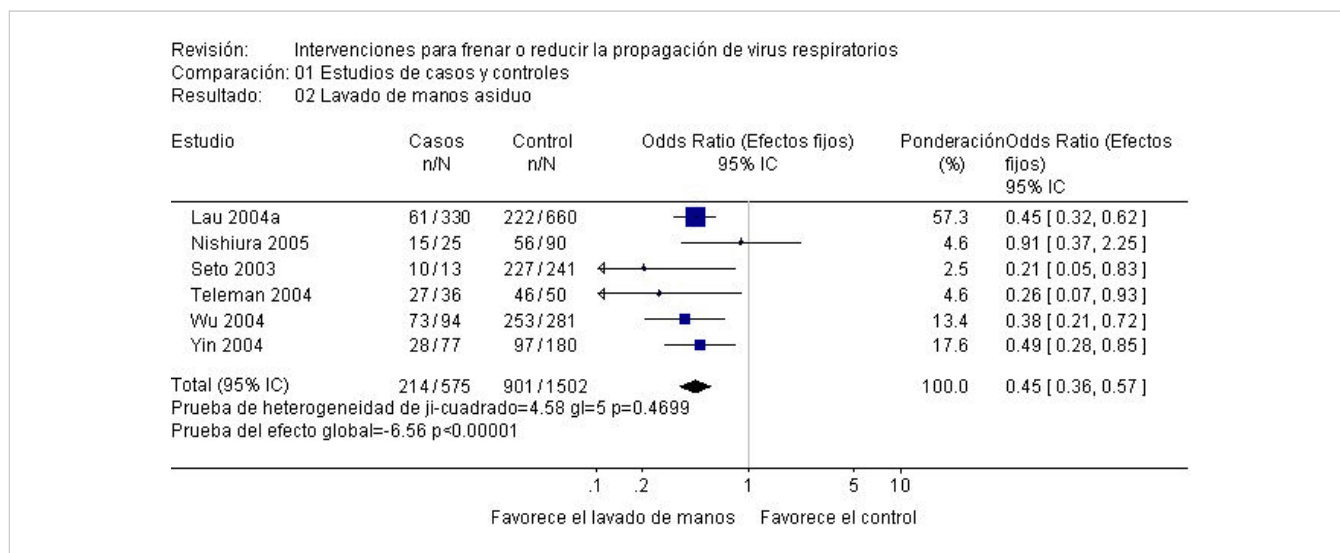
GRÁFICOS Y OTRAS TABLAS

Fig. 01 Estudios de casos y controles

01.01 Desinfección profunda de las viviendas

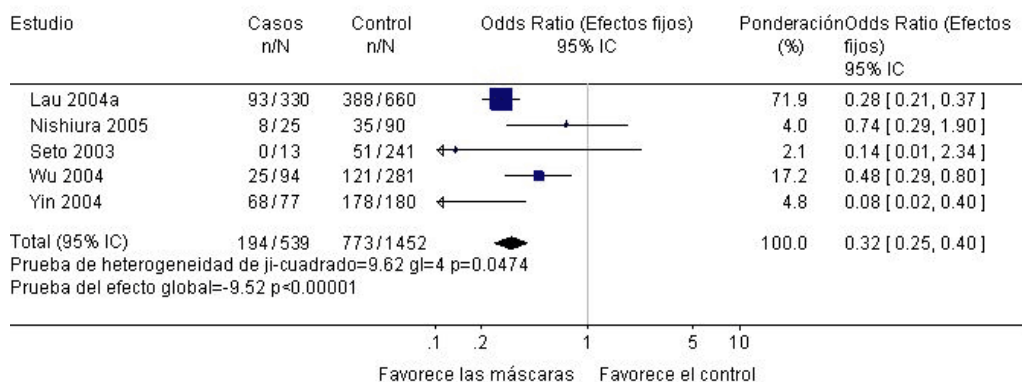


01.02 Lavado de manos asiduo



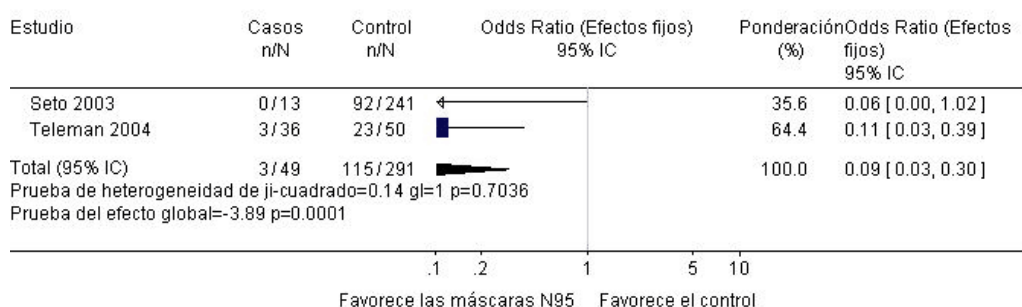
### 01.03 Uso de máscaras

Revisión: Intervenciones para frenar o reducir la propagación de virus respiratorios  
 Comparación: 01 Estudios de casos y controles  
 Resultado: 03 Uso de máscaras



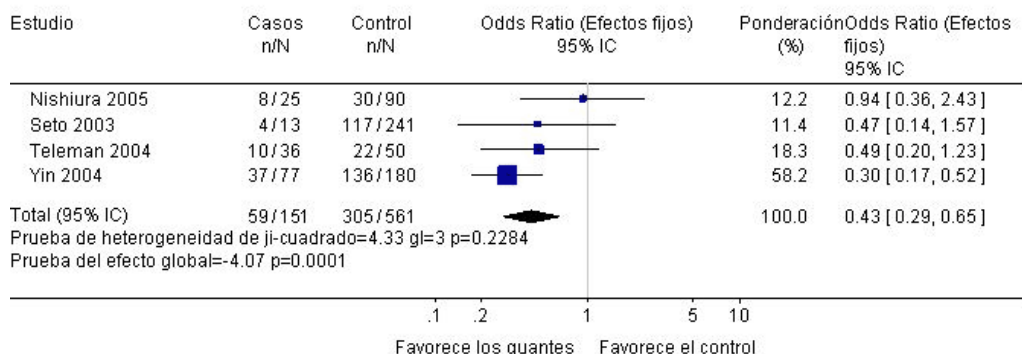
### 01.04 Uso de máscaras N95

Revisión: Intervenciones para frenar o reducir la propagación de virus respiratorios  
 Comparación: 01 Estudios de casos y controles  
 Resultado: 04 Uso de máscaras N95



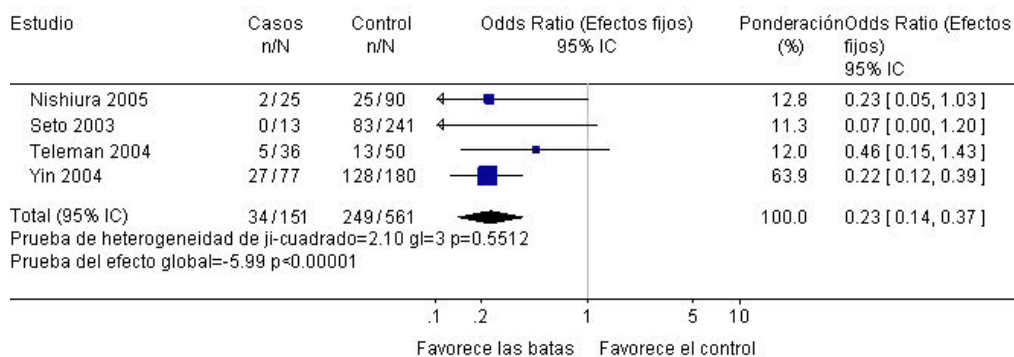
### 01.05 Uso de guantes

Revisión: Intervenciones para frenar o reducir la propagación de virus respiratorios  
 Comparación: 01 Estudios de casos y controles  
 Resultado: 05 Uso de guantes



01.06 Uso de batas

Revisión: Intervenciones para frenar o reducir la propagación de virus respiratorios  
 Comparación: 01 Estudios de casos y controles  
 Resultado: 06 Uso de batas



01.07 Todas las intervenciones

Revisión: Intervenciones para frenar o reducir la propagación de virus respiratorios  
 Comparación: 01 Estudios de casos y controles  
 Resultado: 07 Todas las intervenciones

