UNIVERSITY OF
BIRMINGHAM

Simple interventions to prevent respiratory and gastrointestinal infection in children in day care and school settings: a systematic review and economic evaluation

Jayne Wilson, Dechao Wang, Catherine Meads

Department of Public Health and Epidemiology
West Midlands Health Technology Assessment Group

Simple interventions to prevent respiratory and gastrointestinal infection in children in day care and school settings – a systematic review and economic evaluation.

A WEST MIDLANDS HEALTH TECHNOLOGY ASSESSMENT COLLABORATION REPORT

Report commissioned by: West Midlands Regional Evaluation Panel

Produced by: West Midlands Health Technology Assessment Collaboration
Department of Public Health and Epidemiology
The University of Birmingham

Authors: Ms. Jayne Wilson – Main Reviewer
Dr Dechao Wang – Statistician and Economic Modeller
Dr Catherine Meads – Senior Reviewer

Correspondence to: Ms Jayne Wilson
West Midlands Health Technology Assessment Collaboration
Department of Public Health and Epidemiology
The University of Birmingham

Date completed: July 2006

Expiry Date: July 2010

Report Number: 57

ISBN No: 0704426102
9780704426108

WEST MIDLANDS HEALTH TECHNOLOGY ASSESSMENT COLLABORATION (WMHTAC)

The West Midlands Health Technology Assessment Collaboration (WMHTAC) produce rapid systematic reviews about the effectiveness of healthcare interventions and technologies, in response to requests from West Midlands Health Authorities or the HTA programme. Reviews usually take 3-6 months and aim to give a timely and accurate analysis of the quality, strength and direction of the available evidence, generating an economic analysis (where possible a cost-utility) of the intervention.

CONTRIBUTION OF THE AUTHORS:

Jayne Wilson – Main reviewer, wrote protocol, undertook the search strategies, data extraction, data analysis, wrote the first draft.

Dechao Wang – Statistician and modeller, advised on statistics and analysis, checked analysis for accuracy, undertook sensitivity analysis, wrote section on cluster studies, responsible for the modelling section.

Catherine Meads – Senior reviewer, advised on protocol, searched for studies, double data extracted, edited and revised drafts and worked on model.

The authors take responsibility for this work.

CONFLICTS OF INTEREST:

None

ACKNOWLEDGMENTS:

The authors would like to thank Ann Massey and Natalie Rowles for providing administrative assistance also Sharlene Ting for double data extraction and tabulation of the health economic papers. Thanks also to Martin Connock for providing technical assistance to the review methods, Gavin Rudge for advice on epidemiological statistics and Janine Dretzke for proof reading the final version.

The authors wish to thank the Local Healthy Schools Coordinators for replying to the survey regarding simple hygiene practice in West Midlands schools in particular Wendy Jeffreys.

Thanks also to the peer reviewers, Prof Barry Cookson, and Tina Endericks from the Health Protection Agency, Jenny Hagues from South Birmingham PCT, Rachel Jordan from the University of Birmingham and Dr Rod Taylor from the University of Birmingham.

West Midlands Regional Evaluation Panel

Recommendation

Handwashing – supported

Current evidence – borderline

Multifaceted trials – less supported

Anticipated expiry date: 2010

ABBREVIATIONS

CDCC	Child day care centres
CI	Confidence interval
GI	Gastrointestinal
HPA	Health Protection Agency
ICC	Intra-cluster correlation coefficient
ILI	Influenza like illness
prn	As required
ITT	Intention to treat analysis
NHSP	National Healthy Schools Programme
OTC	Over the counter medicines
PSHE	Personal, social and health education
RCT	Randomised control trial
RR	Relative risk
URTI	Upper respiratory tract infections
WHO CEHAPE	World Health Organisation – Children Environment & Health Action Plan for Europe

EQUIVALENT PHRASES

Primary schools	Elementary schools

DEFINITIONS

Fomite	Inanimate object which can carry pathogens
Quasi - randomisation	Where intervention allocation is alternate, or based on information e.g. date of birth already known to the trialist

EXECUTIVE SUMARY

BACKGROUND - Children typically can expect to suffer approximately four to eight episodes of respiratory infection annually and are also vulnerable to gastrointestinal infections. The cost to the NHS is substantial. Approximately, one third of GP consultations are for patients under 15 years of age, with 50% of these consultations relating to infections. The total annual cost for treating children with infections in primary care was estimated to be £757 million in 2003. Institutions such as child day care centres and schools have been identified as sources of infection. It is hypothesized that the introduction of simple hygiene measures such as hand hygiene, and surface cleaning could reduce the incidence of respiratory and gastrointestinal illness in children attending such institutions.

AIM - To investigate by systematic review whether simple hygiene interventions introduced in primary schools or child day care centres reduce respiratory and gastrointestinal diseases in children aged between 2 and 11. Also to assess the cost effectiveness of such interventions.

METHODS - Systematic review methods were employed. Medline, Embase, CINAHL, and the Cochrane library were searched from inception to August 2005. Included were studies that investigated the role of simple interventions in reducing respiratory and gastrointestinal illness in children aged two to eleven years. Settings were schools and child day care centres comparable to UK practice. Inclusion criteria, quality assessment and data abstraction were undertaken in duplicate. Clinical outcomes included a reduction in respiratory, gastro intestinal infections and sickness related absenteeism. Economic outcomes sought were cost effectiveness analysis and cost data to input into a new economic model relevant to the West Midlands.

RESULTS - Twelve studies met the clinical effectiveness inclusion criteria. Eight considered hand hygiene interventions and four multi-component hygiene interventions. Of the hand hygiene studies, one investigated scheduled handwashing, three looked at hand sanitizer use and four examined educational interventions. All of the multi-component hygiene interventions involved handwashing and recommendations to clean toys at regular intervals, with some studies specifying cleaning regimens, food serving practices, daily air exchange and aseptic nose-wiping. Trial duration ranged from five to sixty weeks.

Five hand hygiene studies reported a reduction in sickness related absenteeism with estimates of effect ranging from 20% to 51% reduction. The cluster design was not factored into the reported results. On sensitivity analysis, when a weak Intra Cluster Correlation Coefficient of 0.01 was applied to the results of four trials the results became non statistically significant. The only study that remained statistically significant was by Guinan and colleagues which investigated hand hygiene education in addition to hand sanitizer.

The multi-component hygiene trials did not show any overall trends. The trial by Roberts and colleagues reported a 44% reduction in GI infections but no reduction in respiratory infections, conversely the studies by Kotch and colleagues and Uhari and colleagues showed a reduction in respiratory infections but not GI infections. It was not possible to account for the cluster design effect in these studies because the results came from subgroup analyses.

All of the studies had important threats to validity, which could have impacted on the trial results.

ECONOMIC EVALUATION - Two economic evaluations were identified. Both found that simple hygiene interventions were cost saving with estimated savings ranging from £106 to £387 per child per year. However, their usefulness to the UK NHS setting and specifically the West Midlands is limited as both are USA based, both are more than five years old and included children younger than 2 years of age. Two cost studies were also identified, with the aim of using the data to furnish a Birmingham economic model. Again it was assessed that the data was not relevant for a UK NHS perspective model.

CONCLUSIONS – The study results suggest that hand hygiene interventions (i.e. handwashing, hand sanitizers and education) can reduce infections and absenteeism substantially. However, these findings are undermined by methodological problems within the studies, which seriously reduce validity of the results. Clustering effects must be considered when quality is assessed. When clustering effects are taken into account, results reduce the confidence that the observed results could not have occurred by chance. This inability to demonstrate clear benefit may be caused more by the difficulty in conducting good quality research in this area, rather than the ineffectiveness of hand hygiene *per se*. A Birmingham model simulation only was developed which suggested that hand sanitizer may be more cost effective than scheduled hand washing. However, due to lack of costs and the lack of good quality studies as mentioned above, these results are tentative at best. Further primary research with a UK perspective is needed. Future research should include better quality studies with more appropriate analysis of the results.

CONTENTS

APPENDICES

TABLES

FIGURES

1 AIMS OF THE REVIEW

A. To investigate by systematic review whether simple hygiene interventions instigated in child day care institutions and primary schools are effective in reducing respiratory and gastrointestinal infections in children aged between 2 and 11 years.
B. To investigate the cost effectiveness associated with simple hygiene interventions particularly relating to the NHS in the West Midlands area of the UK.
C. To inform further primary research.

2 BACKGROUND

Children typically can expect to suffer approximately four to eight episodes of respiratory infection annually[1] and are also vulnerable to gastrointestinal infections.[2] Children are thought to be at increased risk because they have immature immune systems; they tend to be in close contact with each other and share facilities and equipment, particularly in institutions such as schools and nurseries; and they may not have an understanding of personal hygiene practices.[2]

2.1 Types of Infection

There are several types of respiratory and gastrointestinal infections that cause disease in children (Table 1, page 12).

2.1.1 Respiratory infections

The common cold is the most frequent cause of respiratory illness in children.[1] Caused by rhinoviruses, of which there are approximately 100 types, it is classed as an upper respiratory tract infection (URTI) and involves the respiratory tract from the larynx and above. Symptoms include nasal discharge, nasal obstruction, sore throat, headache, and cough.[3] Sequelae can include otitis media (infection of the middle part of the middle ear), tonsillitis and pharyngitis (often due to secondary infection by Group A Streptococcus), sinusitis (causing headache and facial pains)[4] and exacerbation of pre-existing asthma.[5, 6] Other respiratory infections to which children are susceptible are influenza, caused by either influenza A or influenza B virus and bacterial infections such as *S. pneumoniae* and *B. catarrhalis*.[7]

2.1.2 Gastrointestinal infections

Children are also prone to gastrointestinal illness, which manifest as bouts of diarrhoea, nausea and vomiting. Likely causative organisms are viruses (e.g. enteroviruses, rotaviruses, Norwalk virus), protozoan infections (e.g. *Gardia lamblia* and[4] bacterial infections (e.g. *Shigella sonnei, Shigella flexneri*[8]). Severe illness can lead to dehydration occasionally requiring hospital treatment.[4]

2.2 Modes of Infection Spread

Infections can be transmitted in a number of ways: direct contact spread (including bloodborne transmission), contact spread (including faecal-oral transmission), endogenous infection (auto infection), droplet contact spread, airborne spread (droplet nuclei, skin squames, or rafts of fungal spores) common vehicle (common source) spread and vector spread.[1] Whilst hands have been cited as the main culprit in the spread of gastrointestinal and respiratory infectious agents, it is thought that the hands, particularly in the case of rhinoviruses, pick up the infections from contaminated surfaces. Surfaces such as carpets, desks, door handles and objects (known as fomites) such as toys and more recently computer keyboards[9] can act as reservoirs of infection.[1]

Table 1 Common respiratory and GI infections in children.

	Pathogen	Disease/symptoms	Mode of transmission	Risk of transmission
Respiratory				
Virus	**Rhinovirus	Common cold.	P: respiratory droplets, fomites.	Universal susceptibility, particularly in overcrowded institutions.
	**Coronovirus	Cold symptoms.	P: respiratory droplets, fomites.	Universal susceptibility, particularly in overcrowded institutions.
	*Influenza	Cough, fever, malaise.	P: respiratory droplets, airborne.	High. Epidemics are often explosive. Children are important reservoir of infection.
Bacteria	***Streptococcus pneumonia*	Fever, pleural pain, dyspnoea, cough.	P: direct oral contact, fomites.	Increased incidence after influenza epidemics.
	*Streptococcus sp.	Sore throat/fever	P: respiratory droplets, direct contact, fomites. E: food borne.	Moderate risk. Outbreaks can occur in schools.
GI infections				
Virus	*Enterovirus	Varies. Usually febrile illness.	P: faeco-oral, fomites, airborne. E: waterborne.	Moderate in families & nurseries. Children important in transmission.
	*Adenovirus	Diarrhoea	P: possible faeco-oral.	Outbreaks usually in children <2yrs old.
	*Rotavirus	Diarrhoea	P: faeco-oral, possible respiratory droplets.	High, 45% in families.
	*Norwalk virus	Vomiting or diarrhoea	P: faeco-oral, possibly airborne. E: waterborne, food borne.	Moderate to high. Attack rate 4-32% in outbreaks. Attack rate >50% in outbreaks among children.
Bacteria	**Shigella sonnei, *Shigella flexneri*	Diarrhoea	P: faeco-oral (via hands), fomites. E: waterborne, foodborne.	School outbreaks can be controlled by hygiene measures.
Protozoa	**Gardia lamblia*	Gardiasis – diarrhoea, abdominal cramps or flatulence.	P: faeco-oral. E: waterborne, food borne, animals	Attack rate up to 50% in nurseries.

* HPA report[10], **Benenson[11] [P= person to person, E=environmental spread].

2.3 Incidence of Infection

2.3.1 Respiratory and GI infections

It is difficult to quantify the exact number of respiratory and gastrointestinal infections in the community. In the UK there are data collection systems that record service use in hospitals, primary care and for recent NHS call-service initiatives such as NHS direct. Whilst this data can estimate the number of illnesses due to infections that cause parents to seek medical advice, there will be an underestimate of the total number because many infections such as the common cold are treated at home without recourse to the health service. A recent survey by Saunders and colleagues found that in Toronto, Canada, only 56% of parents sought medical advice when children had respiratory symptoms. Factors predicting whether parents sought medical advice were child age less than 48 months, or unusual symptoms, such as earache, high fever or persistent symptoms.[12]

The UK Health Protection Agency (HPA) has collated data from NHS sources and and in 2005 published a report which looked at the burden of disease from infections.[10] The data reported in Table 2, below, is taken from that publication. Data for adults has been included so that the proportions of infections occurring in children can be compared with adults.

Table 2 UK health services costs for respiratory and GI infections

		0-14 yrs	15-59 yrs	60-74 yrs	75+ yrs
Hospitalisations for infections.	% due to infection	12%	2%	2%	4%
	Rate/100,000 population	1,916	452	754	2,162
	Total annual cost	£360m	£268m	£99m	£162m
	Cost/100,000 population	£3.3m	£0.7m	£0.01m	£3.6m
GP consultations for infections.	% due to infection	50%	39%	21%	20%
	Rate/100,000 population	1,776	1,675	1,267	1,230
	Total annual cost	£757m	£2,190m	£372m	£207m
	Cost/100,000 population	£6.9m	£6.1m	£4.7m	£4.6m

Notes: "HPA states that hospital admission, particularly in children, is often dependent upon the perceived deprivation status, with judgements being made about the quality of care available at home and the likelihood of return for outpatient treatment".[10] Original data from RCGP.org.uk and hesonline.nhs.uk

Approximately a third of GP consultations are for patients aged less than 15 years, with 50% of these consultations relating to infections. The most common infections presenting to primary care in children are respiratory infections (in excess of 20,000 per 100,000 population) with gastrointestinal disease infections presenting to GPs at a rate less than 2,500 per 100,000.

Other options for seeking health care in the UK are NHS direct or NHS walk-in centres. NHS direct is a telephone triage/advice line and data is available on the number of consultations for respiratory infections. The total mean annual numbers of calls for colds and influenza to NHS direct for 2003 was 30,373 (for all ages) with an estimated cost of £450,000 (at £15.11/call). For coughs (all ages) the total mean annual number of calls was 95,289 at an estimated cost of £1,400,000. Whilst calls to NHS direct cannot confirm diagnosis, they can indicate disease trends within the population.[10]

2.3.2 Absence data

Another possible source of information on the incidence of infections in children is sickness absence data. Schools collect data on school absence, which can be used as a proxy for illness. In the UK, absences are classed as either authorised absences or unauthorised absences. The number of authorised absences (measured as half days) recorded for Birmingham primary schools in 2004/2005 was 5.03% with the national average at 5%.[13] However, even authorised absence figures do not record the reason for the absence. Authorised absences can be for reasons that are not due to infectious disease. The decision to keep a child off school or out of day care is also related to the severity of the illness, the parents' judgement of the severity of the illness and the circumstances of the parents regarding childcare provision, especially if they usually work during school hours. There may be other reasons for absence, which may be put down to infections, for example, a child may feign stomachache, to avoid situations at school such as bullying. Absence data can also be inaccurately recorded. This can be due to human error, or be deliberate. Blyth and Milner[14] have noted that with the introduction of school performance tables, schools that have a greater number of unauthorised absences have been viewed less favourably than schools with less unauthorised absences. They suggest that this encourages schools to record unauthorised absences as authorised absences. For all of the above reasons therefore, official absence data as a proxy for sickness rates is an unreliable measure.

2.4 Costs of Infection

2.4.1 NHS costs

As Table 2, page 13 shows, the cost of infections to the NHS is substantial. The total annual cost in 2003 for treating children aged between 0 and 14 years with infections in hospital was £360 million and the cost for GP consultation was £757 million.

2.4.2 Societal costs

NHS costs do not consider costs borne by the patient. Over-the-counter medicines (OTCs) can be administered for respiratory and gastrointestinal infections. The survey by Saunders and colleagues 2003[12] found that about 18% of parents administered OTCs to their children. Exact data on OTCs are difficult to obtain on a population level because this type of data is commercially sensitive and may also be subject to company marketing strategies, making it an unreliable indicator of patient borne costs.[10]

Another calculable cost associated with childhood infections is parental absence from work.[15,16] In a cost study of children in a day care centre up to the age of 36 months, illness in a child accounted for 40% of parental absenteeism from work.[16] Cost of seeking healthcare has also been considered.[17] Outbreaks of infection can lead to serious disruption to a child's education due to them feeling unwell and leading to absenteeism.[18,19,20] Moreover, increased stress within the family unit has also been observed if the child has to be unexpectedly cared for at home.[21]

2.5 School and Child Day Care Centres as Sources of Infection

2.5.1 School surveys

There is survey evidence that schools and child day care centres are a source of infection of common respiratory and gastrointestinal diseases within the community.[22,23] A survey of 20 primary schools in Leeds found that faecal streptococci were detected on the hands of children who did not regularly wash them, and that classroom surfaces, in particular classroom carpets, were commonly contaminated. The schools with the highest faecal contamination were also more likely to have had a reported outbreak of gastroenteritis.[24] In another survey, this time in a child day care facility, faecal coliform bacteria were found on the hands of 50% of the children and staff, with 11% of surfaces also contaminated.[22] A 19 month prospective study of children attending 20 day care centres (age 0 to 5 years), found that nine centres had 15 gastrointestinal outbreaks involving 195 persons. An enteropathogen was identified in all outbreaks, shigella was detected in five outbreaks, rotavirus in two, giardia in one, and in the remaining seven multiple enteropathogens were identified.[25] Respiratory pathogens have also been found to be present in schools and child day care centres. Colombet and colleagues[26] surveyed 212 school children aged 9 to 10 years and found that 22 carried *Staphylococcus aureus* on their hands. Studies looking at the types of respiratory pathogens that have been detected in child care facilities have found respiratory syncytial virus, parainfluenzae viruses, adenoviruses, rhinoviruses, enteroviruses, influenza viruses, bacteria, *S. pneumoniae*, *H. influenzae* type b, *B. catarrhalis*, Group A Streptococcus and *M. tuberculosis.*[7]

Petersen and colleagues[22] found that the age of children made a difference to the amount of contamination within a day care centre. They examined a child day centre with children ranging from infants to 4 year olds. The classrooms were grouped by age with contamination being greatest in the younger age groups particularly in children still in nappies. Again they found that hands were the main foci for contamination, and advocated handwashing to reduce transmission of infections. Surface decontamination was also cited as a measure that could reduce infection rates.

The effects of contaminated hands and surfaces can be seen with the number of children within these institutions contracting upper respiratory tract infections and gastrointestinal infections. Many studies have been undertaken investigating the level of infection, particularly in child day care centres.[5, 27-38,]

All suggest that child day care attendance is associated with an increased risk of contracting either a respiratory or gastrointestinal infection. For example, in Norway, Kvaerner and colleagues[39] found that acute otitis media, tonsillopharyngitis and the common cold were common in children aged 4 to 5 attending day care. Similarly, children in day care were more likely to experience a cough at night (adjusted odds ratio 1.89; 95% CI 1.34 – 2.67) and blocked nose without the common cold (1.55; 1.07-1.61) compared to children in home care.[35]

2.5.2 Other causes of illness in schools

There may be other causes of illness such as damp and mouldy school buildings, particularly associated with respiratory infections. For example, Taskinen and colleagues[40] found that children aged 7 - 13 in a school environment that had mould problems, suffered from wheezing and prolonged cough. Another study looking at environmental risk factors for respiratory and ear infections, found that in 304 children aged 4-5 yrs, humid home conditions were a significant risk factor for cold, sore throat, and otitis media (odds ratios = 2.71, 3.03, and 2.77 respectively), mould in the home was a significant risk factor for otitis media (odds ratio = 2.80) and attending day care centres was a significant risk factor for cold and bronchitis (odds ratio = 1.36 and 1.89 respectively).[41]

Children exposed to tobacco smoke may also be more susceptible to respiratory infections.[4] The number of children who live with at least one adult smoker has been reported to be has high as 92% in one West Midlands school. (Wendy Jeffreys – personal communication).

2.5.3 Spread of infections into the community

As well as the burden to children of having an increased number of infections whilst attending day care and school, there are studies that have found that there is an increase in risk of other family members contracting an infection. For example, Nafstad and colleagues[42] undertook a survey of lower respiratory tract infections in infants in Norway during the first year of life. They found that infants who had siblings at day care were at an increased risk of a lower respiratory tract infection, particularly if they shared a bedroom, compared with infants who did not have siblings attending day care. Similarly, this risk can also be to older relatives, such as grandparents.[42,43]

2.5.4 Long term effects of school hygiene practices

Out of home child care and the attendance of school have been viewed as places of opportunity for children and their parents to be exposed to health education. “Proper hand washing techniques can be taught to the child and if the emphasis is on family participation this practice could be taken up in the home and thus reduce transmission of infection within the home environment”.[44] Good health habits acquired early in life may promote long term health.[44] By targeting young children the hope is that this will equip them to follow a healthy lifestyle.[45,46] Today’s children are tomorrow’s parents, food industry workers, health care workers etc. Poor hygiene practice has been noted in all of these areas. For example, in a survey of mothers in the home it was found that only 42% washed their hands following a nappy change, with subsequent spread of faecal contamination throughout the home environment.[47] In 2002 the Food Standards Agency undertook a survey of 1,000 catering staff. They found that 39% of staff did not wash their hands after visiting the toilet whilst at work and that 53% did not wash their hands prior to handling food.[48] Hospital surveys have found that only 9% of doctors wash their hands between patients, with senior doctors washing their hands only twice during 21 hours of ward rounds.[49]

2.6 Prevention Strategies

In order to cause disease, a pathogen must gain entry into the body, and also resist any body defences that are designed to prevent its growth. To avoid disease two options are available. One is to enable the immune system to fight off infections once they have entered the body, the second is to stop the transmission of the infection.

2.6.1 Vaccination/chemo prophylaxis

To enhance the body's ability to fight infection vaccinations are given, and to help stop the pathogens growing within the body treatments such as antibiotics or antivirals (such as Tamiflu) can be administered.

Vaccinating children to prevent influenza has been recently reviewed.[50,51] The review concluded that overall there is the potential that vaccination affords protection particularly for direct contacts and that some degree of herd immunity is developed, but the limitations in quality of the studies meant that this was not possible to quantify.

The use of antibiotics as a chemoprophylaxis is an unlikely course of action in preventing respiratory and gastrointestinal in school children, due to the potential side effects of antibiotics and the risks of the emergence of antibiotic resistance. The use of antivirals in the prophylaxis of influenza has recently been topical in the media particularly in relation to pandemic influenza. Antiviral treatment would have to be given over an extended period of time, which would be a costly exercise. Additionally, antivirals such as Tamiflu have side effects such as nausea, which could diminish compliance in a preventative scenario and there is also the theoretical risk of drug resistance.

2.6.2 Simple hygiene interventions

Definition of hygiene

Hygiene is defined as the principles and practice of health and cleanliness.[52] Simple hygiene interventions relevant to this review are hand hygiene via handwashing or using hand sanitizers and multi-component hygiene interventions, which include handwashing but also involve activities that reduce environmental contamination such as surface disinfection or cleaning fomites.

Hand hygiene interventions

I. Handwashing

Most respiratory and intestinal infections gain entry into the body via the mouth, nose and eyes. The hands act as an inoculation tool, which pick up pathogens from the environment then transfer them to the mouth, nose and eyes. By cleaning the hands regularly, the chances of inoculation are reduced. The UK Department of Health has issued guidance on infection control in schools and nurseries.[53] They recommend that staff and children should wash hands after using the toilet, and before eating or handling food. Hands should be washed using warm water and soap (preferably liquid soap). The hands should be rubbed vigorously to form a lather for at least 15 seconds and all parts of the hands should be covered in the lather. The hands should be rinsed under running water and dried using either an air dryer or towel (preferably a disposable paper towel). There is the potential for adverse events such as drying and chapping of hands especially if frequent handwashing occurs.

Costs associated with handwashing

Handwashing has associated costs, such as water supply and water heating, provision of soap and drying facilities. Maintenance of the facilities including anti-vandalism strategies would create additional costs. Providing disposable paper towels also involves the cost of disposal, and has environmental considerations i.e. a school of 1,000 pupils would use at least 4,000 additional paper towels daily if each pupil washed their hands on arrival at school before lunch and after lunch and before leaving school. If handwashing facilities are in poor repair there may be capital expenditure to consider to bring washing facilities up to standard.

II. Hand sanitizers

Whilst hand sanitizer use has been recommended in the health care setting[54], no UK recommendations for use were identified in the school and child day care setting. Hand sanitizers are chemical preparations, which are designed to reduce the number of micro-organisms on the hands, most often without the use of water. They are not recommended for hands that are visibly soiled. Most preparations are alcohol based, which act by denaturing proteins within the micro organisms. The efficacy of alcohol based products is determined by several factors such as the type of alcohol used, the alcohol concentration, the amount of product used and the contact time.[54]

Safety considerations with alcohol based products have been highlighted.[55] Alcohol based products are flammable, therefore precautions in storage and site of use should be taken.[55] Flash points[*] can vary depending upon the dilution of the alcohol.[56] The alcohol content of the hand sanitizer if ingested can also cause intoxication, something to consider if used by unsupervised children.[57] Some hand sanitizers do not contain alcohol but contain a benzalkonium chloride based disinfectant. This ingredient has not been passed as safe to use by the FDA in the USA.[58] No data relating to its use in the UK was identified. Other safety aspects relate to the product drying the skin of the hands.

[*] Flash point is the minimum temperature at which a liquid produces a sufficient concentration of vapour above it that it forms an ignitable mixture with air (www.ptcl.chem.ox.ac.uk/MSDS - accessed 4 - 12-06)

Cost implications of hand sanitizers
Costs would include buying the products and installing dispensers. However, companies supplying the products often install dispensers as part of the product costs. Safe storage of the product would also be an additional expenditure.

III. Multi-component hygiene interventions.
Multi-component hygiene interventions include hand hygiene, but also include such activities as cleaning surfaces and fomites. A variety of cleaning and disinfection products can be used for these purposes.

Cost implications of multi-component interventions.
Costs associated with this intervention would depend on the intervention components. If the intervention involved surface cleaning this may be undertaken in-house or by specialist cleaning companies, either way would involve a cost.

2.7 Current Service Provision

2.7.1 Hand washing
Two recent surveys have suggested that handwashing is not possible in many schools due to a lack of handwashing facilities. A recent campaign group called ‘The Bog Standard Campaign’[59], suggests that there is a poor level of toilet provision in schools in the UK including provision for washing hands. Similarly, a survey undertaken by the Welsh Assembly[60], found that there was an approximate 25% shortfall in handwashing facilities within schools.

2.7.2 Hand sanitizer use
No data was located regarding the use of hand sanitizers in UK schools and child day care centres.

2.7.3 Education
Formal education in primary schools in the UK is based around the Key Stage system, which is set through the government Qualifications and Curriculum Authority.[61] One of the curriculum subject areas is that of “Promoting personal, social and health education and citizenship (PSHE)”. Whilst Key Stage Workbooks do suggest handwashing as a curriculum activity, hygiene is not specifically highlighted as a major goal within the curriculum overview.

2.7.4 National Healthy Schools Programme
There is a voluntary programme called the National Healthy Schools Programme (NHSP). Within this initiative schools are asked to demonstrate standards in the following: PSHE (including sex and relationship education, and drug, alcohol and tobacco education), healthy eating, emotional health and well being, and physical activity.[61] Again, hygiene interventions are not specifically highlighted.

During the course of this systematic review, the local contacts for the National Healthy Schools Programme within the West Midlands region[62] were emailed and asked whether simple hygiene interventions were taught in schools within the area. All thirteen co-ordinators replied (see Appendix 1, page 64). Overall, there seemed to be variation in hygiene interventions with some co-ordinators involved in hygiene initiatives particularly handwashing and some not involved in hygiene interventions. One co-ordinator identified from school health survey work that handwashing in primary school children was poor after using the toilet and that the frequency of handwashing reduced particularly in boys as they got older. They undertook a project to supply six schools with frothy soap and encouraged the staff to promote handwashing. Whilst supplying soap increased handwashing, the project did not evaluate the impact of the intervention on infection rates. Other school co-ordinators have worked alongside the school nursing teams and used machines to check for dirt on hands, and then combined this with an educational programme. Interest in hand hygiene interventions seemed to be dependant upon the interest of the Healthy Schools Programme Co-ordinator and how they have interpreted the curriculum and also the individual schools taking part in the scheme.

2.7.5 Health Protection Agency Initiative

The Health Protection Agency (HPA) recognises that children are a vulnerable group and that their health should be considered a priority and so have a Corporate Goal (Goal 5) to “improve the health of those who are children now, and to establish good practice and healthier lifestyles which will improve long term health”. Within this the HPA have set up a project on handwashing and hygiene for children in primary schools, which is currently being piloted in the North West region. At the time of writing the HPA are producing a report investigating the level of hygiene within schools[46] and have also produced a report on the Burden of Disease which includes a section on respiratory and gastrointestinal infections in the UK.[10]

2.8 Previous Systematic Reviews

2.8.1 Effectiveness reviews

There have been two relevant previous systematic reviews and there is one protocol registered with the Cochrane Collaboration. The review by Curtis and Cairncross[63] looked at the effects of washing hands with soap on diarrhoea risk in both adults and children and estimated potential reductions in diarrhoea on communities. Seven intervention studies, six case control, two cross sectional and two cohort studies were included. It was found that hand washing could reduce diarrhoea risk by 47%. In studies that specifically mentioned soap the risk reduction ranged from 42-44%. All but two of the studies were conducted in developing countries.

The second systematic review[64] investigated the effectiveness of antimicrobial rinse-free hand sanitizers, for the prevention of illness related absenteeism in elementary school children. All of the studies used a cluster design (see Appendix 2, page 64). They found a reduction in illness related absenteeism. However, the quality of the included studies was poor, therefore the authors advised caution when considering the results. The review only investigated hand sanitizers, rather than a range of simple interventions.

The Cochrane protocol[65] appears to be answering a very similar question to the systematic review by Curtis and Cairncross.[63]

2.8.2 Cost effectiveness reviews

No previous systematic or narrative reviews regarding cost effectiveness were identified. The National Patient Safety Agency recently undertook an economic analysis of hand sanitizer use in the hospital setting.[66] Hospital infections cost the NHS £1bn per annum. Hand sanitizer use in hospitals was estimated to save £140million per year. However, extrapolation of this analysis into child day care and school settings is not possible, mainly due to differences in the pathogens present and the population i.e. healthy children compared with hospital patients who have comorbidities. With an estimated £757million annual spend on childhood infections just in primary care it is important that the cost effectiveness of potential interventions is addressed.

3 EFFECTIVENESS REVIEW

3.1 Methods

3.1.1 Protocol development

The project was undertaken in accordance with a pre-defined protocol (see Appendix 3 Protocol page 67). The protocol was developed by discussion between Rachel Jordan, Dr Carole Cummins and Jayne Wilson, with further refinements incorporated by Catherine Meads. There were no major departures from the protocol except for the addition of an economic analysis.

3.1.2 Search strategy

The following electronic databases were searched: MEDLINE, EMBASE, Science Citation Index, CINAHL, Cochrane Library, and National Research Register. See Appendix 4 page 70 for search strategy. Citation lists from all identified reviews and included primary studies were searched. No language or date restrictions were applied.

3.1.3 Inclusion criteria

Population	• Children - aged from 2 to 11 years (general population). Studies with a wider age range were included if subgroup data were available for 2 to 11 year olds – only data from relevant age group included. • Setting - Schools, Child Day Care Centres, Play Groups, Nurseries, Crèches. • Country – UK based studies and studies from other countries where childcare is comparable to UK practice.
Intervention	• Any simple hygiene intervention that children and /or staff and others undertake to prevent the spread of infection e.g. hand washing, surface disinfection, aseptic tissue disposal.
Control	• Placebo. • No intervention. • Other simple hygiene interventions.
Outcomes	• Any public health or clinical related outcomes e.g. reduction in respiratory infections, reduction in gastrointestinal (GI) infections, reduction in respiratory and GI infection related absenteeism. • Teacher or parental infections.
Study Designs	• Any design, but must have a comparator. Ideal = cluster randomised controlled trial (see Appendix 2, page 64 for definition).

3.1.4 Exclusion criteria

Population.	• Specialist settings e.g. hospitals. • Children < 2 years old and > 11years.
Intervention.	• Food handling hygiene measures from canteen staff. • Interventions designed to prevent specific tropical infections. • Health education delivery techniques.
Control.	• Home care.
Outcomes.	• Laboratory results.
Study design.	• Studies with no comparator practice e.g. cross sectional surveys.

3.1.5 Study identification

Two reviewers (JW) and (CM) independently assessed the papers for inclusion using the title and, where available, the abstract. Full paper copies of potentially relevant studies were obtained for detailed examination. Foreign language publications were assessed for inclusion using English abstracts where available. Translations were obtained where possible within the resources and timeframe of the project. A list of excluded studies can be found in Appendix 5, page 74.

3.1.6 Data extraction strategy

Data extraction was independently carried out by two reviewers (JW & CM) using a standardised data extraction form which can be found in Appendix 6, page 76. The data was tabulated by JW who also checked discrepancies within the data extraction. Discrepancies were resolved by referral to the original paper and through discussion between reviewers.

3.1.7 Study quality assessment

Quality was assessed according to selection bias, performance bias, attrition bias, detection bias and whether the cluster design effect was accounted for in the analysis[67] (See Appendix 2, page 64 for cluster information). The results were tabulated and a critically appraised regarding potential threats to validity.

3.1.8 Methods of analysis/synthesis

Study characteristics and results were tabulated. Results were collected as crude data where possible – e.g. number of events and number of student days lost, as well as worked data. Where sufficient data was supplied, the crude data was converted to relative risks (RR) using StatsDirect.

Outcomes
Outcomes sought were incidence of respiratory infections, incidence of GI infections and absence related to sickness due to respiratory or GI infections. Respiratory and GI infections were taken as defined by each study (see Appendix 7, page 80).

Incidence rates are defined as the number of new episodes of illness. There are two types of incidence statistic, cumulative incidence, which is the number of new cases of disease over a specified time period and incidence rate (or incidence density), which is the number of events observed divided by the total individual person years.[68] Both measures have been used by the included studies.

Absence rates can be recorded in different ways i.e. they can be expressed as the number of episodes of absence or be measured according to the number of days spent absent. In addition the number of absence episodes per individual can be calculated. Reason for absence i.e. because of respiratory or GI infections can also be measured if the study has sought the reason for the absence. In some cases this can lead to double counting if the child has respiratory and GI symptoms. Because this review included studies where infections were reported by parents on symptoms alone rather than laboratory confirmation of infection, an overestimation of disease may have occurred. With absence data there may be other factors such as the severity of illness, parental judgement and social circumstances that lead to the decision to keep the child at home (see section 2.3.2, page 14).

Cluster design
In studies with a cluster design, the results were assessed using the following steps:

1. **Have the results given in the paper been analysed by taking cluster design into account?** (see Appendix 2, page 65)

IF THE RESULTS HAVE NOT TAKEN ACCOUNT OF THE CLUSTER EFFECT STEPS 2 TO 4 SHOULD BE CONSIDERED

2. **Is it possible for the review team to reanalyse the results to take into account the cluster design?** Notes – If the studies have provided enough information re-analyse by using a Two Sample t-test. Studies need to have given sufficient data to enable re-analysis, such as the number of events and size of the cluster.

3. **If the paper does not report sufficient data for a re-analysis of the results, undertake a sensitivity analysis by applying an Intra Cluster Correlation Coeffiecient (ICC) to test if the results are robust in different cluster scenarios.** Notes – use adjusted chi-squared method of analysis.

4. **If none of the above are possible, report the results as stated in the paper, but note that they do not take into account the cluster design.** Notes - reiterate that without adjustments for cluster design within the analysis, the significance of the result tends to be overstated producing an over precise standard error.[69]

For further information on cluster designs see Appendix 2, page 65.

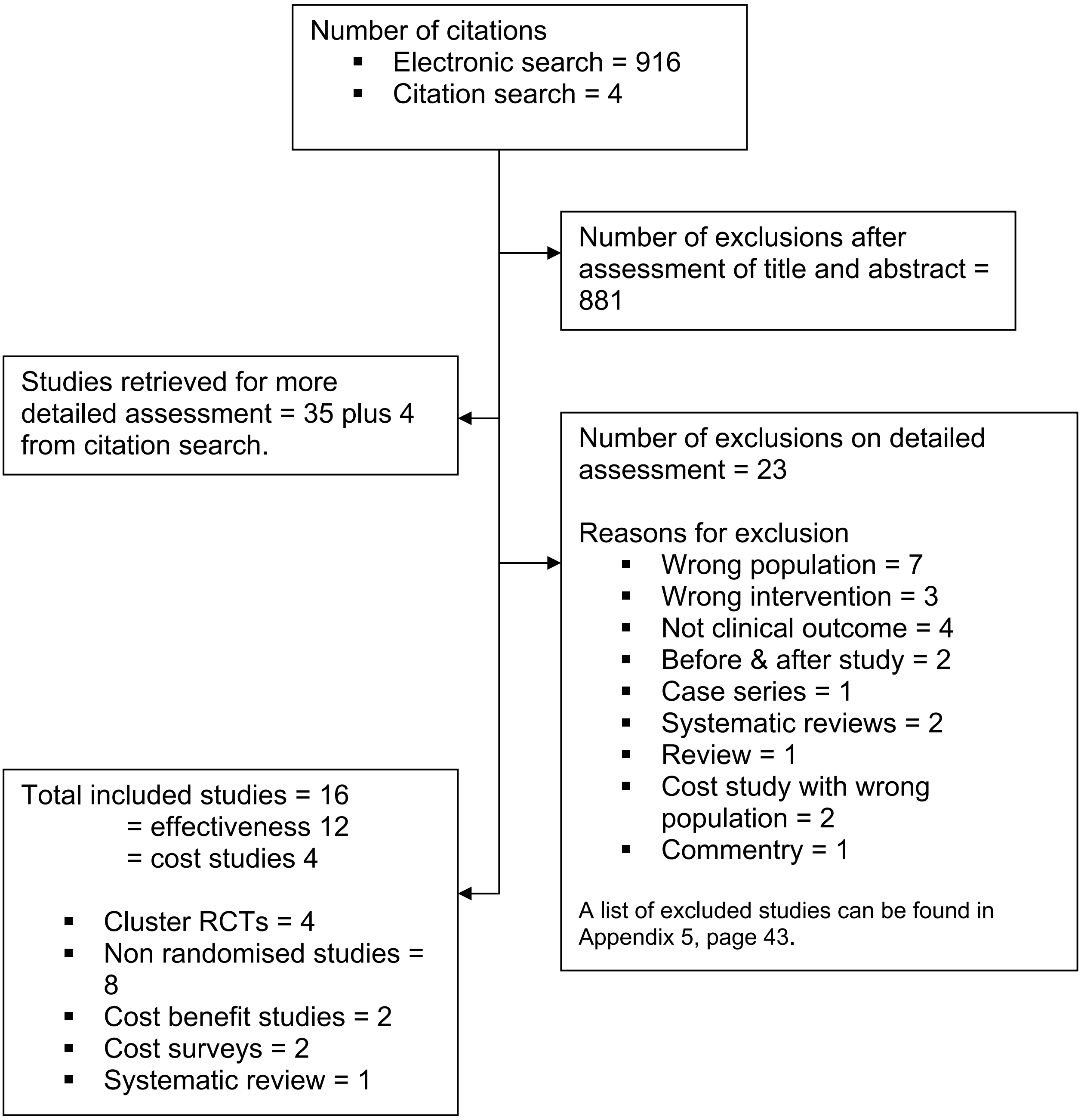
Meta-analysis.
It was envisaged at protocol stage that the studies would be heterogeneous in populations and interventions. It was found during the review that the study characteristics were more uniform than expected. However, the results were presented in different formats therefore it was not possible to pool results and a critical description was undertaken instead.

3.2 Results

3.2.1 Search results.

Figure 1 Flow diagram.

Twelve studies met the clinical effectiveness inclusion criteria and four cost studies were identified.



3.2.2 Characteristics of clinical effectiveness included studies

In total 12 studies met the inclusion criteria. Of these, eight investigated the effectiveness of hand hygiene interventions and four investigated multi component hygiene interventions. All of the studies involved a cluster design i.e. the intervention was applied at group level (e.g. classroom or institution). The main characteristics of the included studies can be found in Table 3, page 28, and Table 4 page 32 and a fuller description of the individual studies is given in Appendix 8, page 82.

HAND HYGIENE STUDIES (EIGHT STUDIES)

Study design
Whilst all of the studies involved a cluster design i.e. the intervention was applied at a group level, within this there were a variety of study designs. Two studies employed the ideal study design i.e. cluster randomisation.[70, 71] One was a randomised placebo controlled trial[70], the other[71]was a cluster randomised cross over trial. Quasi randomised methods were used in five studies[72, 73, 74, 75,76] with one study using a non-randomised crossover design.[77]

Population
All of the hand hygiene studies were conducted in the USA. One was set in a child day care centre[72] the remaining studies were set in primary schools (ranging from kindergarten classrooms to grade 6 which is approximately 4 to 11 years[78]) (see section Hand hygiene studiespage 54 for discussion points).

Interventions
Within the hand hygiene studies three interventions were apparent. Ordered by increasing complexity they are:

- Handwashing – where children were instructed to physically wash hands with soap and water at specified times as an adjunct to regular handwashing.[75]
- Hand sanitizer use – children were instructed to use a hand sanitizer as an adjunct to their regular handwashing regimen.[70, 76, 77]
- Education regarding hand hygiene (with or without hand sanitizer use[71,72, 73, 74]).

(See Appendix 10, page 93 for specific details).

Length of studies ranged from five weeks to nine months. All were undertaken during winter periods.

Control
For the study where the intervention was scheduled handwashing, the control group undertook normal practice.[75] However, all of the children in the study initially received instruction on handwashing three weeks before the start of the study. One of the hand sanitizer studies used a placebo for the control group.[70] In two of the three hand sanitizer studies, again all the children taking part initially received education regarding hand hygiene[70, 77] whereas for the

third hand sanitizer study[76] usual practice served as the control. All of the educational studies had as controls usual handwashing practice.

Outcomes

All of the hand hygiene studies set in primary schools measured sickness related absenteeism rates. The study set in day care centres[72] measured the level of respiratory infections not specifically related to absenteeism.

Funding source

Four studies had industry input. In two of the studies[70, 76] study authors worked within the companies that donated the materials. The remaining two studies[74,71] had had the hand sanitizer and educational materials donated by industry. See Appendix 9, page 92, for further details.

Study size.

The number of child participants in the hand hygiene studies ranged from 38 to 6,080. The number of institution clusters ranged from 3 to 18 and the number of classroom clusters ranged from 2 to 17.

Table 3 Study characteristics hand hygiene studies.

Arranged by intervention. Randomised trials = shaded.

Study ID	Study Design [Total number]	Population/setting	Intervention	Control	Outcomes	Dates of trial / duration
A. Scheduled hand washing.						
Master 1997[75]	Quasi randomised controlled study. [305 students, 14 classroom clusters].	Kindergarten to grade 5 (4-10yrs*). Elementary school x 1 – USA.	Instruction on handwashing 3 wks before study. Scheduled handwashing.	Instruction on handwashing 3 wks before study. Not prompted to hand wash during study.	**Absence,** categorised into respiratory or GI infections.	Jan 8th 1996 to Feb 29th 1996. Study length 37 days (just over 5 wks).
B. Scheduled use of hand sanitizer						
White 2001[70]	Cluster randomised double blind placebo controlled trial. [769 students, 16 classroom clusters].	Kindergarten to grade 6 (5 -12 yrs). Elementary school x 3 - USA.	Hand sanitizer scheduled times. All received instruction regarding germ theory & hand washing 3 wks prior to start of trial.	Placebo hand sanitizer-scheduled times. All received instruction regarding germ theory & hand washing 3 wks prior to start of trial.	**Absence**, defined as respiratory or GI infections or non infectious illness/absence.	Mar to Apr 1999. Trial length 5 wks.
Hammond 2000[76]	Matched paired cluster controlled study. [6,080 students, 18 institution clusters].	Kindergarten to grade 6 (4 - 11 yrs*). Elementary school x 9 – USA.	Hand sanitizer – scheduled times.	Usual hand washing practice.	**Absence** defined as the aggregate number of nonattending school days due to illness defined as colds, flu & GI infection, excluding non infectious absences, also pink eye, skin infections and abscesses excluded.	Sept 2000 to May 2001. Study length 36 wks.
Dyer 2000[77]	Cross over. [420 students, 14 classroom clusters].	Children 5-12 yrs. Elementary school x 1 – USA.	Hand sanitizer – scheduled times.	Instruction to wash hands before eating, after visiting the toilet, and prn during the day – not supervised.	**Absence**, defined as respiratory or GI infections or non infectious illness/absence.	Mar to May 1998. Study length 10 wks.

wks = weeks, yrs = years
* estimatated age range taken from http://www.fulbright.co.uk/eas/studyus/schoolstudy/structure.html [accessed 3-2-06]

Study ID	Study Design [Total number]	Population/setting	Intervention	Control	Outcomes	Dates of trial / duration*
Ci. Education.						
Niffenegger 1997[72]	Controlled study [38 students, 2 classroom clusters].	Age 3-5 yrs. Child day care centres x 2 – USA.	Education re: hand hygiene plus encouragement to wash hands.	Normal handwashing practice.	**Infections** Incidence of colds. Reported by teachers & parents.	Aug to Dec 1994 & Jan to Apr 1995. Study length 36 wks.
Kimel 1996[73]	Quasi controlled [199 students, 9 classroom clusters] (note: control group were study refusers).	Kindergarten & grade 1 (4-6 yrs*). Elementary school x 1 – USA.	Education re: hand hygiene.	Usual practice.	**Absence** due to flu like symptoms. Information from daily school absentee logs.	Intervention delivered to 2 kindergarten and 2 first grade classes Nov 20th and Dec 3rd 1992 with 2 other kindergarten classes and one first grade class receiving education during the third and fourth weeks in January 1993.
Cii. Education plus use of hand sanitizer.						
Guinan 2004[74]	Controlled study. [190 students, 9 classroom clusters].	Kindergarten to grade 3 (4 - 8 yrs*). Elementary school x 5 – USA.	Education re: hand hygiene plus encouragement to use hand sanitizer located in classrooms.	Usual practice.	**Absence**, due to infectious illness such as cold, flu or GI infection. Also a cost analysis.	Mar to May 2000. Study length 12 wks.
Ciii. Education plus scheduled use of hand sanitizer.						
Morton 2004[71]	Cross over Phase I = 46 days, phase II = 47 days. [253 students, 19 classroom clusters].	Kindergarten to grade 3 (4 - 8 yrs*). Elementary school x 1 – USA.	Education re: hand hygiene plus scheduled use of hand sanitizer.	Normal handwashing practice. (All children received the Germ Unit education intervention at start of trial).	**Absences**, categorised into respiratory or GI infections, or non infectious illness/absence. Asthma exacerbations excluded. Adverse events also assessed.	Dates not stated, trial length was 15 wks.

wks = weeks, yrs = years
* estimatated age range taken from http://www.fulbright.co.uk/eas/studyus/schoolstudy/structure.html [accessed 3-2-06]

MULTI-COMPONENT INTERVENTIONS – FOUR STUDIES[□]

Study design
As with the hand hygiene studies all four of the multi-component studies involved a cluster design. Three of the studies used random methods for intervention allocation [79,80,81,82] the fourth study involved an open controlled cluster design.[83]

Population
All of the multi-component hygiene intervention studies were set in the child day care setting, making this population younger than the hand hygiene study populations. All of these studies included children less than 2 years old, therefore all of the data relevant to this review comes from subgroup analyses of children over 2 years. Theoretically these studies are more methodologically robust than the hand hygiene studies where only 2 studies used a randomised design[70, 71] but this advantage may be negated because the data relevant to this review is derived from subgroup analysis.

One study was conducted in the USA[79], one in Australia [81, 82] and two studies conducted in Finland.[80, 83]

Intervention
Whilst there was variation within the multi-component interventions, all involved handwashing and recommendations to clean toys at regular intervals, with some studies specifying cleaning regimens[79], food serving practices[79,81,82,83],daily air exchange regimens[83] and aseptic nose wiping practice.[81,82] Aseptic nose wiping involved the day care staff wiping childrens noses using a tissue and plastic bag. It is of concern that if this behaviour were mimicked by the children themselves that this would be potentially very unsafe. The details of each intervention can be found in Appendix 11, page 95.

The length of studies ranged from 6 to 15 months. All included winter periods, (Oct to May – northern hemisphere, March to November – southern hemisphere).

Control
All studies had usual practice as controls. None were described in detail.

Outcomes
Three studies investigated the level of infections[79, 80, 81,82] the fourth study[83] investigated absenteeism.

Funding source
In only one study[79] was there industry involvement. Within this study a waterless disinfectant scrub Cal Stat™ was used, which had been donated by Calgon Vestal Laboratories. (see Appendix 9, page 92).

[□] Please note: reference 81 and 82 are the same study

Study size.

When compared to the hand hygiene studies, this set of studies had higher numbers of participants with a range from 371[79] to 17,388[83] The number of institutional clusters ranged from 20 to 511. Therefore the multi-component studies were much larger than the hand hygiene studies, and included a greater number of clusters. It must be remembered however, that all of the multi component hygiene studies included children younger than 2 years old, therefore data relevant to this review was from subgroup analysis.

Table 4 Study Characteristics multi-component hygiene studies.

Randomised trials = shaded.

Study ID	Study Design	Population/setting	Intervention	Control	Outcomes	Dates of study / duration
Roberts 2000 (2 papers)[81,82]	Cluster randomised controlled trial [558 students, 23 institutional clusters].	Age 3 yrs or younger. Results given as ≤2 yrs & > 2yrs – approx 56 % aged over 2 years. Day care centre x 23 - Australia.	Multi-component hygiene intervention.	No intervention.	**Infections** - Parent reported illness: GI – diarrhoea. URTI – respiratory illness symptoms. Secondary = implementation of intervention.	Mar 1996 to Nov 1996. Trial length 36 wks.
Kotch 1994[79]	Cluster randomised controlled trial [371 students, 24 institution clusters].	Mean age of intervention children 15.9 mths, controls 16.8 mths. Results given as <24 mths & > 24mths – 21% aged over 2 years. Day care centres x 24 - USA.	Multi-component hygiene intervention.	Usual practice, observation only.	**Infections** GI – parent reported diarrhoea. Respiratory infections.	Oct 1988 to May 1989. Trial length 28 wks.
Uhari 1999[80]	Matched pair cluster randomised controlled trial. [1,522 students, 20 institution clusters].	Mean age 3.5 yrs +/- 1.9mths. Results given as ≤ 3 yrs & > 3 yrs – 56% aged over 2 years. Day care centres x 20 – Finland.	Multi-component hygiene intervention. Parents had a symptom diary.	Assume no intervention, parents had a symptom diary.	**Infections** GI – vomiting, diarrhoea. URTI – cough, fever, earache, conjunctivitis. Other – visits to Dr, parental absence from work, day care personnel infections, compliance. Childrens symptoms = daily diary kept by parents.	Mar 1991 to May 1992. Total trial length 60 wks.
Ponka 2004[83]	Open controlled cluster. [17,388 students, 511 institution clusters].	Children in 2 groups, <3 yrs and > 3 yrs – 55% aged over 2 years. Day care centre x 60 – Finland.	Multi-component hygiene intervention.	Usual hygiene policy and practice.	**Absence**, due to all infections, subgroups URTI, otitis media, conjunctivitis, diarrhoea.	Dec 1999 to Feb 200 (run in), Feb 2000 (training), Mar to May 2000 (study period). Study length = 24 wks, duration of intervention = 12 wks.

wks = weeks, yrs = years

3.2.3 *Quality Assessment*

Quality was assessed by examining the methodology of the studies to identify areas of potential bias. Also of interest was how the cluster effect was taken into account in the study conduct and analysis. For full details see Appendix 12, page 97. Table 5, below and Table 6, page 35, highlight particular areas of study methodology identified from the quality assessment that were thought to be important threats to the validity of each study.

HAND HYGIENE STUDIES

Table 5 Threats to validity, hand hygiene studies

Study ID	Important threats to validity	Implications
A. Master 1997[75]	1. Non randomised. 2. Low numbers of clusters (n= 14). 3. Not analysed by cluster.	1. Possible selection bias. 2. Reduced power. 3. Overestimates the precision of the effect.
B. White 2001[70]	1. RCT but methods of randomisation not stated. 2. Total of 72 classes enrolled (1,626 children), but only 32 classes (16 int, 16 con) – 769 children) were included in analysis. 3. Not analysed by cluster.	1. Possible selection bias. 2. Major problem with this trial - 55% of the clusters dropped from analysis due to non-compliance, overestimate of effect likely. 3. Overestimates the precision of the effect.
Hammond 2000[76]	1. Non randomised 2. Matched pair design. 3. Not ITT, low sample size, 6 clusters in study, with one omitted from analysis due to non compliance. 4. Not analysed by cluster.	1. Selection bias possible. 2. Assumes that prognostic factors have been correctly matched, questionable design with small numbers of clusters.[69] 3. Not ITT therefore could overestimate the effect. 4. Overestimates the precision of the effect.
Dyer 2000[77]	1. Non randomised. 2. Cross over study. 3. Numbers of clusters = 14 4. Not analysed by cluster.	1. Selection bias possible. 2. Assumes no carry over effect* – can this be assumed for handwashing practice? May also be a problem because of seasonality. 3. Possible reduced power. 4. Overestimates the precision of the effect.
Ci. Niffenegger 1997[72]	1. Non randomised study. 2. Involved only 2 cluster groups. 3. Missing incidence data. 4. Not analysed by cluster.	1. Selection bias. 2. Equivalent to a non cluster study having 2 patients. 3 & 4. Overestimates the precision of the effect.
Kimel 1996[73]	1. Quasi controlled – control group = refusers. 2. Results given for Dec/Jan, but 3 classes had yet to receive intervention. 3. Number of clusters = 9 4. Not analysed by cluster.	1. High likelihood of selection bias. 2. Missing intervention -underestimates effect? 3. Possilbe reduced power. 4. Overestimates the effect.
Cii Guinan 2004 [74]	1. Non randomised study 2. Number of clusters = 9	1. Possible selection bias. 2. Possible reduced power.
Ciii. Morton 2004 [71]	2. Randomised crossover trial, but methods of randomisation not stated. 2. Cross over trial. 3. Not analysed by cluster.	1. Possible selection bias. 2. Assumes no carry over effect – this is an educational intervention?, may also be a problem because of seasonality. 3. Overestimates the precision of the effect.

Shaded - RCTs
*carry over effect - where the estimated effects of the intervention are dependent of the order in which they are assigned.

Comments
The ideal study design is the cluster randomised control trial. Only two hand hygiene studies were cluster randomised studies. However, there were many methodological problems with the randomised hand hygiene trials, which have consequences on the validity of the trial outcomes. (See Table 5, page 33). The main problem with the trial by White and colleagues[70] was the number of clusters excluded from the final analysis because of non-compliance issues. The main problem with the trial by Morton and colleagues[71] was its cross over design. This design assumes that there are no “carry over” effects of the intervention i.e. that the estimated effects are independent of the order in which they are assigned. This trial involved education regarding hand hygiene where theoretically one would expect that an educational intervention would have carry over effects.

The remaining hand hygiene studies were not randomised. Without randomisation all of the studies are susceptible to selection bias. Other notable problems were that one study[73] used study refusers as their control groups, one study only had two clusters[72] which is the equivalent of a non-cluster study with two participants and four studies[72, 73,75,77] did not analyse the data by cluster.

MULTI-COMPONENT HYGIENE STUDIES

In total there were three cluster randomised studies[79, 80, 81,82] and one cluster study with non random allocation.

Table 6 Threats to validity, multi-component hygiene interventions

Study ID	Important threats to validity	Implications
Roberts 2000[81,82]	**RCT but** 1. Allocation concealment not stated. 2. Baseline characteristics not stated. 3. Blinding of participants not stated. 4. Only a subgroup of children >24 mths.	1. Possible selection bias. 2. Unable to check for selection bias. 3. At risk of measurement bias. 4. Subgroup analysis may be underpowered to detect an effect. Also unclear where the older children were placed within the cluster groups, which could influence the results despite ICC being used.
Kotch 1994[79]	**RCT but** 1. Methods of randomisation not stated. 2. Allocation concealment not stated. 3. Only a subgroup of children >24 mths.	1. Possible selection bias. 2. Possible selection bias due to non concealed allocation. 3. Subgroup analysis may be underpowered to detect an effect – children >24mths account for only 21% of the total trial population.
Uhari 1999[80]	**RCT but** 1. Matched pair cluster RCT. 2. Allocation concealment not clear. 3. Unclear regarding blinding. 4. No adjustment for clusters in sub group analysis. 5. Only a subgroup of children >36 mths.	1. Assumes that prognostic factors have been correctly matched. 2. Possible selection bias. 3. At risk of measurement bias. 4. Overestimates the effect. 5. Subgroup analysis may be underpowered to detect an effect, >3 yrs age group accounts for approx 56% of the total trial population.
Ponka 2004[83]	1. Open controlled cluster. 2. Only a subgroup of children >24 mths.	1. Possible selection bias, however the study had a baseline run in period where there was no intervention to establish if the intervention group was comparable to the control group – groups were reasonably balanced with slight differences in age groups. 2. Subgroup analysis may be underpowered to detect an effect – the 3-6 age group accounts for approx 55% of the total study population.

Shaded = RCTs.
Please see Appendix 12, page 97 for full quality assessment.

Comments

The main problem with all of the multi-component hygiene studies is that only parts of the study included children over two years of age. Therefore all of the data relevant to this review are derived from subgroup analyses.

3.2.4 Effectiveness results

HAND HYGIENE STUDIES

A. Scheduled handwashing

The single study in this category sought only sickness absence data. The RR for the total number of days absent for all infections was 0.75 (95% CI 0.59, 0.96) (p=0.0193), which equates to a 25% reduction in days absent compared with the control group. The RR for the total number of days absent for respiratory infections was 0.79 (P=0.075), which was not statistically significant. The RR for the total number of days absent for GI infections was 0.43 (P=0.0024), which was statistically significant. (See Table 7, page 37).

B. Scheduled use of hand sanitizer

The three studies in this category all sought sickness absence data. All favoured the intervention. The RR for the total number of days absent for all infections was as follows: White = 0.68 (95% CI 0.55, 0.84), Hammond = 0.80 (95% CI 0.78, 0.83), Dyer = 0.58 (95% CI 0.45, 0.75). For the trial by White and colleagues[70] data was also available for absences related to respiratory and GI infections. The RR for the total number of absences related to respiratory infections was 0.69, and for GI infections it was 0.62. (See Table 7, page 37).

C. Hand hygiene education

Of the four studies in this category, one reported the incidence of the common cold, the remaining three reported sickness related absence. Niffenegger and colleagues[72] found no difference in cold incidence between intervention and control groups, the RR was 0.99 (95% CI 0.76, 1.28). For the three studies reporting sickness absence, Kimel and colleagues[73] found a 53% reduction in the total days absent, with a RR of 0.47 but this was not statistically significant (95% CI 0.03, 3.53 P = 0.41). Guinan and colleagues[74] found a 49% reduction in total days, with the RR of 0.51 being statistically significant (95% CI 0.39, 0.65 P<0.001). Morton and colleagues[71] also reported a 43% difference in the number of absences in favour of the intervention but the RR was not calculable due to lack of data reported in the paper. (See Table 7, page 37).

Table 7 Effectiveness results hand hygiene studies

Study	Results – URTI	Results GI infections	Absenteeism related to all sickness.	Absenteeism related to URTI	Absenteeism related to GI infections
HAND HYGIENE.					
A. Scheduled handwashing.					
Master 1997[75]			^Total days absent RR 0.75 (P=0.0193) (*95% CI 0.59, 0.96)	^Total days absent RR 0.79(P=0.075)	^Total days absent RR 0.43 (P=0.0024)
B. Scheduled use of hand sanitizer.					
White 2001[70]			^Total days absent RR = 0.68 (*95% CI 0.55, 0.84)	^Total days absent RR = 0.69 (variance not given)	^Total days absent RR = 0.62 (variance not given)
Hammond 2000[76]			*Total days absent RR = 0.80 (95% CI 0.78, 0.83)		
Dyer 2000[77]			*Total days absent RR= 0.58 (95% CI 0.45, 0.75)		
Ci. Education re: handwashing					
Niffenegger 1997[72]	*Cold incidence rate RR = 0.99 (95% CI 0.76,1.28).				
Kimel 1996[73]			* Total days absent RR = 0.47 (95% CI 0.03, 3.58)		
Cii. Education plus use of hand sanitizer.					
Guinan 2004[74]			* Total days absent RR = 0.55 (95%CI 0.44, 0.68)		
Ciii. Education plus scheduled use of hand sanitizer.					
Morton 2004[71]			**No. of absences intervention = 39, control 69, chi squared 7.787, p=0.053. % diff = 43%.		

^ Result given in study report, * Results calculated from data given in study report – ICC not incorporated, ** unable to calculate RR due to lack of data.
Shaded = randomised trials. NOTE: NONE OF THE STUDY RESULTS IN THIS TABLE ACCOUNT FOR THE CLUSTER EFFECT.
See Appendix 13, page 99 and Appendix 14, page 101 for raw data and StatsDirect calculations.

CLUSTER ANALYSIS – HAND HYGIENE STUDIES

None of the hand hygiene trials took account of the cluster design in their analyses, therefore the results presented in Table 7 could overestimate the precision of the estimate. In one study[74] it was possible to re-analyse the data in cluster level, and in four studies[70,75,76,77] it was possible to undertake a sensitivity analysis exploring the effect of incorporating ICC.

Re-analysis
The study by Guinan and colleagues[74] was reanalysed. This study involved nine classroom clusters in five schools and reported the outcomes of each individual student within the clusters. The absenteeism data were collected for 3 months (March, April, and May 2000).

The analysis was redone taking into account the cluster level and results for all data collected in March, April, and May 2000 are shown in Table 8, page 38. The results show a 47% reduction of infection due to education plus with hand sanitizer use, which is significantly different to the control with a p-value of <0.001. When the analyses were carried out separately for each month, the results show a 40-51% reduction of infection due to education plus hand sanitizer use. The reductions in April and May 2000 were statistically significant with p-values of 0.015 and 0.037, respectively. The reduction in March 2000 was not statistically significant with p-values of 0.08, but the trend is strong.

Table 8 Cluster level analysis Guinan and colleagues 2002

Period	Proportion of sickness related absenteeism		Favours	P-value
	Education & Sanitizer	Control		
March 2000	0.35	0.58	Intervention	0.08
April 2000	0.30	0.61	Intervention	0.015
May 2000	0.31	0.61	Intervention	0.037
March - May 2000	0.32	0.60	Intervention	<0.001

Sensitivity analysis

For four studies[70,75,76,77] it was not possible to identify data pertaining to individual clusters therefore an adjusted chi-square approach was used to investigate the relationship between the significance of the clinical effectiveness results of the hand hygiene intervention and the ICC. The sensitivity analysis results are shown in Table 9, below.

Table 9 Hand hygiene – cluster sensitivity analysis – adjusted chi-squared method

Study	Proportion of sickness absence		Reduction of infection (%)	Favours	Uncorrected P values	Corrected P-values		
	Hand hygiene	Control				ICC = 0.0001	ICC = critical value	ICC=0.01
Master 1997[75]	0.023	0.030	25	Hand hygiene	P=0.0193	p=0.0192	p=0.05 (ICC=0.00068)	p=0.4094
White 2001[70]	0.016	0.023	32	Hand hygiene	P=0.0002	p=0.0004	p=0.05 (ICC=0.00195)	p=0.3263
Hammond 2000[76]	0.013	0.017	20	Hand hygiene	P<0.0001	P<0.0001	p=0.05 (ICC=0.00075)	p=0.5866

Dyer 2000[77]	0.012	0.020	42	Hand hygiene	P<0.0001	P<0.0001	p=0.05 (ICC=0.00334)	p=0.2233

The results indicate that 20-42 % of reductions of sickness related absenteeism are statistically significant *if and only if* the ICC is less than 0.0033. When an ICC of 0.01 is applied to the data, the reductions of sickness related absenteeism turn out to be not statistically significant.

MULTI-COMPONENT HYGIENE INTERVENTIONS

Three studies in this category reported incidence of infections. The fourth measured sickness related absenteeism (see Table 10, page 40). Roberts and colleagues[82] found that for the cumulative incidence of respiratory infections the RR was not statistically significant at 0.98 (95% CI 0.89, 1.07), however it was statistically significant in favour of the intervention for GI infections RR 0.56 (95% CI 0.44, 0.71)[81]. Kotch and colleagues[79] found only small differences between intervention and control groups for the incidence rate of respiratory and GI infections which all favoured the control group. Uhari and colleagues[80] combined respiratory and GI infections and found that the percentage mean difference in favour of the intervention for the number of episodes of infections per person years at risk was 8%, which was just statistically significant.

The study by Ponka and colleagues[83] was the only multi component study to report sickness related absenteeism. They found no significantly significant differences between intervention and control. Insufficient data for the latter three studies meant that a relative risk could not be calculated (see Appendix 13, page 99).

Because the data came from subgroup analyses within the multi-component hygiene trials it was not possible to explore the effects of the cluster design on the results.

Table 10 Effectiveness results multi-component interventions.

MULTI-COMPONENT HYGIENE INTERVENTIONS.					
Study	**Results – URTI**	**Results GI infections**	**Absenteeism related to all sickness**	**Absenteeism related to URTI**	**Absenteeism related to GI infections**
Roberts 2000 [81,82]	^Incidence RR = 0.98 (95% CI 0.89,1.07) Cumulative incidence.	^ Incidence RR = 0.56 (95% CI 0.44, 0.71) Cumulative incidence.			
Kotch 1994[79]	*Number of episodes per child per year. Intervention = 12.87, control = 11.77. Mean difference =1.11, RR=1.09, favouring control. Incidence rate.	*Number of episodes per child per year. Intervention = 2.85, control = 2.79. Mean difference =0.06, RR=1.02, favouring control. Incidence rate.			
Uhari 1994[80]	Combined URTI and GI **% diff mean no. of episodes of infection per person years at risk = 8% (95% CI 0.0, 15, p=0.049) favouring intervention (no difference GI infections) Cumulative incidence.				
Ponka 2004[83]			**Mean diff between no. of abs per 1 mth per 1,000 children = 14 (95% CI - 23, 51 p=0.451)	**Mean diff between no. abs per 1 mth per 1000 children = 1 (95% CI = -31, 33 p=0.941).	**Mean diff between no. abs per 1 mth per 1000 children = 19 (95% CI -2, 40 p=0.072).

^ Result given in study report, * Results calculated from data given in study report – ICC not incorporated, ** unable to calculate RR due to lack of data. abs = absences.
Shaded = randomised trials. NOTE: NONE OF THE STUDY RESULTS IN THIS TABLE ACCOUNT FOR THE CLUSTER EFFECT.
See Appendix 13, page 99 and Appendix 14, page 101 for raw data and StatsDirect calculations.

3.2.5 Adverse events

Table 11 Adverse events – all studies

Study	Events reported.	Comments.
HAND HYGIENE		
A. Scheduled handwashing.		
Master 1997[75]	Not reported	
B. Scheduled use of hand sanitizer.		
White 2001[70]	7 children had skin irritation – group assignment not reported – children left study once irritation occurred	Monitored weekly
Hammond 2000[76]	No adverse events found	
Dyer 2000[77]	No adverse events found	
Ci. Education.		
Niffenegger 1997[72]	Not reported	
Kimel 1996[73]	Not reported	
Cii. Education plus use of hand sanitizer.		
Guinan 2004[74]	Not reported	
Ciii. Education plus scheduled use of hand sanitizer.		
Morton 2004[71]	10 children had skin irritation – not clear if they were in the intervention group at the time of drop out (crossover trial design) – children left study once irritation occurred	Monitored weekly by school nurse
MULTI-COMPONENT HYGIENE INTERVENTIONS.		
Roberts 2000[81,82]	Not reported	
Kotch 1994[79]	Not reported	
Uhari 1999[80]	Not reported	
Ponka 2004[83]	Not reported	

Shaded = randomised trials.

Four studies reported adverse events data. All were in the hand hygiene studies. In two studies no adverse events were found[76, 77] however, in the two studies that stated that they monitored adverse events weekly skin irritation was found. White and colleagues[70] noted seven children with skin irritation and Morton and colleagues[84] noted 10 children with skin irritation. In neither study was it stated whether the skin irritatation occurred in the intervention or control group. Both studies used an alcohol free hand sanitizer.

4 REVIEW OF PREVIOUS ECONOMIC EVALUATIONS

4.1 Aim

1. To identify published economic evaluations of simple hygiene interventions in the prevention of infections in children aged between 2 and 11 years.
2. To identify cost data to populate a new economic model relevant to the West Midlands.

4.2 Methods

A search for previous economic evaluations and cost data was undertaken, using the same search terms as for the effectiveness part of the review (Appendix 4, page 70). Citation lists from all identified reviews and included primary studies were searched.

4.2.1 Inclusion criteria for economic analysis

Population	• Children from the general population. No age restrictions applied. • Setting - Schools, Child Day Care Centres, Play Groups, Nurseries, Crèches. • Country – only included were studies where childcare is comparable to UK practice.
Intervention	• Any simple hygiene intervention that children and /or staff and others undertake to prevent the spread of infection e.g. hand washing, surface disinfection, tissue disposal.
Control	• Placebo. • No intervention. • Other simple hygiene interventions.
Outcomes	• Cost effectiveness of simple hygiene interventions. • Costs that could be utilized in the Birmingham model.
Study Designs	• Any type of economic evaluation (i.e. cost minimization, cost effective analysis, cost utility analysis, or cost benefit analysis). • Any primary study that has measured costs associated with respiratory or GI infections in the child day care setting or schools (either with or without the simple hygiene interventions)

4.2.2 Exclusion criteria

Population.	• Specialist settings e.g. hospitals.
Intervention.	• Food handling hygiene measures from canteen staff. • Interventions designed to prevent specific tropical infections. • Health education delivery techniques.
Control.	• Home care.
Outcomes.	• Laboratory results.
Study design.	• Studies with no comparator practice e.g. cross sectional surveys.

Excluded studies are described in Appendix 5, page 74. The quality of the economic evaluations identified was evaluated according to the Drummond checklist.[85] Results were tabulated (see Appendix 15, page 103 and Appendix 16, page 109) and discussed with respect to the appropriateness of the economic analysis to the West Midlands setting and whether any cost data would be able to be used in the Birmingham model.

Current UK prices are given in square brackets [£] inflated to 2006 using the retail price index and exchange rate for February 2006.

4.3 Results

Six papers were identified, which described four potential studies. Two were cost benefit studies and two were cost surveys.

Table 12 Previous economic evaluations

Study ID	Content.
Economic Evaluations.	
Ackerman SJ 2001[86] Related publications: Rubino 2002[87], Duff 2000[88]	Economic evaluation, Markov model employed.
Guinan 2002[74]	
Cost surveys.	
Carabin H 1999[89]	Cost survey.
Lambert S 2004[90]	Cost survey.

4.3.1 Economic evaluations

There were two cost benefit studies identified, full details are given in Appendix 15, page 103.

ACKERMAN AND COLLEAGUES 2001[86]

This was a USA cost benefit analysis, which used a Markov model to primarily investigate the cost of an intensive multi-component hygiene intervention in a specialist preschool for children with Downs Syndrome. This initial model was adapted for use in non specialised settings and used effectiveness estimates derived from three studies[79,80,81&82] which are included within this review and one study which was excluded from this review[89] (see Appendix 5, page 74).

The model took a societal perspective. The cost year was 1999. Costs included absenteeism and direct medical costs, such as child GP visits, hospitalisation. Other costs included lost parental working time, calculated at 80% opportunity cost (defined as parents' lost wages at $117 per day [£134.06]) and 20% replacement costs (defined as babysitter time at $58.5 per day [£67.03]). Intervention costs were taken from Krilov and colleagues[86] and included the cost of the personnel who conducted an initial assessment of in-service training for day care staff, cleaning and disinfection product use, and educational materials such as posters and handouts. Control costs consisted of cleaning product cost (calculated at 25% of the intervention). Time period was one year.

The results were as follows:

Table 13 Cost analysis by Ackerman

Mean Annual Costs of Illness per Child.

Study	Baseline Year	Intervention Year	Cost savings
Uhari 1999	$1,002 [£652.37]	$814 [£529.97]	$188 [£122.39]
Carabin 1999	$1,212 [£789.08]	$825 [£537.13]	$387 [£251.94]
Kotch 1994	$2,604 [£1935.74]	$2,398 [£3137.37]	$206 [£153.14]
Roberts 2000	$1,672 [£1066.72]	$1,337 [£852.99]	$227 [£144.83]

The intervention was cost saving for all of the studies.

Comment
The analysis was well conducted with costs derived from study data, literature searches and physician consultation. Because the non specialist day care centres were secondary analyses, costs are not tabulated in the publication making it difficult to check the data. It was presumed that all of the study data was used in the effectiveness assessment, which would include children less than 2 years old. The population included were children from 0 to 5 years, which is younger than the populations included in this review. Higher costs may be associated with infants. Additionally, the economic evaluation took a societal perspective and was based in the USA. Care should be taken when extrapolating the results to the UK.

GUINAN AND COLLEAGUES 2002[74]

This was a cost benefit analysis based on the study by Guinan and colleagues.[74] Set in a primary school in the USA, the economic analysis looked at the costs of an education plus hand sanitizer intervention. The cost year was 2000.

Cost of absenteeism was calculated according to teacher time (cost of remedial work, take home assignments) given as an hourly rate of $50 [£56.14]. Cost of intervention included school nurse time at $35 [£39.30] per intervention. Cost of hand sanitizers were calculated as one fourth the cost of the yearly cost of soap per child ($2 [£2.25] per year or 50 cents per quarter). Activity booklets and cards were costed at 50 cents per child.

The results were as follows:

Table 14 Cost analysis by Guinan

	Teacher time	School nurse time	Hand sanitizer	Activity sheets	Total cost per quarter	Total cost projected yearly
Intervention	$7000 [£4,465.91] (140 hrs)	$630 [£401.93] (18 hrs)	$72.50 [£46.25]	$72.50 [£46.25]	$7,775 [£4,960.35]	$31,100 [£19,841.42]
Control	$13,850 [£8,836.14] (277hrs)	-	-	-	$13,850 [£8,836.14]	$54,400 [£34,706.54]
Cost savings	$6,852 [£4,371.49]	-	-	-	$6,075 [£3,875.77]	$24,300* [£15,503.11]

*Yearly cost saving per student = $167 [£106.54]

The intervention was cost saving.

Comment
This cost benefit analysis is limited because it takes only the educational perspective, and doesn't consider the costs of illness to the health service. It is useful, however, that it gives an estimate of hand sanitizer costs from one of the studies included in this review.

4.3.2 Cost surveys

There were 2 cost surveys with potentially useful information that could be incorporated into the Birmingham model (see Appendix 16, page 109 for further details). The earliest study by Carabin and colleagues 1999[89] was set in Quebec, Canada and was a cost survey carried out ahead of a study investigating a multi-component hygiene intervention. The survey was set in a childcare centre with a mean child age range of 24.8 months (SD 6.1). Outcomes included were URTI, GI related illness and illness related absenteeism. Costs calculated were direct costs (medication, physician visits) and indirect costs (carer costs). Two hundred and seventy three children were included. The study was conducted from 1st September 1996 to 1st March 1997. The total cost of illness was $206.77 [£114.46] (SD $217.30 [£120.29]) per child per 6 months (replacement cost method) or $260.96 [£144.98] (SD $302.00 [£167.17]) per child per 6 months (opportunity cost method).

The second cost survey by Lambert and colleagues 2004[90] was set in Melbourne, Australia and was not related to any intervention study. Children were aged between 12 to 71 months (only 8/122 children were under 24 months). Outcomes sought were the number and duration of influenza like illness (ILI), with disease burden quantified. Costs calculated were direct costs (medication, physician visits and diagnostic tests) and indirect costs (carer time, travel and time seeking health care). One hundred and twenty two children were included. The study was conducted between July 2001 and December 2001. The total cost per ILI was calculated at Aus$240.88 [£104.53].

<u>Comments</u>
Both cost studies were initially thought to be potentially relevant, particularly because the health care systems of Canada and Australia are comparable with the UK NHS in terms of reimbursement making it feasible to use the results to populate the Birmingham model. However, there are problems within both surveys that make the costs given less relevant to the Birmingham model. For instance, the costs included in both studies do not take into account recent NHS initiatives such as NHS direct, or NHS walk in facilities.

Additionally, both cost surveys included children younger than 2 years old, with neither cost survey including children older than 6 years. In the earlier survey[89], it is difficult to ascertain what proportion of the children are younger, therefore inputting costs relating to children younger than the target population into the model would not be appropriate. The main problem with the later survey is that 70% of the costs come from an undefined cost described as “time away from usual activities of the main carer”. Putting in an undefined cost within the Birmingham model, particularly one that accounts for 70% of the data, was not considered to be reasonable.

4.4 Conclusions

Two economic evaluations and two cost studies met the inclusion criteria. However, their usefulness to the UK NHS setting and specifically the West

Midlands is limited because the studies are more than 5 years old, none are UK based and three include children less than two years old. Additionally, none are explicit in how the costs were calculated making it difficult to generalise the results to the UK.

5 BIRMINGHAM ECONOMIC MODEL

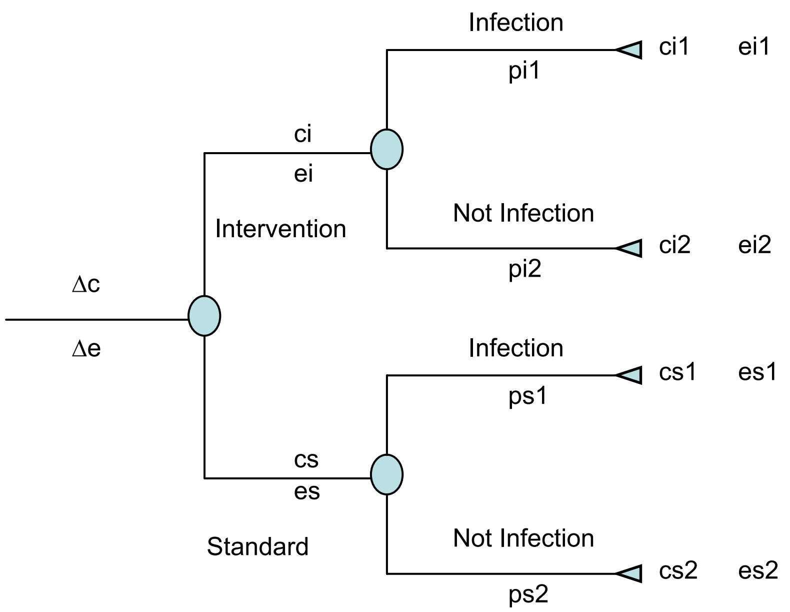
5.1 Introduction

This section provides a basic model structure that could be used to assess the cost-effectiveness of the simple interventions included in this review compared to standard care. The parameters required for economic analysis are described. A simulated data set is shown to give an example of how the model works. However, it must be stressed that this is only a simulation. At the present time cost data relating to the West Midlands is not available (see section 4.4.2, page 45). Additionally the studies included in this review do not provide reliable effect estimates because of quality issues (see section 3.2.3, page 33). The Birmingham model therefore provides a working model framework should this information become available.

5.2 Methods

The model chosen for the cost effectiveness analysis was a decision tree. Its basic structure is shown in Figure 2, below. The model was constructed with two branches, one for the intervention group, and the other for the control (assumed standard care) group. The intervention arm represents either handwashing, hand sanitizer, education regarding hand hygiene, or multi component hygiene interventions.

Figure 2 Basic structure of the Birmingham decision tree model for cost effectiveness analysis.



The parameters **pi1** and **pi2** are the probabilities of infection and not infection in the intervention group, **ci1** and **ei1** are the average yearly cost and the effectiveness (with effectiveness expressed as the number of infections or absenteeism prevented) if a child gets an infection, **ci2** and **ei2** are the average yearly cost and the effectiveness if a child does not get an infection. The parameters **ps1** and **ps2** are the probabilities of infection and not infection in the standard care group, **cs1** and **es1** are the average yearly cost and the effectiveness if a child gets an infection, and **cs2** and **es2** are the average yearly cost and the effectiveness if a child does not get an infection. The parameters **ci** and **ei** are cost effectiveness in the intervention group, and **cs** and **es** are the corresponding cost effectiveness in the standard care group. ∆**c** is the cost difference between the intervention and the standard care group, ∆**e** is the effectiveness difference between the intervention and the standard care group. The incremental cost effectiveness ratio (ICER) is evaluated by:

$$ICER = \frac{\Delta \mathrm{c}}{\Delta \mathrm{e}}$$

The time horizon is one year. This was chosen for convenience and because it is highly likely that any hygiene initiative in young children would need to be repeated very frequently. For the studies in which the follow-up period is less than 1 year, the probabilities of infection and not infection for the period of 1 year are assumed to be the same as those reported in the studies.

To estimate which intervention offers the greatest cost effectiveness different interventions can be compared to each other indirectly according to their ICERs to the standard care treatment.

5.3 Examples

To test whether the model worked, two simulations were conducted. Inputs consisted of effectiveness data from two studies[70,75]and arbitrary costs (see Table 15, page 48 and Table 16, page 48). Sensitivity analyses were conducted using the combination of probabilities of infection derived from the 95% CI and higher cost data for the control group (see cost setting 2 below).

Table 15 Model inputs – effectiveness probabilities (taken from included studies).

Study	Intervention		Standard care	
	Probability of infection	**95%CI**	**Probability of infection**	**95%CI**
White 2001[70]	0.25	(0.20, 0.29)	0.38	(0.33, 0.43)
Master 1997[75]	0.55	(0.46, 0.63)	0.69	(0.61, 0.76)

(Note: studies chosen because probability data was available)

Table 16 Model inputs – arbitrary costs (not evidence based).

	Intervention	Standard care
Cost setting 1		
With infection	£600	£400
Without infection	£500	£300
Cost setting 2		
With infection	£600	£500
Without infection	£500	£400

(Note: Cost setting 1 = £200 difference between intervention and control. Cost setting 2 = £100 difference between intervention and control)

Example 1. Data from the scheduled handwashing study by Master and colleagues[75] was used in this example. Probabilities were based on the point estimate and 95% CI. In this study sickness absenteeism is taken as a proxy for infection.

Table 17 Example 1 – Simulated cost effectiveness results for scheduled handwashing (absenteeism related to all sickness)

Cost setting	Probability of infection (intervention)	Probability of infection (control)	Cost difference (£)	Difference of sickness prevented	ICER (£/sickness prevented)
Cost setting 1					
Point estimate	0.55	0.69	186	0.14	1328.57
Estimates derived from 95% CI	0.46	0.69	177	0.23	769.57
	0.63	0.69	194	0.06	3233.33
	0.55	0.61	194	0.06	3233.33
	0.55	0.76	179	0.21	852.38
	0.46	0.61	185	0.15	1233.33
	0.46	0.76	170	0.3	566.67
	0.63	0.61	202	-0.02	-10100.00
	0.63	0.76	187	0.13	1438.46
Cost setting 2 (Sensitivity analysis)					
Point estimate	0.55	0.69	86	0.14	614.29
Estimates derived from 95% CI	0.46	0.69	77	0.23	334.78
	0.63	0.69	94	0.06	1566.67
	0.55	0.61	94	0.06	1566.67
	0.55	0.76	79	0.21	376.19
	0.46	0.61	85	0.15	566.67
	0.46	0.76	70	0.3	233.33
	0.63	0.61	102	-0.02	-5100.00
	0.63	0.76	87	0.13	669.23

Table 17 above, shows the parameters and the corresponding cost effectiveness for hand washing in terms of incremental cost effectiveness ratio (ICER). For the cost setting of £600 and £500 in the intervention group with and without infection, and £400 and £300 in the control group with and without infection, ICER had a range of £10100 to £3233 per sickness prevention. For the cost setting of £600 and £500 in the intervention group with and without infection, and £500 and £400 in the control group with and without infection, ICER had a range of -£5100 to £1567 per sickness prevention.

Example 2. Data was taken from the hand sanitizer trial by White and colleagues 2001[70] for this example. Probabilities were based on the point estimate and 95% CI. In this trial sickness absenteeism is taken as a proxy for infection.

Table 18 Example 2. Simulated cost effectiveness results of hand sanitizer (absenteeism related to all sickness).

Cost setting	Probability of infection (intervention)	Probability of infection (control)	Cost difference (£)	Difference of sickness prevented	ICER (£/sickness prevented)
Cost setting 1					
Point estimate	0.25	0.38	187	0.13	1438.46
Estimates derived from 95% CI	0.2	0.38	182	0.18	1011.11
	0.29	0.38	191	0.09	2122.22
	0.25	0.33	192	0.08	2400.00
	0.25	0.43	182	0.18	1011.11
	0.2	0.33	187	0.13	1438.46
	0.2	0.43	177	0.23	769.57
	0.29	0.33	196	0.04	4900.00
	0.29	0.43	186	0.14	1328.57
Cost setting 2 (Sensitivity analysis)					
Point estimate	0.25	0.38	87	0.13	669.23
Estimates derived from 95% CI	0.2	0.38	82	0.18	455.56
	0.29	0.38	91	0.09	1011.11
	0.25	0.33	92	0.08	1150.00
	0.25	0.43	82	0.18	455.56
	0.2	0.33	87	0.13	669.23
	0.2	0.43	77	0.23	334.78
	0.29	0.33	96	0.04	2400.00
	0.29	0.43	86	0.14	614.29

Table 18 above, shows the parameters and the corresponding cost effectiveness for hand sanitizer in terms of incremental cost effectiveness ratio (ICER). For the cost setting of £600 and £500 in the intervention group with and without infection, and £400 and £300 in the control group with and without infection, ICER had a range of £770 to £4900 per sickness prevention. For the cost setting of £600 and £500 in the intervention group with and without infection, and £500 and £400 in the control group with and without infection, ICER had a range of £335 to £2400 per sickness prevention.

In order to evaluate the cost effectiveness for hand washing, hand sanitizer, and education on hand washing based on the parameters derived from the two studies, samples with a size of 1,000 were randomly generated by assuming a normal distribution with a mean and standard deviations which were calculated from 95% CI for each type of interventions. These parameters were then input into the models. The values of cost effectiveness for different combination of parameters were obtained.

Figure 3 Simulation of cost effectiveness results for hand washing (absenteeism related to all sickness).

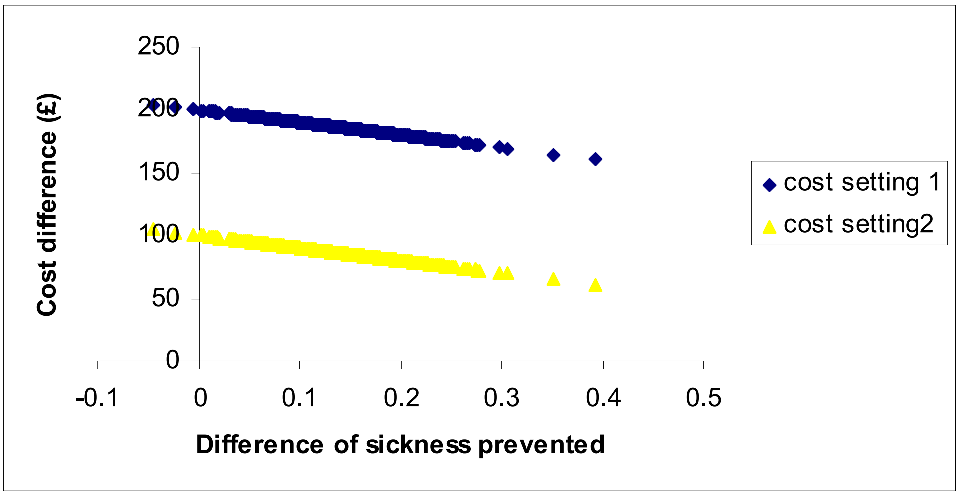
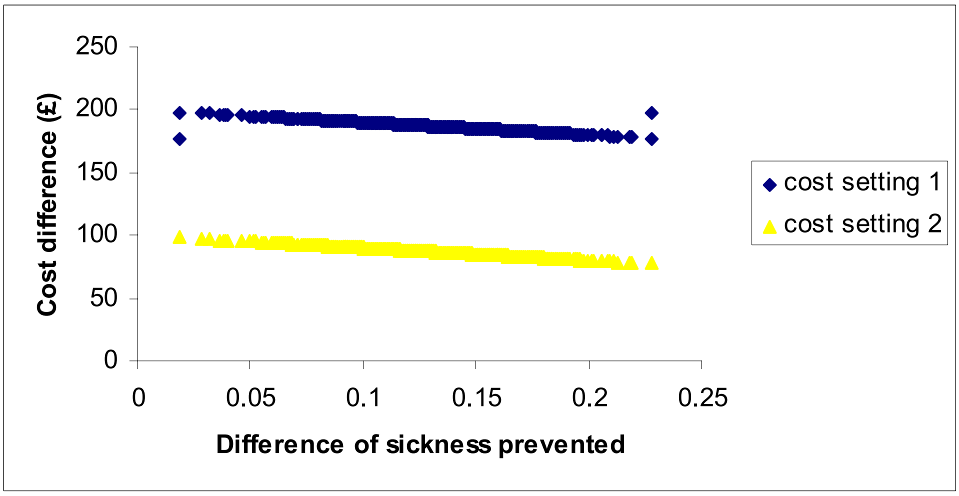


Figure 4 Simulation of cost effectiveness results for hand sanitizer (absenteeism related to all sickness)



The mean and standard deviation of the cost effectiveness for hand washing were £1875±4952 per sickness prevented (see Figure 3, page 51). The mean and standard deviation of the cost effectiveness for hand sanitizer were £1570±639 per sickness prevented (see Figure 4, page 51). The simulated results suggest that hand sanitizer was more cost effective than scheduled hand washing.

Please note that due to lack of the cost data and the small number and poor quality of the studies, the simulation results are only for demonstration purposes. The results from simulation simulation should not be used to assist decision making.

5.4 Comments

Data regarding the costs of infection could be taken from the NHS perspective, from a societal perspective as described from the Ackerman study[86] or educational perspective as described by Guinan and colleagues.[74] The choice of perspective would depend upon user requirements. It may be appropriate in the UK to take a NHS perspective and combine it with an educational perspective, particularly as the money for the intervention would principally be derived from an education budget, and any savings would be from the NHS budget. Further work regarding these parameters is needed, but is outwith the remit of this review, as it would require primary research on costs. Ideally, this work should be taken by a mutli-disciplinary group to take into account healthcare, education and societal perspectives.

6 DISCUSSION

6.1 Review Summary

This review identified 12 primary studies that investigated the effectiveness of simple hygiene interventions on respiratory and GI infections in children attending either day care or primary school. Eight studies investigated the role of hand hygiene interventions and four studies investigated multi-component hygiene interventions. Two economic evaluation and two cost studies were identified.

Hand hygiene studies
All but one hand hygiene study investigated the effects on sickness absenteeism. They all found that illness related absenteeism was reduced during the intervention. The hand hygiene study investigating respiratory illness found no difference between intervention and control groups.[72] However, none of the trial results took into account the cluster design. It was possible to factor in the cluster design in five of the studies which measured absenteeism. Guinan and colleagues[74] presented sufficient data to allow for a reanalysis of the results taking account of the cluster. The results remained statistically significant in favour of the intervention, but with a reduced variance. For the remaining four studies (one handwashing[75] and three hand sanitizer studies[70,76,77]) an ICC of 0.01 was applied to the results. This turned highly statistically significant results into non statistically significant results. An ICC of 0.01 is commonly applied to cluster trials undertaken in schools.[91]

Multi-component hygiene interventions
Of the multi-component hygiene studies only one investigated absenteeism, which did not find a significant difference between intervention and control groups.[83] The remaining multi-component hygiene studies investigated the incidence of respiratory and GI infections. The results did not show any overall trends. The trial by Roberts and colleagues[81] found a statistically significant reduction in GI infections but not respiratory infections[82], conversely the studies by Kotch and colleagues[79] and Uhari and colleagues[80] showed a reduction in respiratory infections but not GI infections.

Economic evaluation
The two previous economic analyses found that simple interventions such as multi-component hygiene regimens were cost effective in societal terms and educational terms. However, both were based in the USA. A Birmingham model was developed but due to lack of robust data to populate it, only a simulation could be achieved. Further primary research with a UK perspective is needed.

Overall
Taken at face value the results show that simple interventions, particularly hand hygiene interventions, are effective in reducing sickness related absenteeism. However, there are several factors other than the interventions that could have impacted on the results of the studies included. There are also

problems which limit the generalisability of the study results in this review. These are discussed below.

6.2 Population

6.2.1 Hand hygiene studies

Institution characteristics
Seven of the eight studies were based in primary schools and included children aged between 5 and 12 years. The eighth study was based in a child day care centre and included children aged between 3 and 5 years.[72] All the studies were conducted in the USA. All of the studies give the name and location of the schools, therefore inferences could be made regarding the population characteristics. The study by Hammond and colleagues[76] describe the school locations as rural, suburban and urban. Three studies state that the school populations were middle class.[73,74,75]

Only one study gave a description of the hand hygiene facilities available prior to the study.[73]

Child characteristics
Only Kimel and colleagues[73] supplied a table of population characteristics describing the intervention and control groups. They reported sex distributions, number with chronic illness, income status and ethnicity. None of the other studies reported any details of the children within the studies. In their discussion Guinan and colleagues[74] state that data on variables such as smoking status of parents, home hygiene practices and social circumstances would have been useful aid interpretation of the results.

In general the hand hygiene studies underreported population characteristics. This makes the generalisability of study results difficult.

6.2.2 Multi-component hygiene studies

Institution characteristics
All four studies were set in child day care centres. The size of the centres recruited was stipulated in two studies. Roberts and colleagues only included centres with more than 50 children who attended for at least 9 hours per day, 5 days a week.[81,82] Kotch and colleagues[79] included centres that had less than 30 children attending for at least 20 hours per week. Both required that at least 5 children should have been using nappies. Nappy use is a risk factor for GI infections.

Only Kotch and colleagues[79] describe the characteristics of the intervention and control centres. They reported that the number of centres with a written diarrhoea policy was greater in the intervention centres (33% versus 18%). However, controls had a better access to sinks: 70% of the controls had sinks less than 3ft way from nappy changing areas compared to 35% for the intervention groups and 91% of controls had classroom sinks compared to 70% of the intervention groups. In addition 25% of intervention groups were open to other classrooms, compared to 91% for the control groups. Difficulties in access to sinks and mixing of age groups have been cited as factors for the spread of infection. Without a description of the centre characteristics it is difficult to independently assess such confounding factors within the study.

Child characteristics

Child day care in Finland is state sponsored, which may have had implications for the population make up of these studies compared with the Australian and American studies. Neither of the Finnish studies[80,83]described the economic status of the parents. Roberts and colleagues[81,82] described their population as affluent and Kotch and colleagues[79] described participants has having moderate socio-economic status.

Risk factors associated with respiratory infections were reported in two studies. Kotch and colleagues[79] reported that 24% of children had at least one parent who smoked, and 49% of children had siblings in day care or school. Uhari and colleagues[80] reported that 50% of children had at least one parent who smoked and 3% of children had siblings in day care. In both studies these characteristics were balanced between intervention and controls.

The age ranges of the multi-component hand hygiene studies were from 0 to 6 years. All of the studies assessed gave data on subgroups of children older than 2 years. Unfortunately subgroup analyses can be misleading as they are underpowered[92] and often undertaken post hoc. Only Roberts and colleagues[81,82] described the reasons for the subgroup analyses. In addition, it was not clear how the data for these subgroups related to the cluster structure of the studies as the clusters within the studies are were not described by age. By ignoring the cluster effect, the treatment effect could be overestimated.

6.3 Interventions

6.3.1 Defining interventions

As a descriptive framework, this review arbitrarily split the studies into two groups, hand hygiene studies and multi-component hygiene studies. Hand hygiene studies were defined as studies where the intervention focused on reducing hand contamination. Hand contamination was reduced by introducing scheduled handwashing with soap and water, by using a hand sanitizer product or by educating children about the importance of cleaning the hands and giving them the means to undertake hand hygiene either by washing with soap and water or using hand sanitizers. Handwashing and hand sanitizer use were a supplement to normal handwashing such as after using the toilet. Multi-component studies were studies that included hand hygiene plus other interventions such as environmental cleaning. It could be argued that the heterogeneity of the interventions makes the arbitrary grouping unwise. However, the hands are the prime suspects in spreading many infections. It seemed sensible to group interventions that concentrated on this mode of spread to see if any of them were effective, and then compare them to interventions that looked at ways of reducing infection by means other than hand hygiene. As it happened, the multi-component hygiene interventions had as core activity hand hygiene. Therefore only the added value of interventions such as surface cleaning, fomite cleaning, aseptic nose wiping and air exchange systems could be evaluated.

Because the multi component studies used a variety of interventions it is also difficult to tease out which elements worked, and if there were any that complemented each other or others that had opposing effects. It may be that in hygiene interventions the whole is greater than the sum of the parts. For instance, teaching children about handwashing is not going to be effective if handwashing facilities are not available.

6.3.2 Safety issues

Some of the interventions may have had risks associated with them. The safety of using hand sanitizers in children has not been evaluated. Hand sanitizers containing alcohol are also a fire hazard[55] and an intoxicating substance[57]so care has to be taken when managing storage and use of these products around children. In all of the studies that used hand sanitizers the children were under the supervision of the teachers and the hand sanitizers were placed in classrooms. The trial by Roberts and colleagues[82] used plastic sandwich bags to aseptically wipe the noses of young children. This is also a potential hazard particularly if other children mimic the actions of the staff and place plastic bags over the noses of themselves and other children, particularly infants.

6.4 Controls

All of the studies had control groups. One study had a control group made up of refusers.[73] This may not be appropriate as often refusers are different from the people willing to take part in the study.

Control group activities varied. White and colleagues[70] used a placebo hand sanitizer. Of the hand hygiene studies, four had usual practice as controls but usual practice was not described. It could be that usual practice consisted of alot of handwashing or very little handwashing. This would create variation in the results. In the remaining four hand hygiene studies the control groups received education regarding germ theory,[70,71,75]or instructions to wash hands after going to the toilet and before eating.[77] All of the multi-component hygiene studies had usual practice as control. Details of usual practice were not given. Kotch and colleagues[79] observed the hygiene behaviour of the control group, and expressed concern that this could be acting as an intervention. However, they also observed the intervention group in the same manner therefore this should not have affected the overall study results.

Within the intra-school studies there was also the potential for cross contamination from one classroom with another. This, however, would have reduced the effect estimate and in all of these studies the effect estimates were large.

6.5 Outcomes

6.5.1 Data collection

Outcomes measuring respiratory infections, gastrointestinal infections and infection related absenteeism were reported in the studies in this review. To collect information on these outcomes the studies relied on reports from parents, schools or actively gathered information by telephoning parents. For the studies collecting infection data, the parents were asked to keep symptom diaries and report symptoms to the study staff. This involved a lot of commitment from the parents. It would have been useful to know how many diaries were correctly completed.

All of the methods for data collection had the potential for bias, particularly where blinding did not occur. For example, the study by Guinan and colleagues[74] had a very large effect size of up to 50% difference in absence rates between intervention and control with the data collected by the teachers who would have known the intervention allocations. In the study by Ponka and colleagues[83] data was collected via the usual absence reporting route, well away from the study mechanisms and the effect size was very much smaller.

6.5.2 Infections

Parents and in some cases teachers were advised which signs and symptoms they should report. This varied between the studies, therefore could have led to discrepancies between the studies. However, as both intervention and control groups were working to the same criteria within the studies and it is the reduction in infection between these groups that is of interest this should not have affected the results of each study. However, reporting illness using only signs and symptoms is a subjective measure that may be prone to reporting biases, particularly if blinding has not been undertaken. A less subjective measure could have been laboratory conformation of infection.

6.5.3 Absenteeism

The number of children absent on any day is a relatively straightforward statistic to collect and in most of the studies this was undertaken using the schools usual reporting system. Determining if the absence was due to respiratory or gastrointestinal symptoms is more difficult and is a subjective measure. Using absence data as a proxy for illness can be difficult to validate. Superficially one would think that a child is absent because they are too ill to attend school. However, as described in the background (see section 2.3.2, page 14), determining whether the child can attend school is based on social as well as health grounds. The study scenario also complicates the situation.

6.5.4 Interpretation of outcome data

A further challenge in interpreting the outcome data was that the studies reported the data using different measures, which made it difficult to compare effect sizes. Care had to be taken to define the events reported. For example, absence data was reported as the number of episodes of illness, but also the number of days absent, the latter being the larger number. Similarly, infections were reported as incidence rates but also as incidence density. Additionally, absence data was reported as absence related to respiratory illness or gastrointestinal illness. In many of the study reports this was not immediately obvious. In some studies the data was also split into time slices, for example, Niffenegger and colleagues[72] presented data in two segments, the reason given was that the intervention needed a run in time. Indeed the first segment showed a favouring of the control (weeks 1 to 11 = RR 1.53 (95% CI 1.03, 2.29) but the second segment showed a difference in favour of the intervention (weeks 12 to 21 = RR 0.68 (95% CI 0.47, 0.99) in reducing the incidence of colds. The whole result taken together shows no difference (RR = 0.99 (95% CI 0.76, 1.28). Presenting the data in this manner could overestimate the overall effect, and could be misconstrued as a data dredging exercise particularly if it is not clearly stated that the time slices had not been anticipated in the *a priori* data analysis plan.

6.5.5 Adverse events

Only four studies reported adverse events data with two of the hand sanitizer studies reporting a total of 17 children with skin irritation[70, 71] Unfortunantly neither of these studies state whether the irritation occurred in the intervention or control group. As White and colleagues[70] used a placebo control, and Morton and colleagues[71] used a cross over design it is feasible that the irritation could have occurred in the intervention or control arms. If the irritation had occurred only in the intervention groups, a simple conclusion would be that adverse events occur with hand sanitizer use. But this could be an artefact of the data collection in that only these two studies reported that the children were monitored weekly for adverse events. The other studies may have had adverse events but these may have been missed if monitoring did not occur.

6.6 Study Design/Study Quality

6.6.1 Hierarchy of evidence

At the top of the hierarchy of evidence is the RCT. This review included five studies that were cluster RCTs.[70,71,79,80,81,82] Two were hand hygiene studies and three were multi-component interventions. However, there are problems with each of these included randomised studies, which make the data from them no more reliable than the data from the studies that were not randomised (see section 3.2.3, page 33 for details). The three multi-component hygiene studies that were randomised whilst being of reasonable quality regarding internal validity (i.e. study conduct) caused a problem for this review in that the study populations ranged from 0 to 6 years, therefore data relevant for this review was obtained from subgroup analysis.

The remaining studies were non randomised designs, and are therefore open to selection bias. Each study had individual problems that could have an effect on the internal validity of the study (see Table 5, page 33 & Table 6, page 35) therefore the results of this review should be treated with caution.

6.6.2 Cluster designs

All of the interventions included in this review were given at the cluster level (i.e. at classroom or institutional level). This has implications on how the study is conducted and how the data is analysed. In cluster randomised studies it is the clusters not the individuals who are the unit of randomisation. Whilst the outcomes are assessed on individuals within the cluster, the effects of the cluster must be incorporated into the analysis. This is done by modelling or incorporating the ICC when analysing individual data. Data from clusters not analysed in this way can result in an overestimate of the effect. This is because clusters exert an effect on the behaviour on the individuals within them, making individuals within clusters more alike than individuals not within the clusters. In this review it would be likely that teacher behaviour, group conformity, teacher/child ratio[72] and the level of infection within the clusters would play a key role determining the cluster make up.

To allow for this variation between the cluster make up there should be sufficient number of clusters within the study. Unfortunately most of the hand hygiene studies had small numbers of clusters with the smallest study Niffengger[72] only including two clusters. A study with only two clusters equates to a non cluster study having just two participants. This situation excludes replication within the study and any result may simply be due to the natural variation between the two clusters in the absence of an intervention.[69]

The degree of alikeness within the clusters is also determined by the size of the cluster and their location.[69] Clusters at the classroom level within this review would be more alike than clusters at the level of the institution. There were seven studies with clusters at the classroom level and five studies where clusters were at the level of the institution (school or day care centre), therefore a higher ICC would be more likely required at the classroom level. By taking into account the type of cluster within the analysis and adapting the ICC accordingly it would be possible to cross compare the results within the review. Unfortunately, ICCs were rarely used within the data analysis. The sensitivity analysis undertaken in this review demonstrates the importance of accounting for cluster in the analysis (see section 3.2.4, page 36).

Whilst information regarding the size of the clusters was given, only one study[72] described the stability of the clusters, i.e. how many children left and joined the clusters during the study. New children may be more prone to infections in an established group or may bring new infections into the group. If the level of movement was high, this may have affected the groups. In the case of Niffenegger and colleagues[72] the control group was the most stable cluster.

6.6.3 Compliance

Whilst lack of compliance caused problems for individual studies, particularly in validating their data analysis,[70] it also suggests that this type of intervention is very difficult to instigate. Compliance appeared to be improved where there was a higher ratio of teachers to students[72,80]). Other studies analysed their data according to the degree of compliance. [76,81,82] They found that the intervention was most effective in reducing infections in the most compliant groups and least effective in the least compliant groups. Related to compliance is duration of effect, particularly in studies that had educational elements in them. None of the studies measured long-term effect, and all of the studies were of short duration.

6.6.4 Seasonality

Infections such as colds and influenza are prone to seasonality. Particularly for the studies that used a crossover design, this may have had an effect on the incidence of respiratory infections.

6.6.5 Funding sources

Two studies had authors from industry[70,76] and three studies had products donated from industry.[71,74,79] The studies with author involvement were well designed studies, with large sample sizes compared to most of the studies without industry involvement. The effect sizes particularly the study by Hammond and colleagues[76] are more conservative than in studies without industry involvement.

6.7 Cost Effectiveness

6.7.1 Publications

Two economic evaluations[74,86] and two cost surveys were identified.[89,90] Both economic evaluations were from a USA perspective. One looked at the effect of a multi-component hygiene intervention in day care taken from a societal perspective. This included cost of care of the child at home, and was made up of parental working days lost. The other economic evaluation looked at the costs of teacher time in coaching children who were absent. Costs identified in the cost surveys, included health service costs, costs borne by parents such as work time lost, and also time spent seeking health care and cost of OTC medicines.

The range of costs included in these studies highlight the complexity associated with illness in children. As well as affecting health services, it also affects educational systems and community and family life. When considering costs the most appropriate perspective in this case would be societal. It would need to be tailored to take into account recent UK initiatives such as NHS direct, NHS walk in centres and recent school based initiatives such as the healthy schools programme.

6.7.2 Birmingham model

Because previous economic evaluations have been based in the USA, ideally this health technology assessment should have incorporated an economic model to fully assess the impact of simple hygiene interventions in the West Midlands. Whilst it has been possible to suggest a model layout, it was not possible to populate the model with the data found. The effectiveness estimates have problems as described above, so to include them in a model would lead to spurious cost estimates. In addition more primary research is needed to properly assess UK costs.

6.7.3 NHS perspectives

The costs associated with respiratory and GI infections in children just from the NHS perspective are enormous, with the bill from GP consultations alone estimated at £757 million per annum. If these costs can be reduced by even 1% this would represent a massive saving. The cost of the intervention would be borne by the education system and the beneficiaries would be the health care system and families. This would need to be considered if interventions are introduced that could reduce infections in children.

6.8 Review Limitations

As with all systematic reviews, there may have been studies that were not identified, particularly as much of the research was not published in mainstream journals. Much of the information required to populate an economic model may be in the education literature, which was not systematically searched. Not undertaking a meta-analysis could also be seen as a limitation. Differences in population, differences in the comprehensiveness of the interventions and differences in definitions of outcome measures made it difficult to compare the results between studies quantitatively and a meta-analysis with this amount of clinical heterogeneity would have probably been inappropriate.

6.9 Recommendation for Further Research

6.9.1 Future primary studies

Four studies have shown that it is possible to design a randomised control trial in this area of research and that when using cleaning products such as hand sanitizers it is even possible to introduce a placebo. By the nature of the intervention the design would be a cluster trial and care should be taken during the planning of the trial that adequate numbers of clusters are recruited and that the cluster design is factored into the analysis (Appendix 2, page 64).

Only one study investigated handwashing. Therefore there is scope for further studies to investigate this basic intervention. There is also further scope to investigate elements of the multi-component studies such as surface or fomite cleaning, none of which were investigated singly.

In future studies care should be taken when considering outcome measures. Whilst absenteeism data is the most practical to collect, its usefulness as a proxy for illness needs to be considered. Methods of data collection should also be very carefully considered, and should ideally be undertaken by staff who do not know the treatment allocations.

The studies in this review did not undertake adequate follow up to investigate the sustainability of any effects. Further investigation regarding issues of compliance would also be a useful outcome to measure in future studies. Reasons for the differing levels of compliance within the studies such as lack of handwashing opportunities or facilities may well be a useful avenue of exploration.

Future studies also need to improve reporting procedures. There has been a recent Consort statement regarding the reporting of cluster studies[92] which recommends that the level of inference (i.e. cluster or individual) should be explicitly stated in all parts of the study report. Without knowing the inference level, interpreting results is difficult. Within the studies included in this review, reporting of basic information such as population details (both at cluster and individual level) was very poor. This makes the generalisability of findings problematical.

6.9.2 Economic analysis
Further research is required into the costs associated with respiratory and GI infections, particularly from a societal perspective, including health service and educational costs.

6.9.3 Secondary research methods
Undertaking this review highlighted the need to develop review methods for cluster studies. Particular areas of concern were lack of validated quality assessments for cluster studies, lack of accessible information concerning data analysis of cluster studies, and difficulties in reporting studies that had multiple levels i.e. cluster and individual levels. Further research is recommended in this area.

7 REVIEW CONCLUSIONS

7.1 Effectiveness Review

A total of 12 studies met the inclusion criteria. Of these, eight investigated hand hygiene interventions (i.e. handwashing, hand sanitizer use and education) and four investigated multi-component hygiene interventions.The results of five studies suggest that hand hygiene interventions can reduce sickness related absenteeism substantially, particularly in children at primary school and thus by proxy reduce respiratory and gastrointestinal infections. When measured directly, one multi-component hygiene intervention study found a reduction in GI infections in pre-school children. However, these findings are undermined by methodological problems within the studies, which seriously reduce the validity of the results. Clustering effects must be considered when quality is assessed. Accounting for cluster in sensitivity analyses, the results of four studies were not found to be statistically significant, thus diminishing the confidence that the observed results could not have occurred by chance. This inability to demonstrate clear benefit may be caused more by the difficulty in conducting good quality research in this area, rather than the ineffectiveness of simple hygiene interventions *per se*. The studies in this review can offer insight on how confounding factors can influence results and how difficult it is to evaluate community interventions of this nature. Future research should include better quality studies with more appropriate analysis of the results.

7.2 Cost Effectiveness Review and Model

Two previous economic analyses and two cost surveys were identified. The economic analyses found that simple interventions such as multi-component hygiene regimens were cost effective in societal and educational terms but both were based in the USA. The two cost surveys provided cost information that could potentially be used to populate a model. However, the children within the surveys included infants under 2 years of age, which is outside the age group under study in this review, therefore the survey results, whilst of interest, are not directly relevant to the population of this review. A Birmingham model was developed but due to lack of robust data to populate it, a simulation only was performed. The model did suggest that the cost effectiveness of hand washing is sensitive not only to the effectiveness of hand washing but also the cost difference between intervention and comparator. The results also suggested that hand sanitizer may be more cost effective than scheduled hand washing. However, due to lack of costs and the lack of good quality studies as mentioned above, these results are tentative at best. Further primary research with a UK perspective is needed.

Appendix 1 Survey of Local Healthy Schools Programme Co-ordinators

Programme Contacts – West Midlands Region January 2006

In January 2005 the thirteen Local Healthy Schools Programme Contacts in the West Midlands Region were contacted for information regarding hand hygiene interventions in the Region. The following information was requested:

I am a researcher in the Department of Public Health at the University of Birmingham, presently undertaking a systematic review looking at whether simple hygiene interventions (e.g. hand washing, using hand sanitizers, hygiene education), are effective in preventing common infections such as colds, influenza and diarrhoea. Could you tell me:

1) *Are any of these interventions already in place in the schools that you are involved with?*

2) *If so what effect do you think they have had?*
3) *If not, do you think simple hygiene interventions should be part of the school curriculum?*

Selection of Replies

“We have a machine for checking for 'clean hands' and many schools do work on hygiene but it is non-statutory and a choice for the school. Personally I think it is crucial and have done work with nurses in a village school in Africa where this is what parents and children were taught and resources put into place for soap and water to be available for children when they went to the toilet during the school day. Clearly in those conditions there was a massive effect.”
“Through use of the health related behaviour questionnaire we discovered that hand washing was poor after using the toilet, particularly in boys and that this poor behaviour increased as they became older. Whilst younger children are encouraged to wash their hands prior to eating this happens less/becomes more difficult to manage when children are coming to eat at different times from a variety of activities. Talking to schools the issue of soap was a concern: misuse/lack of/ messy looking bars after some use, poor hand drying facilities. I discussed with infection control and ran a pilot during one term (6 schools) - installing hand washing dispensers and providing frothy soap and encouraged staff to promote hand washing. We did a small evaluation, which showed that hand washing had increased but it was difficult to identify as to whether this had an impact on non attendance in relation to chest infection or gastro-intestinal infections. Unless the basic practical facilities are in place any hand hygiene messages through the curriculum will be lost.”
“Unfortunately this is not the type of data we collect from schools so I am unable to help you directly. You could possibly contact the schools nursing service who might be able to help. The only place where it might be included within our remit of work would be within early years sex and relationships education/science curriculum - the bit about passing on infections etc.”
Response from a school nurse. “School nurses have traditionally taught hand washing in reception and KS1 and briefly during puberty talks. I have worked with nurses doing a whole school approach unfortunately time is the issue.”

Appendix 2 Cluster Trials Theory

1 Correlation and contamination

The clustering of subjects into groups can lead to two major effects: correlation and contamination. Correlation within clusters may affect the results of individually randomized trials and cluster randomized trials differently. Contamination leads to the attenuation of the treatment effect because the control group and intervention group are more alike. The result is a reduced ability to detect an effect. [69, 93, 94, 95, 96, 97,]

2 Individually randomized trials and cluster randomized trials

Assuming positive correlation, subjects within clusters will be more like each other than subjects in other clusters. [93]

If all the intervention subjects and all the control subjects are pooled and are compared, without consideration of clustering, the variance due to differences between clusters is mixed in with variation between subjects within clusters. This usually results in unnecessarily large standard deviations, larger p-values, wider confidence intervals, and false negative results. Accounting for clustering can remove a significant source of variance and create more precise estimates. [93]

In cluster randomized trials, failing to account for clustering may even lead to false positive results with erroneously small p-values. In this case, each cluster has either intervention subjects or control subjects but not both. Comparing intervention to control subjects therefore requires comparisons across clusters, and the variance due to differences between clusters contributes to the variance of the estimates. Ignoring clustering in the analysis will mix cluster variance with variance between subjects within clusters and lead to an underestimate of the overall variance, with inappropriately small p-values and narrow confidence intervals. [93]

3 Design and analysis of cluster randomised trials

3.1 Design effect

Applying standard sample size formulae to cluster randomised trials can lead to an underestimation of the required sample size. For completely randomised cluster design, we multiply standard sample size estimates by a design effect. There are two components of variance: within-cluster variance S_w^2, and between-cluster variance S_b^2. Intra-cluster correlation coefficient $r = S_b^2 /$ ($S_b^2 + S_w^2$). The correlation coefficient can be obtained from previously published studies or from the analysis of pilot data. The design effect D is defined as: $1+(m-1)r$, m is the average number of individuals within clusters. [69, 93]

3.2 Handling correlation

It is important to account for correlation within clusters in cluster randomized trials otherwise misleading conclusions may be drawn. There are two overall approaches to the analysis: cluster-level analyses and individual-level analyses that account for clustering.[93]

Cluster-level analyses aggregate the individual observations using cluster means, proportions, or log odds, resulting in a single value per cluster. Standard statistical methods are then applied. Although cluster-level analyses address the problem of correlation within clusters, individual-level covariates cannot be analysed because the data have been aggregated.[93]

3.2.1 Cluster-level analysis

The standard two-sample t-test can be used to test whether the difference between the average values of the outcome in the intervention and control groups is statistically significant. The underlying assumptions are that the cluster-specific outcomes are normally distributed with equal variances. Simulation research has shown that the t-test is remarkably robust to violations of the underlying assumptions. A non-parametric method, Mann-Whitney U-test can be used without making any assumptions about the distribution of the outcome. [69,93]

3.2.2 Individual-level analysis

Individual-level analyses preserve the individual observations but still account for the correlation within clusters. The adjusted chi-squared approach, random effects models and generalized estimating equations are commonly used. Individual-level analyses can be applied to any of the randomized cluster designs.[69]

The adjusted chi-squared approach introduces clustering correction factors into the standard Pearson chi-squared test. The random effects model is a generalized linear mixed model, in which clustering is considered to be a random effects variable. Generalized estimating equations can be used as an extension of standard logistic regression that adjusts for the effect of clustering, and it does not require parametric assumptions.[69,93]

Appendix 3 Protocol

Simple interventions to prevent respiratory and gastrointestinal infections in children in day care or school settings

Primary Aim

To find evidence to support the hypothesis that simple hygiene interventions are effective in reducing infection in children in day care settings and schools.

Secondary Aim

To inform further primary research, particularly in areas of study design, intervention and outcome measures.

Methods

Systematic review methods will be employed.

Search Strategy

Electronic databases: MEDLINE, EMBASE, Science Citation Index, CINAHL, Cochrane Library, and National Research Register.
Citation lists from all identified reviews and included primary studies will be searched.
No language restrictions will be applied.
No date restrictions will be applied.

Search Terms

Start with settings, to be inclusive rather than exclusive. Predicted difficulty of inadequate indexing in this area.

Population	General population of children. Aged from 2 to 11 years old. Sub – group – children aged 3 to 5 years old.
Settings	Schools, reception class, day care centres, play groups, nurseries, crèches.
Country	Only include studies from countries where the childcare setting would be comparable to UK practice.

Interventions

Include

Primary interventions
Simple hygiene interventions that the children undertake to prevent the spread of infection e.g. hand washing, toilet use, and tissue disposal.
Secondary interventions

Hygiene policy of the school.

Exclude
Food handling hygiene measures from canteen staff.
Health education delivery techniques.

Outcomes
Primary outcomes
Reduction in gastrointestinal infections
Includes bacterial, viral and protozoan pathogens
Reduction in respiratory infections
Includes colds, influenza and influenza like illnesses
Absenteeism
Secondary Outcomes
If mentioned in the paper, include teacher and parental infections as above.

Study design
All included studies must have a comparison practice.
Ideal design would be RCT with cluster randomisation. However other designs with comparator practice will be included.

Exclude studies with no comparator e.g. cross sectional survey.
Exclude studies where comparator = home care.
Exclude before and after designs – as may have a problem of temporality.

Quality Measures

Not to exclude studies on quality, but do a sensitivity analysis.
Suggest Jadad scale; adapt it if there are non-RCT papers.

Study Identification

One reviewer (JW) will assess papers for subject relevance using the title and where available the abstract. Completely inappropriate papers will be excluded. The modified lists will then be independently assessed, by two reviewers (JW, and CM) using the inclusion/exclusion criteria. Where disagreements exist a third reviewer will be asked to decide on inclusion. Full paper copies of included and possibly included studies will be obtained for detailed examination. Foreign language publications will be screened using English abstracts where available. Translations will be obtained where necessary and where possible within the resources and timeframe of the project.

Data Extraction Strategy

Data extraction will be carried out by one reviewer (JW) using a standardised data extraction form, then checked by a second reviewer using independent sampling.

Methods of Analysis/Synthesis

It is envisaged that the studies will be heterogeneous therefore it may not be possible to pool results. A qualitative narrative assessment is likely to be most informative.

Terms that could be used to search for studies used to develop search strategy.

Setting	Population	Intervention	Outcomes	Study design	Misc.
Preschool	Child	Hand washing	Absenteeism	Comparative study	School nursing
Education	Human	Health education	Gastrointestinal diseases	RCT	Sanitation
Schools	Students	Hand	Intestinal diseases	Controlled trial	Transmission
Community	Parents	Gels	Diarrhoea	Cluster randomisation	Family
Primary school	Teachers		Gastroenteritis	Intervention study	Hygiene
Nurseries	Family		Respiratory tract diseases/infections		Hygiene infection control
Child care			Respiration disorders		Teaching
Infant care			Bacterial infections		Bacteria
Child day care centres			Infection		Communicable diseases
School children			Streptococcal infections		Communicable disease control
Nursery school children			Streptococcus		Community – Acquired Infections control
Reception class			Incidence		Health behaviour
Play groups			Prevention		Toilet facilities
Crèche			Infection control		Faecal contamination
			Virus diseases		Microbiology
			Acute disease		Environmental microbiology
			Common cold		Epidemiology
			Otitis media		Learning
			Pneumonia		Reward
			Cross infection		Disease outbreaks
			Morbidity		Transmission
			Cytomegalovirus Infections		Disinfection
			Campylobacter		Primary prevention
			Enterovirus		
			Respiratory Syncytial Viruses		
			Respirovirus		
			Influenza		
			Rhinovirus		
			Aseptic nose wiping technique		

Appendix 4 Search strategies.

Database: Ovid MEDLINE(R) <1966 to 29-7-05>
Search Strategy:
----
1 handwashing.mp. or HANDWASHING/ (2526)
2 hygiene.mp. or HYGIENE/ (29486)
3 soap.mp. or SOAPS/ (2233)
4 Detergents/ or Disinfectants/ or Disinfection/ or surface disinfection.mp. or Infection Control/ (33533)
5 health education.mp. or Health Education/ (47401)
6 Anti-Bacterial Agents/ or Anti-Infective Agents/ or antimicrobial.mp. (164848)
7 infection control.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (16122)
8 1 or 2 or 3 or 4 or 5 or 6 or 7 (274956)
9 SCHOOLS/ or school$.mp. or SCHOOLS, NURSERY/ (119778)
10 Child, Preschool/ or Child Day Care Centers/ or child day care.mp. (536888)
11 NURSERIES/ or nursery.mp. (4797)
12 creche$.mp. (221)
13 kindergarten$.mp. (2019)
14 9 or 10 or 11or 12.mp. or 13 [mp=title, original title, abstract, name of substance word, subject heading word] (641391)
15 absenteeism.mp. or ABSENTEEISM/ (5672)
16 gastrointestinal diseases.mp. or Gastrointestinal Diseases/ (22069)
17 Diarrhea/ or diarrhoea.mp. (34757)
18 gastroenteritis.mp. or GASTROENTERITIS/ (10638)
19 respiratory tract disease$.mp. or Respiratory Tract Diseases/ (13909)
20 respiratory tract infection$.mp. or Respiratory Tract Infections/ (25377)
21 15 or 16 or 17 or 18 or 19 or (respiratory tract infection$ or Respiratory Tract Infections).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (106901)
22 infection.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (464943)
23 8 and 14 and 22 (4492)
24 randomized controlled trial.pt. (203054)
25 controlled clinical trial.pt. (68748)
26 randomized controlled trials.sh. (38090)
27 random allocation.sh. (53343)
28 double blind method.sh. (82188)
29 single-blind method.sh. (9079)
30 or/24-29 (345457)
31 (animals not human).sh. (3764342)
32 30 not 31 (318269)
33 clinical trial.pt. (409385)
34 exp clinical trials/ (167347)
35 (clin$ adj25 trial$).ti,ab. (111403)
36 ((sing$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. (81548)

37 ((sing$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. (81548)
38 placebo.sh. (0)
39 placebo.mp. (89238)
40 placebo$.ti,ab. (89420)
41 random$.ti,ab. (312410)
42 research design.sh. (41049)
43 cohort stud$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (66872)
44 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 (4473275)
45 44 and 23 (846)
46 from 43 keep 1-395 (395)
47 from 46 keep 1-395 (395)

Database: EMBASE <1980 to 29-7-05>
Search Strategy:
----
1 handwashing.mp. or HANDWASHING/ (1910)
2 hygiene.mp. or HYGIENE/ (17973)
3 soap.mp. or SOAPS/ (1575)
4 Detergents/ or Disinfectants/ or Disinfection/ or surface disinfection.mp. or Infection Control/ (30619)
5 health education.mp. or Health Education/ (22296)
6 Anti-Bacterial Agents/ or Anti-Infective Agents/ or antimicrobial.mp. (60070)
7 infection control.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (19457)
8 1 or 2 or 3 or 4 or 5 or 6 or 7 (128600)
9 SCHOOLS/ or school$.mp. or SCHOOLS, NURSERY/ (158600)
10 Child, Preschool/ or Child Day Care Centers/ or child day care.mp. (88268)
11 NURSERIES/ or nursery.mp. (2458)
12 creche$.mp. (139)
13 kindergarten$.mp. (1067)
14 9 or 10 or 11or 12.mp. or 13 [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (216978)
15 absenteeism.mp. or ABSENTEEISM/ (4572)
16 gastrointestinal diseases.mp. or Gastrointestinal Diseases/ (12187)
17 Diarrhea/ or diarrhoea.mp. (55133)
18 gastroenteritis.mp. or GASTROENTERITIS/ (8018)
19 respiratory tract disease$.mp. or Respiratory Tract Diseases/ (13788)
20 respiratory tract infection$.mp. or Respiratory Tract Infections/ (25752)
21 infection.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (561649)
22 15 or 16 or 17 or 18 or 19 or 20 or 21 (628866)

23 randomized controlled trial/ (96871)
24 exp clinical trial/ (352494)
25 placebo/ (78929)
26 single blind procedure/ (5394)
27 (control$ adj (trial$ or stud$ or evaluation$ or experiment$)).mp. (2032882)
28 (placebo$ or matched communities or matched schools or matched populations).mp. (124082)
29 (comparison group$ or control group$).mp. (122495)
30 ((singl$ or doubl$ or trebl$) adj5 (blind$ or mask$)).mp. (95217)
31 (clinical trial$ or random$).mp. (572216)
32 (quasiexperimental or quasi experimental or pseudo experimental).mp. (1178)
33 matched pairs.mp. (1729)
34 cohort stud$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (21267)
35 or/24-34 (2399332)
36 8 and 14 and 22 and 35 (747)
37 from 36 keep 1-747 (747)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to 29-7-05>

----

1 handwashing.mp. or HANDWASHING/ (1688)
2 hygiene.mp. or HYGIENE/ (3824)
3 soap.mp. or SOAPS/ (425)
4 Detergents/ or Disinfectants/ or Disinfection/ or surface disinfection.mp. or Infection Control/ (10007)
5 health education.mp. or Health Education/ (31846)
6 Anti-Bacterial Agents/ or Anti-Infective Agents/ or antimicrobial.mp. (1733)
7 infection control.mp. [mp=title, subject heading word, abstract, instrumentation] (9589)
8 1 or 2 or 3 or 4 or 5 or 6 or 7 (48312)
9 SCHOOLS/ or school$.mp. or SCHOOLS, NURSERY/ (29867)
10 Child, Preschool/ or Child Day Care Centers/ or child day care.mp. (35262)
11 NURSERIES/ or nursery.mp. (654)
12 creche$.mp. (9)
13 kindergarten$.mp. (331)
14 9 or 10 or 11or 12.mp. or 13 [mp=title, subject heading word, abstract, instrumentation] (63074)
15 absenteeism.mp. or ABSENTEEISM/ (1039)
16 gastrointestinal diseases.mp. or Gastrointestinal Diseases/ (1131)
17 Diarrhea/ or diarrhoea.mp. (1765)
18 gastroenteritis.mp. or GASTROENTERITIS/ (446)
19 respiratory tract disease$.mp. or Respiratory Tract Diseases/ (1304)
20 respiratory tract infection$.mp. or Respiratory Tract Infections/ (1684)

21 infection.mp. [mp=title, subject heading word, abstract, instrumentation] (27949)
22 15 or 16 or 17 or 18 or 19 or 20 or 21 (33282)
23 exp clinical trials/ (31727)
24 Clinical trial.pt. (14365)
25 (clinic$ adj trial$1).tw. (7407)
26 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$3 or mask$3)).tw. (4504)
27 Randomi?ed control$ trial$.tw. (6131)
28 Random assignment/ (10356)
29 Random$ allocat$.tw. (821)
30 Placebo$.tw. (6244)
31 Placebos/ (2765)
32 Quantitative studies/ (2319)
33 Allocat$ random$.tw. (75)
34 or/23-33 (44558)
35 8 and 14 and 22 and 34 (32)
36 from 35 keep 1-32 (32)

Appendix 5 Excluded studies.

Study	**Reason for exclusion.**
Butz,A.M., E.Larson, P.Fosarelli, and R.Yolken. 1990. "Occurrence of infectious symptoms in children in day care homes." *American Journal of Infection Control*. 18:347-353.	Wrong population and setting
Barker,R.N. and D.P.Thomas. 1994. "A practical intervention to address ear and lung disease in Aboriginal primary school children of central Australia." *Journal of Paediatrics & Child Health*. 30.	Before and after study.
Barros,A.J.D., D.A.Ross, W.V.C.Fonseca, L.A.Williams, and D.C.Moreira-Filho. 1999. "Preventing acute respiratory infections and diarrhoea in child care centres." *Acta Paediatrica*. . 88.	Wrong age group.
Bartlett,A.V., B.A.Jarvis, V.Ross, T.M.Katz, M.A.Dalia, S.J.Englender, and L.J.Anderson. 1988. "Diarrheal illness among infants and toddlers in day care centers: Effects of active surveillance and staff training without subsequent monitoring." *American Journal of Epidemiology*. . 127.	Wrong age group (<2 yrs).
Black,R.E., A.C.Dykes, K.E.Anderson, J.G.Wells, S.P.Sinclair, G.W.Gary, Jr., M.H.Hatch, and E.J.Gangarosa. 1981. "Handwashing to prevent diarrhea in day-care centers." *Am J Epidemiol.* 113:445-451. Found via handsearching.	Wrong age group (<2 yrs).
Carabin, H., T.W.Gyorkos, J.C.Soto, L.Joseph, P.Payment, and J.P.Collet. 1999. "Effectiveness of a training program in reducing infections in toddlers attending day care centers. [see comment]." *Epidemiology*. 10:219-227.	Wrong age group (< 2 yrs).
Colombet,G., J.Croize, P.Pavese, V.Chanteperdrix, and J.P.Stahl. 2003. "Screening bacterial hand carriage in schools. A tool for hygiene education." *Medecine et Maladies Infectieuses*. . 33:01.	Not a clinical outcome (bacterial load).
Coulthard,M.G. and C.M.Mellis. 2004. "Does probiotic milk prevent infections in children attending daycare centres?" *Medical Journal of Australia*. . 181:15.	Not hygiene intervention.
Early,E., K.Battle, E.Cantwell, J.English, J.E.Lavin, and E.Larson. 1998. "Effect of several interventions on the frequency of handwashing among elementary public school children." *AJIC: American Journal of Infection Control*. 26.	Not clinical outcome.
Early,E., K.Battle, E.Cantwell, J.English, J.E.Lavin, and E.Larson. 1998. "Effect of several interventions on the frequency of handwashing among elementary public school children." *AJIC: American Journal of Infection Control*. 26.	Not clinical outcome.
Ferguson,J.K., L.R.Jorm, C.D.Allen, P.K.Whitehead, and G.L.Gilbert. 1995. "Prospective study of diarrhoeal outbreaks in child long-daycare centres in western Sydney." *Medical Journal of Australia*. . 163.	Wrong study design (case series).
Hatakka,K., E.Savilahti, A.Ponka, J.H.Meurman, T.Poussa, L.Nase, M.Saxelin, and R.Korpela. 2001. "Effect of long term consumption of probiotic milk on infections in children attending day care centres: double blind, randomised trial.[see comment]." *BMJ*. 322:1327.	Not hygiene intervention (probiotic)
Kaltenthaler,E.C., A.M.Elsworth, M.S.Schweiger, D.D.Mara, and D.A.Braunholtz. 1995. "Faecal contamination on children's hands and environmental surfaces in primary schools in Leeds." *Epidemiology & Infection*. . 115.	Not clinical outcome.
Koefoed,B.G., A.M.Nielsen, and L.M.Keiding. 2002. "The impact of selected environmental factors on the morbidity of children in day-care centres." *Ugeskrift for*	Review.

Study	Reason for exclusion.
Laeger. . 164:02.	
Ladegaard,M.B. and V.Stage. 1999. "[Hand-hygiene and sickness among small children attending day care centers. An intervention study]. [Danish]." *Ugeskrift for Laeger*. 161:4396-4400.	Wrong age group (include <2yrs).
Mygind,O., T.Ronne, A.Soe, C.H.Wachmann, and P.Ricks. 1913. "Comparative intervention study among Danish daycare children: the effect on illness of time spent outdoors." *Scandinavian Journal of Public Health*. 2003; 31:439-443.	Not hygiene intervention .
Shaughnessy,A. 2002. "Can the use of a hand sanitizer by children decrease absenteeism from school due to illness?... commentary on Dyer DL, Shinder A, Shinder F. Alcohol-free instant hand sanitizer reduces elementary school illness absenteeism. FAM MED 2000;32:633-8." *Evidence-Based Practice*. 2001 Jan; 4:10.	Not a study, commentary on the Dyer study.
Soto,J.C., M.Guy, D.Deshaies, L.Durand, J.Gratton, and L.Belanger. 1994. "A community-health approach for infection control in day-care centers." *Pediatrics*. Vol. 94.	Before and after study.
White,C., R.Kolble, R.Carlson, N.Lipson, M.Dolan, Y.Ali, and M.Cline. 2003. "The effect of hand hygiene on illness rate among students in university residence halls." *AJIC: American Journal of Infection Control*. 31.	Wrong population (university students).

Howard, D.H., McGowan, J.E., 2004 “Initial and follow-up costs of treatment outcomes for children with respiratory infections. Pediatrics. Vol 113. No. 5.	Cost survey – includes antibiotic use only N/A.
National Patient Safety Agency, “The economic case – Implementing near-patient alcohol hand rub in your trust”. Clean your hands campaign - http://www.npsa.nhs.uk/cleanyourhands [accessed 3/2/06]	Relating to hospital infections.

Appendix 6 Data extraction form

Data extraction – simple interventions to prevent infections in schools

Extractor: Date:

Paper details

Paper title:	
First Author:	
Journal etc	
Publication year	
Authors contact address (if available)	
Full text article or only published as an abstract	
Does the trial meet all inclusion criteria (see separate abstract sheet)	
Number of trials included in this paper: (if more than one, complete separate extraction forms for each, and add letters A, B, C, etc to the paper name)	
Papers of other trials with which this may link: (if other papers report further results of this trial, incorporate them onto this form, and note what has been here)	
Funding:	

Aim of Study

Study Design

	Yes	Describe
Cluster randomised		
Randomised		
Quasi randomised		
Cross over		
Cohort		
Other		

Population/setting

{describe}	Intervention {}	Control {}	Intervention {}
Please give numbers and percentages	Group 1 [n=]	Group [n=]	Group 2 [n=]
Type of school/child care centre			

Age of children (state if mean; median; range)			
Gender of children M / F			/
Location of school (e.g. Birmingham, England)			

Intervention

	Yes	Describe
Hand washing/disinfectant		
Toilet use		
Tissue disposal		
Surface disinfect		
Hygiene policy		
Alteration in facilities		
Other		

Control (exclude if home care)

	Yes	Describe
No intervention		
Other interventions		
Different policy implementation		

Duration of intervention	
Duration of follow up	
Total length of trial	
Dates when trial commenced	
Dates when trial completed	
Data collected – daily, weekly, monthly?	

Outcomes Sought

Primary outcomes	Yes	Definition given in paper
1. Gastrointestinal infections defined symptomatically or by laboratory testing		
2. Respiratory infections		
3. Asthma		
4. Absenteeism		
5. Other		

Statistical analysis

Describe

Results

	Intervention	Control
Number of schools enrolled		
Number of schools in final analysis		

Number of classrooms per school		
Number of classrooms per school in final analysis		
Number of children enrolled		
Number of children in final analysis		

Event rate

	Intervention Number of events (variance)	Control Number of events (variance)	Difference (variance)
1. Gastrointestinal infections.			
2. Respiratory infections			
3. Asthma			
4. Absenteeism			
5. Other			

Analysis – seek crude data where possible i.e. number of events, number of student days lost.

Study Quality

	Yes	No	Unclear	Comments
SELECTION BIAS				
Treatment allocation				
Randomisation				
1. Was the trial described as randomised?				
2. Was allocation truly random? Yes: random numbers, coin toss, shuffle etc. No: by pt number, dob, alternate allocation Unclear: method not stated or unclear				
Concealment of allocation				
3. Was the treatment allocation concealed? Yes: central allocation at trials office or pharmacy, sequentially numbered or coded vials, other methods where the trialist allocating treatment could not be aware of the treatment. No: allocation was alternate, or based on information e.g. dob already known to the trialist Unclear: insufficient information given.				
Similarity of groups				
4. Were the pts characteristics at baseline similar in all groups?				
PERFORMANCE BIAS				
Masking/blinding				
5. Was the trial described as double blind?				
6. Was the treatment allocation masked from participants? (either stated explicitly or an identical placebo is used)				
7. Was treatment allocation masked from investigators?				
8. Was treatment allocation masked from outcome				

assessors?				
ATTRITION BIAS				
Completeness of trial				
9. Were the number of withdrawals, dropouts and lost to follow up in each group stated? NB: yes if there have not been any drop outs or lost to follow up				
10. Were the drop out rates similar in both groups?				
11. Was an intention to treat analysis done?				
12. If not ITT were there less than 10% of patients per study arm excluded?				
OTHER				
13. Was the appropriate analysis undertaken on the data, particularly if cluster randomised?				

Appendix 7 Outcome definitions

HAND HYGIENE TRIALS

Study ID	Definition of outcome measure as given in the study report.
A. Scheduled handwashing.	
Master 1997[75]	**Absence** – parents were telephoned by investigators to determine the nature of any illness. Illnesses included = abdominal pain, diarrhoea, vomiting. cough, sneeze, sinus trouble, bronchitis, fever alone, pink eye, headache, mononucleosis, and acute exacerbation of asthma.
B. Scheduled use of hand sanitizer.	
White 2001[70]	**Absence -** defined as gastrointestinal absences (vomiting, abdominal pain, diarrhoea), or respiratory related absences (cough, sneezing, sinus trouble, bronchitis, fever alone, pink eye, headache, mononucleosis, acute exacerbation of asthma) or other (non communicable disease related absences – e.g. vacations, nontransmissible urinary tract infections, sprained or broken limbs)
Hammond 2000[76]	**Absence -** defined as the aggregate number of nonattending school days due to illness with illness defined as colds, flu, and gastrointestinal disease. Excluded were common infectious illnesses such as pink eye, abscesses, skin infections. Other types of absences such as doctors appointments, vacations, accident injuries were excluded.
Dyer 2000[77]	**Absence –** data collected by the teachers (information regarding the nature of the absence supplied by parents to the health secretary's office during the study). Absences were counted as GI (symptoms included vomiting, abdominal pain and diarrhoea), respiratory related (symptoms included cough, sneezing, sinus trouble, bronchitis, fever alone, pink eye, headache, mononucleaosis, acute exacerbation of asthma), or non-transmissible reasons (vacations, non transmissible UTI, sprained or broken limbs etc).
Ci. Hand hygiene - education	
Niffenegger 1997[72]	**Infections -** only the incidence of colds were reported in the results. Outcome assessment measure by the "Teacher Health Assessment Checklist" and "Child Health Assessment Checklist" filled out by the teachers and parents respectively.
Kimel 1996[73]	**Absence –** due to influenza like symptoms. Information from daily school absentee logs.
Cii. Education plus hand sanitizer.	
Guinan 2004[74]	**Absence -** defined as the number of episodes of illness per child per month. Illness was defined as an infectious process such as cold, flu and gastroenteritis. Excluded were personal situations e.g. longer vacation, or other health problems such as an injury.
Ciii. Education plus scheduled hand sanitizer.	
Morton 2004[71]	**Absences -** assessed according to respiration, GI, vacations, or non communicable diseases or injuries. (e.g. influenza (?), diarrhoea, nausea, vomiting, with or without fever, nasal congestion, cough, sore throat, with or without fever). Absences due to asthma excluded. Adverse effects – children in the experimental arm checked weekly by the school nurse for adverse effects such as roughness, redness, excoriation, in addition children were also encouraged to report any adverse affects.

MULTI-COMPONENT HYGIENE STUDIES

Study ID	Definition of outcome measure as given in the study report.
Roberts 2000 [81,82]	**Infections** Diarrhoea defined as 2 or more watery or unusually loose bowel motions in 24 hours. A new episode of diarrhoea was defined as the occurrence of diarrhoea after a period of 3 symptom free days. A diarrhoea episode was defined as the occurrence after a symptom free period of 7 days. Symptoms of upper respiratory illness elicited from the parents were: a runny nose, a blocked nose, and cough. A cold was defined as either 2 symptoms for 1 day or 1 of the respiratory symptoms for at least 2 consecutive days but did not includ 2 consecutive days of cough alone. A new episode of a cold was defined as the occurrence of respiratory symptoms after a period of 3 symptom free days.

Kotch 1994[79]	**Infections.** Diarrhoea defined as a report by parent of an unusually loose or watery stool. "Pure diarrhoea" – without respiratory symptoms "Severe pure diarrhoea" – five or more stools per day, plus fever and/or vomiting – also without respiratory symptoms. "All diarrhoea" = all episodes of diarrhoea symptoms with or without respiratory symptoms "All diarrhoea, severe" = all episodes of diarrhoea with severe symptoms. Respiratory symptoms include coughing, runny nose, wheezing or rattling in the chest, sore throat, or earache. "All respiratory" = all episodes with any respiratory symptoms with or without diarrhoeal symptoms "all respiratory severe" = all such respiratory episodes with fever.
Uhari 1999[80]	**Infections –** e.g. vomiting, diarrhoea, cough, fever (≥38C) earache, conjunctivitis Also measured were visits to the doctor, parental absenteeism from work, infections of personnel and compliance.
Ponka 2004[83]	**Absences -** data on absences due to infectious diseases recorded by the CCDCs included in the study. The CCDCs have reported absences by diagnosis to the health authorities using this method since the 1970s. Data for children over 3 yrs was collected separately by the CCDC personnel, with parents reporting reasons for absence.

Appendix 8 Detailed description of studies

HAND HYGIENE

Handwashing – specified times.

Number of studies
Only 1 study investigated the effect of applied handwashing.[75]

Study characteristics
This study by Master 1997[75] hypothesized that illness related absenteeism would be reduced if children washed their hands as specific times throughout the day. Specified handwashing times were on arrival at school, before eating lunch, after lunch, and after recess. The study involved 305 children attending an elementary school in Detroit, USA. The children were aged 5 to 12 years (kindergarten to fifth grade). The unit of cluster was at the classroom level, with 14 classrooms taking part in the study. Six classrooms received the intervention (143 children) and 8 classrooms were the control group (162 children). The study ran for a total of 37 days from 8th January 1996 to 29th February 1996.

Outcomes sought
Outcomes were measured from daily absence records, with the reason for absences determining the nature of the absence.

Study Quality
This is a non randomised controlled study. The paper states that classrooms were allocated the intervention and control "without formal randomisation" therefore the results are open to selection bias. In addition, it is not possible to check if the groups are balanced as no information was given describing the groups. The results do not take into account the cluster design of this study, which has the potential for an overestimation of the effect size.

Results
All illness absence: RR 0.75 (P=0.0193)
URTI illness related absence: RR 0.79 (P=0.0756)
GI illness related absence: RR 0.43 (P=0.0024)
Therefore there was a 25% reduction in illness related absenteeism, of this GI related absenteeism was statistically significantly reduced by 57% but URTI whilst being reduced by 21% did not reach statistical significance.

Comments
Applied handwashing at specified times was investigated by 1 study. This study used school soap and required the students to wash their hands at specified times, in addition to their regular handwashing practices (e.g. after using the toilet). The results suggest that this simple intervention effectively reduced illness related absenteeism, particularly absenteeism related to GI infections. However, due to several factors such as non randomised study

design and no adjustment for cluster in the analysis, this may be an over estimate of the effect.

HAND HYGIENE

Applied hand sanitizer – specified times.

Number of studies.
Three studies investigated the effects of applied hand sanitizer use at specific times. One was a cluster randomised controlled trial,[70] one was a matched pair
cluster study[76] and the third was a cross over study involving a single elementary school.[77]

White CG 2001[70]

Study characteristics.
Conducted in 3 elementary schools in California, USA, the trial ran from March to April 1999 for a total of 5 weeks. Children were aged between 5 and 12 years. Teachers were instructed to prompt children to use the hand sanitizer on entering the classroom, before and after eating, before leaving at the end of the school day, and after sneezing or coughing. In addition students were encouraged to wash hands with soap and water whenever necessary and possible through the day, although this was not prompted by teachers.

Outcomes sought.
Outcomes sought were GI or URTI illness related absences. The teachers collected absentee data, with parents providing details regarding the reason for absences.

Study Quality.
This was a randomised placebo controlled trial. Methods of randomisation are not stated. Little information except that age and sex were balanced between intervention and control groups was given. Blinding occurred as the control group used a placebo hand sanitizer. Unfortunately, despite the high methodological standard of this trial, the number of dropouts reduces the robustness of the results. A total of 72 classes were enrolled in the trial (1,626 children), but only 32 classes (16 active, 16 control – 769 children) were retained in the analysis. Classes were dropped from the analysis because of non-compliance with minimum adequate product use standards. The results were not analysed by cluster nor ITT. This could over estimate the effectiveness result.

Results.
All illness related absence RR = 0.67 (33% advantage over placebo).
URTI illness related absence RR = 0.69 (31% advantage over placebo).
GI illness related absence RR = 0.62 (38% advantage over placebo),
(no variance figures noted).

Adverse events – not reported.

Hammond B 2000[76]

Study Characteristics.

A total of 9 elementary schools were enrolled involving 6080 children (3075 intervention, 3005 control). Children from kindergarten to sixth grade were recruited. The hand sanitizer was an adjunct to usual handwashing practice. Children were instructed to use hand sanitizer on entering and leaving the classroom, first thing in the morning, before and after lunch, at recess, after using the toilets, before going home and after sneezing and coughing. The study commenced September 2000, and completed May 2001, running for a total length of 9 months.

Outcomes sought.

Outcomes sought were illness associated absenteeism, with illness defined as colds, influenza, and gastrointestinal infections. Absentee numbers were collected from school personnel who identified the reason for absence. In addition teacher absenteeism was monitored from the largest school district.

Study Quality.

Unfortunately the treatment was not allocated randomly, therefore there is the potential for selection bias to be present. The results have been analysed by cluster which is the correct analysis for this type of study. The authors suggest that the schools that had a statistically significant reduction in absenteeism were more compliant with the intervention. This was a matched pair design which has the advantage that a very tight and explicit balancing of potentially important prognostic factors at baseline can be achieved, which may enhance the credibility of the study conclusions.[69] However, this assumption requires that the matching factors are relevant prognostic factors to be matched and matching within cluster studies can be difficult to achieve in practice. Despite the large number of participants included in this study, this only accounts for 6 clusters, one of which was excluded from the analysis, therefore the power of the results are reduced.

Results.

"Overall percentage difference over control in reduction in absenteeism due to illness was 19.8% P<0.05". "Analysed by school the results were as follows: 3 schools had statistically significant reduced absenteeism (Cuyahoga Falls, Ohio (n=2576 [32.96% diff over control]), Athens, Ten (n=1272[19.07% diff over control), Hudson, Ohio (n= 818[32.96% diff over control) the school in Wilmington, Del (n=223), showed a 7.87% difference in absenteeism in the intervention group but this was not statistically significant. The fifth school Irvine, California (n = 1191), showed more absenteeism in the intervention group (-3.75%) but this was not significantly significant". One school district monitored teachers'absence. In the intervention group their was a reduction in teacher absenteeism of 10.1% statistically significant with a pooled 2 sample t test at $\alpha = 0.05$.

Adverse events – not reported.

Dyer DL 2000[77]

Study Characteristics
This was a cross over study involving a single elementary school in California, USA. Children were aged between 5 and 12 years. Fourteen classrooms took part, each averaging 30 children, in total 420 children were included in the study. The intervention was alcohol free instant hand sanitizer (Clean Hands®). The intervention groups were instructed to use the hand sanitizer immediately on entering the classroom, before eating, after sneezing and coughing, and after using the toilet. The control group were instructed to wash hands before eating, after visiting the toilet and as necessary throughout the day. The study ran from March to May 1998, giving a total length of 8 weeks plus 2 weeks in the middle for a washout period.

Outcomes sought
Outcomes sought were illness related absenteeism and adverse events. Illness was defined as GI, URTI and non infectious absences and adverse events were oedema, rash, erythema. The teachers collected absence data with information regarding the nature of the absence supplied by parents to the health secretary's office during the study.

Study Quality
This was not a randomised controlled study and therefore will be prone to selection bias. Other problems may be due to the cross over design. Cross-over designs rely on the assumption that there is no carry over effect i.e. that the estimated effects of intervention are independent of the order in which they are assigned. Within this study the cross over design could have had an effect that in that there may be an element of learning with the intervention group, therefore when they become controls they may be more conscious of ensuring their hands are clean even in the absence of hand sanitizer. In addition the results were analysed by cluster, therefore there may be an over estimation of the effect.

Results
Overall there was a 33.6% reduction in the illness related absences ($p<0.001$) in the intervention group compared to the control group.
Adverse events – no adverse events observed or reported during or following the study.

Education regarding hand hygiene

Number of studies

Four studies investigated the effects of education regarding hand hygiene. Two[72,73] just instigated education programs whereas 2[74, 71] also included hand sanitizer use. Three[72, 73,74] studies were non-randomised controlled studies, the fourth[71] used a cross over design.

Niffenegger 1997[72]

Study characteristics
Set in a child day care centre this study included children aged between 3 and 5 years old. The study was based in Northwest Indiana and involved 2 centres, 1 as the intervention (n=26 children) and 1 as the control (n=12). The intervention group received 3 days of instruction based on the "Hooray for Handwashing" program and washing posters were displayed near handwashing sinks as reminders of when and how to wash hands. Staff and children were also encouraged to wash their hands when they arrived at the centre also to "give their cough the elbow" a simple technique of lifting ones arm and sneezing into it rather than sneezing or coughing onto the hands. The control group undertook normal handwashing procedures and observation of the incidence of colds. The study ran for 21 weeks, with the intervention given throughout the whole period.

Outcomes sought
Incidence rates due to colds were sought. Outcomes were assessed weekly by the teachers and the childrens parents who used either the "Teacher Health Assessment Checklist" or the "Child Health Assessment Checklist" to record the incidence of colds amongst the children.

Quality assessment
This was a non randomised control study. It involved only 2 groups, which is the equivalent of a non cluster study with only 2 patients, which is a very weak study design. The results are also not analysed by cluster. In the analysis it is difficult to assess the results given in this paper because it is not clear from where the totals in the incidence data tables are derived. One presumes that these totals are the number of health assessment checks that were undertaken, however, the text states that more than 700 health assessments were undertaken from the intervention group and more than 400 health assessment checklists were completed in the control group. If this is the case then there must be missing data. In summary, there are many methodological problems with this study.

Results
Cold incidence - All wks combined = 0.99 (95% CI 0.76, 1.28).
Cold incidence - Wks 1 to 11 = RR 1.53 (95% CI 1.03, 2.29) favours control.
Cold incidence - Wks 12 to 21 = RR 0.68 (95% CI 0.47, 0.99) favours intervention.
Results calculated from data given in Table 1 and 2 of the paper.

Kimel 1996[73]

Study Characteristics
Set in an elementary school in Chicago, USA. Four kindergarten and 5 first grade classes were included. Higher numbers of children were included when compared to Niffenegger[72] (N = 112 (43 in kindergarten) intervention, 87 (43 in kindergarten) control. The education program involved a 30 minute presentation developed from materials from the Scrubby Bear Program 1985, and the Ivory Handwashing Program 1987. The presentation consisted of a 20

minute discussion followed by demonstrations. The study ran for a total of 4 months. Absenteeism was measured from school records.

<u>Outcomes sought</u>
Absence due to influenza like symptoms. Information from daily school absentee logs.

<u>Quality assessment</u>
This was a quasi controlled study, where the control group were comprised of the refusers. This is a very poor study design. In addition there seems to be a discrepancy regarding when the intervention was given, in that the results are given for December and January, but at this time 3 classes had yet to receive the intervention. Finally the study design was not analysed by cluster.

<u>Results</u>
The paper reports that that the daily number of absences over the study period was 1.5/87 for the intervention group and 4/112 for the control group. The authors state that the rate of absenteeism was approximately double in the control groups compared to the intervention groups and that this gave a Chi-squared value of 22.225, 1df, p=0.001. Therefore taken at face value this data suggests that handwashing has an effect in reducing absenteeism of influenza like illnesses. However, we have been unable to replicate these results, therefore caution should be exercised when interpreting these results.

Guinan M. 2004G[74]

<u>Study Characteristics</u>
This study investigated the effectiveness of a comprehensive handwashing progamme entitled "Buddies Handwashing Program" plus the use of a hand sanitizer on the rates of absenteeism. Set in an elementary school in Pennsylvania USA, 6 schools were asked to provide 2 test and 2 control classrooms from kindergarten to grade 3. Median cluster size was 15 (range 11 – 20 students), with 190 children in the study (145 intervention). The study ran from March to May 2000.

<u>Outcomes sought</u>
Absentee rates were measured. Data was collected monthly, with absenteeism defined as the number of absentee episodes due to infectious disease illness, such as cold, influenza and gastroenteritis.

<u>Quality Assessment</u>
The study was a non randomised controlled study. It was unclear if the groups were similar at baseline, although the discussion describes the groups as "homogenous student population (middle-class and upper class private school students)". The main total = 50.6% has been analysed individually, (the total is also incorrect – should be 49%), however, this paper does give the data by cluster in table 1, therefore theoretically it is possible for the data to be analysed by cluster (i.e. work out the means then divided by the total clusters i.e. 27).

Results
Total number of episodes of absenteeism over the 3 month study in the intervention group were 140 compared to 277 in the control group. This gives a percentage difference of 50.6% ($p<0.001$) in favour of the intervention. This has been calculated per individual, therefore may be an overestimate.

Morton 2004[71]

Study Characteristics
The study was a cross over design with classrooms in each grade level randomised to begin as either the experimental group or the control group. The study investigated the use of a hand hygiene educational program plus the use of a hand sanitizer at specified times as a way of decreasing absenteeism. The study was divided into phase one (46 days) and phase two (47 days) with a 1 week washout period when no children had access to alcohol gel. The children were from a single elementary school in New England, USA. A total of 17 classrooms were involved (four kindergarten classes, four 1st grade classes, three 2nd grade classes, four 3rd grade classes, plus two classes that combined 1st and 2nd graders), giving a total of 253 children. Analysis was ITT with data consisting of aggregated absences per classroom and per disease category.

Outcomes sought
Outcomes were derived from daily absence reports from parents, with reasons for absence recorded. GI absences were defined as: influenza (?), diarrhoea, nausea, vomiting, with or without fever. Respiratory absences defined as: nasal congestion, cough, and sore throat, with or without fever. Also assessed were adverse events: children in the experimental arm checked weekly by the school nurse for adverse effects such as roughness, redness, excoriation, in addition children were also encouraged to report any adverse affects. Children with adverse effects left the study.

Study Quality
The study was a randomised cross over study. However, it was unclear how the randomisation was undertaken, therefore it could still be open to selection bias. As it was a crossover study, a carryover effect may have been a problem, particularly as one part of the intervention was education. In this study only 1 week was given as a washout period. Finally, it is unclear if the correct analysis was undertaken, as the figures are not clear. There was no ICC correction, therefore it is unlikely that it was analysed per cluster, which could mean the effect size is an overestimate.

Results
The authors report that the odds of being absent due to infections were reduced by 43%. The following results are given by age group and infection:

	total n	URTI % absence intervention	URTI % absence control	GI % absence intervention	GI % absence control
Kindergarten	67	48%	60%	22%	22%
1st Grade	55	44%	38%	44%	36%
Combined	28	44%	46%	42%	25%
2nd Grade	46	36%	50%	46%	41%
3rd Grade	57	26%	46%	36%	26%

Comment: Whilst these results seem impressive regarding the adjunct use of hand gel, it is difficult to verify the data from the information given in the paper.

Adverse events
The number of children with adverse events was 10, all had skin irritation.

Multi-component Hygiene Intervention

Roberts 2000[81],[82]

Study Characteristics
This was a cluster randomised trial, set in Australia. It involved 23 child day care centres (n= 299 children intervention, 259 children control). The trial ran from March 1996 to November 1996, with a total length of trial of 9 months. Ages of the children are given as under 3 years old.

Outcomes sought
Parent reported GI infections causing diarrhoea, and parent reported URTI.

Study Quality
This was a cluster randomised control trial. It was unclear whether allocation was concealed, if the groups were similar at baseline and whether participants were aware of the intervention allocation. The analysis has taken into account the cluster design of this trial. The authors state that the intracluster correlation coefficient for colds in intervention centres was 0.008 and in control centres was 0.016. For diarrhoea the intracluster correlation coefficient in the intervention centres was 0.003 and in control centres 0.022. Whilst the chart on page 740 of the study gives an idea regarding the age distribution, it is not possible to determine the exact number of children that were in the intervention and control grouped by age. This has implications because this systematic review is interested in children of 2 years and over, therefore we do not know where the older children were placed in relation to the clusters and this could have influenced the results despite the ICC being used.

Results
URTI related illness – all children (RR 0.89 (5% CI 0.66, 1.08 p=0.45).
URTI related illness children ≤ 24 months - RR 0.89 (95% CI 0.65, 1.21 p=0.45)
URTI related illness children >24 months RR 0.98 (95% CI 0.55, 1.11 p=0.18).
Whilst all favour the intervention groups, no results are significantly significant.

Diarrhoea incidence – all children (RR 0.50 (95% CI 0.36, 0.68 p<0.001).

Diarrhoea incidence - children ≤24 months RR 0.90 (95% CI 0.67, 1.19 p=0.44).
Diarrhoea incidence - children >24 months RR 0.48 (95% CI 0.29, 0.79 p=0.003).
All favour intervention, with statistically significant results for 'All children' and children > 24 months.

Kotch JB 1994[79]

Study Characteristics
This was a cluster RCT, set in 24 day care centres in North Carolina, USA. Altogether, there were 371 children in the trial, 291 were aged less than 24 months, whilst 80 were over 24 months. The trial ran from October 1988 to May 1989 for a total duration of 7 months.

Outcomes sought
Outcomes assessed were the incidence of URTI, and the incidence of diarrhoea.

Study Quality
This was a cluster randomised trial, however the methods of randomisation are not described, and it is unclear whether concealment of allocation occurred. Parents were blinded therefore illness reports were not subject to observer bias. Our main problem with this trial was that it involved children from 0 to 26 months so only a subgroup of the results are relevant for the purposes of this review (i.e. children >24 months). This only accounts for 21% of the trial population, which will reduce the power of the trial to detect an effect in the population over 24 months. Additionally, incidence rates are stated to have been calculated at the classroom level, but no description of any adjustments for cluster are given.

Results
Reported incidence of diarrhoea in intervention group = 2.85 (unadjusted age >24 months) and 2.79 (unadjusted age >24 months) control. For URTI the incidence density for URTI was 12.87 (unadjusted age >24 months) and 11.77 (unadjusted age >24 months).

Uhari M. 1999[80]

Study Characteristics
This was a randomised trial involving 20 child day care centres in Oulu, Finland with 786 children (509 person years) for the intervention and 736 children (481 person years) for the control. The intervention was a multi-component hygiene intervention, which included the encouragement of staff to take sick leave. The trial ran from March 1991 to May 1992 for a total duration of 15 months. The mean age of the children was 3.5 years +/- 1.9.

Outcomes sought
Outcomes sought were URTI, and GI infections. Parents kept a daily symptom diary, which was collected by the study nurse every 2 weeks.

Study Quality
This was a matched pair cluster randomised controlled trial. It was unclear if allocation was concealed and who was blinded to treatment. Groups were similar at baseline, with ITT analysis undertaken. No adjustment for cluster appears to have been undertaken therefore the results may be an overestimate of effect.

Results
Both URTI and GI infections were analysed together. The % difference for the mean number of days with a symptom per person risk year was 14% (95% CI 11-16, P = 0.001) in favour of the intervention. The % difference for the mean number of episodes of infection per person years at risk was 8% (95% CI 0.0 – 15, P=0.049) in favour of the intervention.

Ponka A 2004[83]

Study Characteristics
The study was undertaken in child day care centres in Helsinki, Sweden. Sixty day care centres (n= <3yrs 679, > 3 yrs 2,335,) were allocated the intervention, with 228 acting as control (n= < 3yrs 2,372, >3 yrs 12,002). The study ran from March to May 2000, total duration of intervention period was 3 months. The intervention was a multi-component hygiene intervention (Appendix 10, page 93).

Outcomes sought
Outcomes sought were illness related absenteeism, due to all infections with subgroups for URTI, otits media, conjunctivitis and diarrhoeal absenteeism. Results were reported separately in age groups <3years and >3years.

Study Quality
This was an open controlled cluster study (the authors stated that for administrative reasons randomisation was not possible). Groups were similar at baseline and the analysis was by cluster. This was a very large study involving day care centres (59 intervention and 227 control – children 3 – 6 years). Altogether, 2.335 children were allocated the intervention and 12,002 children allocated the control. This is probably the best study in the review.

Results
For the children over 3 years, the mean difference between the number of absences per 1 month per 1,000 children was 14 (95% CI = - 23, 51 p=0.451). For URTI the mean difference was 1 (95% CI = -31, 33 p=0.941). For diarrhoea the mean difference was 19 (95% CI = -2, 40 p=0.072). For otitis media the mean difference was –3 (95% CI = -12, 6 p= 0.501). Finally for conjunctivitis the mean difference was –3 (95% CI = -9, 2 p=0.243). Therefore there was no difference between the intervention groups and control groups.

Appendix 9 Funding sources

Study ID	Funder
HAND HYGIENE.	
A. Scheduled handwashing.	
Master 1997[75] (handwashing with soap)	Not stated.
B. Hand sanitizer.	
White 2001[70] (handsanitizer)	Two of the authors from industry.
Hammond 2000[76] (handsanitizer)	Main author works for GOJO industries, maker of the hand sanitizer.
Dyer 2000[77] (handsanitizer)	Not stated
Ci. Hand hygiene – education.	
Niffenegger 1997[72] (hand/edu)	Not stated.
Kimel 1996[73] (hand/edu)	Not stated.
Cii. Education plus hand sanitizer.	
Guinan 2004[74] (hand/edu+ handsanitizer)	GOJO industries supplied the educational materials and hand sanitizer.
Ciii. Education plus scheduled hand washing.	
Morton 2004[71] (hand/edu+ handsanitizer)	Funded by Maine Administrative School District. AlcoSCRUB donated by Erie Scientific.
MULTI-COMPONENT INTERVENTIONS.	
Roberts 2000 [81,82] (multi-comp)	Grant from the Commonwealth Department of Family Services and Health, Research and Development scheme.
Kotch 1994 [79] (multi-comp)	Part funded by a grant from the Maternal and Child Health Programme. Cal Stat™ donated by Calgon Vestal Laboratories, a subsidiary of Merck.
Uhari 1999[80] (multi-comp)	Not stated.
Ponka 2004[83] (multi-comp)	Grant from Paivikki and Sakari Sohlberg Foundation

Appendix 10 Hand hygiene intervention and control details

Study ID	Intervention	Control
HANDWASHING		
A. Scheduled handwashing.		
Master 1997[75]	Three wks prior to the intervention the proper technique and timing of appropriate hand washing was demonstrated to all of the school's students. During this meeting, germ theory was also discussed. The intervention is scheduled handwashing. Children in the intervention group were required by their teachers to wash their hands after arrival at school, before eating lunch, after lunch recess, and before going home. The teacher instructed the children to go to the toilets to wash their hands at these times. (these required hand washings were in addition to normal practice – e.g. after going to the toilet). Hand washing was not monitored and non scheduled handwashings were not quantified. School soap was used which was not antibacterial, Eucerin lotion was used for dry skin after washing. In addition guest lecturers were provided every 2 wks throughout the study period for the hand washing groups. Topics included medieval medicine, the auditory system and a plating experiment in microbial flora so the children could see their clean and dirty hands. Some teachers gave stickers to members of the handwashing group.	Children had instruction on hand washing 3 weeks before the study started, they were then left to wash their hands at their normal frequency with no prompting from the teachers. The frequency was not monitored. School soap was used which was not antibacterial, Eucerin lotion was used for dry skin after washing.
B. Scheduled use of hand sanitizer		
White 2001[70]	Structured hand hygiene education program employing programmed use of the hand sanitizer with current patterns of at will soap and water hand washing practices. Two weeks prior to study initiation, all students attended a 22 minute assembly on proper hand washing techniques, instruction regarding the importance of washing hands with soap and water to prevent the spread of illnesses and the relationship of germs to illness. New coughing and sneezing behaviours were also taught, (i.e. cough/sneeze into the cuff, sleeve or elbow instead of covering their nose and mouth with their hands. They also viewed a 4 minute video tape "The sneeze, how germs are spread" by Francois Chew 1996, which illustrated the hand to hand spread of germs between people. Alcohol free hand sanitizer (SAB formulation). Students were instructed to use the hand sanitizer: immediately on entering the classroom, before and after eating (recess and lunch), before leaving at the end of the day, with additional use when a child sneezed or coughed in the classroom. Teachers verbally reminded the children when to use the product.	Placebo controlled, the product did not contain benzalkonium chloride or preservative compounds.
Hammond 2000[76]	Usual hand wash practice plus the use of a waterless alcohol gel hand sanitizer when entering and leaving the classroom, especially first thing in the morning, before lunch, after recesses, after use of the toilet, and before going home. Also when the students sneezed or coughed. Teachers were responsible for ensuring the hand sanitizer was used per protocol.	Usual handwashing practices
Dyer 2000[77]	Both intervention and control recieved a 30 minute presentation on germs, the relationship of germs to colds and the importance of washing hands with soap and water to prevent illness – 2 weeks prior to the study initiation. In addition the students also viewed an educational videotape presentation that described the	The control group received instruction to wash hands before eating, after visiting the toilet, and prn during the day

	hand to hand spreading of germs between people. SAB sanitizer (clean hands®). Students were instructed to used the spray under teacher supervision to supplement normal, at will handwashing with non-medicated (non antibacterial soap) and water. The situations determining hand sanitizer use were: 1). immediately after entering the classroom, 2). before eating (snacks and lunch), 3). after sneezing and coughing in the classroom 4). after using the restroom facility (presume this means the toilet).	
Ci. Hand hygiene – education		
Niffenegger 1997[72]	Staff and children were encouraged to wash their hands when they arrived at the centre also to "give their cough the elbow" a simple technique of lifting one's arm and sneezing into it rather than sneezing or coughing onto the hands. The children in the intervention group also received 3 days of instruction based on the "Hooray for Handwashing" program (see paper for full details). In addition hand washing posters were displayed near handwashing sinks as reminders of when and how to wash hands.	Normal handwashing practice plus observation
Kimel 1996[73]	"A half hour presentation was developed using materials from the Scrubby Bear Program 1985, and the Ivory Handwashing Program 1987. The presentation consisted of a 20 minute discussion followed by demonstrations. Topics discussed were: what germs are and how they get inside people, how people can help their bodies protect themselves from germs, when to wash hands, how to wash hands properly. Two demonstrations were then conducted, 1st the spread of flour from surface to surface was used to show how germs travel, 2nd students used different handwashing techniques to demonstrate varying degrees of effectiveness in removing dirt and oil. Then a follow up story and activity sheet were given to the class to reinforce information presented. A take home hand washing chart was also given to each student to encourage handwashing at home".	Not described, presume normal routine.
Cii Education plus hand sanitizer.		
Guinan 2004[74]	Educational components = 10 minute talk on the importance of handwashing, then to wash hands and remind your buddy to wash their hands. This was followed by a video on micro organisms and disease transmission. Kindergarten and grade 1 = shown a 2 minute video entitled "The Sneeze" and children in grades 2 and 3 saw a 10 minute video titles "Haley's germs". After the video each student received a "Buddies Handwashing Pamphlet" on which kindergartners and 1st graders completed a dot to dot that formed a hand and bar of soap, the older children completed a word search which included common words such as soap, water and towel. Total training time = 1 hour. The presenter was the same for all of the intervention - a junior high school student. Hand sanitizer – each classroom was equipped with a dispenser of Purell Instant Hand Sanitizer with Aloe (GOJO industries). Active ingredient = ethyl alcohol at 62%. Running water was not available in any of the classrooms. Each child was taught how to use the hand sanitizer and awarded a card identifying them as "Ambassadors of Hygiene".	Usual hygiene practice.
Ciii. Education plus scheduled use of hand sanitizer.		
Morton 2004[71]	1. Education about hand hygiene – 45 minute lesson on hand hygiene called the "Germ Unit" plus practical demonstrations using Glo Germ a cornstarch based product that is luminescent under UV light.	Routine hand washing, children who received the intervention first would have received the Germ Unit

	2. Protocol for using alcohol gel – children to follow healthy hands rules – to wash hands: ▪ on arrival at school ▪ before lunch ▪ after toilet use, if ordinary soap not available ▪ after rubbing the nose, or eyes, or putting fingers in the mouth ▪ after a request from the teacher	education. Monitoring of absences

Appendix 11 Multi-component hygiene intervention and control details

Study ID	Intervention	Control
MULTI-COMPONENT HYGIENE INTERVENTIONS.		
Roberts 2000[81,82]	Handwashing recommended to be undertaken on arrival at the centre, after toileting, before eating, and after changing a diaper (staff and child). Staff members who changed diapers were discouraged from preparing food for the children on the same day. Handwashing practice was: only soap recommended, the duration of a hand wash was of an approximate count of 10 to wash and count of 10 to rinse. Staff members were asked to teach handwashing to the children using nursery rhymes etc to encourage them and to perform hand washes on infants. Aseptic tissue wiping involved wiping – this involved where possible staff using a small plastic bag to cover their hand like a glove. [note: this could be potentially dangerous] Recommended that toys be washed daily using dishwashers where possible. Staff given a 3 hour training session about transmission of infection, hand-washing and aseptic nose wiping at the beginning of the trial. In addition 9 newsletters were distributed to the centre staff with news items from centre staff of how they had incorporated hygiene methods into their daily routines.	Both control and interventions were observed by trial staff for a period of 3 hours in a morning every 6 weeks. [blinded observer]
Kotch 1994[79]	Curriculum for care givers – emphasis on: handwashing of children and staff; disinfection of toilet and diaper change areas; physical separation of diapering areas from food preparation and serving areas; hygienic diaper disposal; availability of soap, running water and disposable towels [waterless disinfection scrub to be used only if the alternative were not washing at all]; daily washing and disinfection of toys, sinks, kitchen and bathroom floors, daily laundering of blankets, sheets, dress up clothes etc ; hygienic food handling practices. A 3 hour training session at the start of the trial, with participants required to demonstrate skills. On site training was given a week after trial start with subsequent 5 week intervals. Monthly meetings with centre directors also given to encourage leadership and support.	Observation only.
Uhari 1999[80]	The hygiene recommendations were: intensified handwashing, use of an alcohol based oily	Assume no intervention, not clear what the control

	disinfectant, directions on the use of disposable towel use, cleaning of the CDCCs and regular washing of toys (if this was not possible, circulation of toys so that they were taken out of use for an at least every other week). One healthy person served food and tooth brushing was withdrawn. Attention was paid to diaper changing practices and the places where this was done. At the beginning the study team visited each intervention CDCC and made an inventory of possible control measures. This was followed by a 1 hour lecture to CDCC personnel on the spread of infections and the possibilities for preventing them accompanied by a slide show. This lecture was given at the beginning, then repeated at 6 months and an additional 3 times by the study nurse. CDCC personnel were encouraged to take sick leave at first appearance of symptoms. [Note – this could initially increase absenteeism]	got other than the parents symptom diary and nurse collecting outcome data.
Ponka 2004[83]	Intensified handwashing, both children and personnel, disposable towels. Recommended to wash hands on arrival, after being outside, sneezing, toileting or after changing a diaper and before eating. Attention given to diaper changing practices and cleaning of these places as well as cleaning toilet bowls, pots and immediate hygienic disposal of diapers. All surfaces that could be reached by children were to be cleaned carefully and regularly, most of them daily. Toys were to be washed weekly or if this was not possible to be taken out of circulation at least biweekly. Teething rings and dummies to be washed daily. Directions for washing and changing of sheets and other linen were given. Instructions were given for good hygiene practice for serving and cleaning up after food. Instructions were given for regulation of a sufficient air exchange rate in the CDCC. Instructions regarding children with symptoms of communicable diseases were also given based around the permanent instructions of the CDCC.	Usual hygiene policy and practice.

Appendix 12 Quality assessment

Study ID	1. Study design random?	2. How randomised?	3. Allocation concealment?	4. Groups similar at baseline?	5. Blinding Who?	9. ITT or >10% dropout	10. Appropriate analysis.
HAND HYGIENE STUDIES							
A. Scheduled handwashing							
Master 1997[75]*	No	N/A	No	Unclear – no info given as to who got the intervention & control	No one	All students accounted for.	No – not accounting for cluster
B. Scheduled use of hand sanitizer							
White 2001[70]	Random	Unclear	Unclear	Unclear – states that age and sex balanced	Yes – placebo hand sanitizer used	Not ITT, only 32/72 classrooms in final assessment	No –not analysed by cluster also not ITT.
Hammond 2000[76]	No	N/A	Unclear	Yes – matched pairs	Unclear	1 school district excluded from analysis for protocol violations (Bozeman, Montana)	Yes – accounted for clustering in the analysis.
Dyer 2000[77]	No	N/A	No	Cross over N/A	Participants – no, others – unclear	Unclear	No
Ci. Education regarding hand hygiene							
Niffenegger 1997[72]	No	N/A	No	Yes – authors stated there was balance.	No one	Unclear	No
Kimel 1996[73]	No	N/A	No	Yes	Unclear	Unclear	Unclear
Cii. Education plus use of hand sanitizer							
Guinan 2004[74]	No	N/A	No	Unclear	Unclear	Unclear	Unsure, not ICC but were assessed by

							grades see para on page 218 of publication.
Ciii. Education plus scheduled use of hand sanitizer							
Morton 2004[71]	Random	Unclear	Unclear	Cross over N/A	None	No	Unclear
MULTI-COMPONENT HYGIENE STUDIES							
Roberts 2000 (2 papers[81,82])	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes – but unclear for subgroups.
Kotch 1994[79]	Random	Unclear	Unclear	**Mostly	Unclear	Unclear	Unclear
Uhari 1999[80]	Random	Yes – paired randomisation	Unclear	Yes	Participants, investigators – no, others – unclear	Yes	Unclear
***Ponka 2004[83]	No	N/A	No	Yes	Unclear	Yes for > 3yrs	Yes – analysed in clusters.

* Clear write up of methods, source of bias may be that the investigators phoned parents to ask why children were absent, the investigators may have known which group the absentee was assigned to and may have caused a bias in the results. “Lack of blinding may have resulted in the handwashing group being less inclined to stay at home with minor illness because they knew they were being studied”.
** Except more non-white children, shorter time since enrolment, sharing a bedroom, single parent, multifamily dwelling, open classroom and inadequate sink access
****Best study in review – large study even for subgroup, well conducted, analysed in clusters.

Appendix 13 Results data given in the papers

Respiratory outcomes

	Ci. Niffenegger 1997[72]		MCHI. Roberts 2000 [81,82]		MCHI. Kotch 1994 [79]	
	Int.	Con.	Int.	Con.	Int.	Con.
Child days at risk	530	425	39,539	30,206		
Infection incidence	102	81	1009	786		
Episodes per child per year			1.2	2.1	12.87	11.77

GI outcomes

	MCHI. Roberts 2000 [81,82]		MCHI. Kotch 1994 [79]	
	Int.	Con.	Int.	Con.
Child days at risk	39,539	30,206		
Infection incidence	127	172		
Episodes per child per year	1.2	1.9	2.85	2.79

Respiratory and GI combined

	MCHI. Uhari 1999 [80]	
	Int.	Con.
Episodes per child per year	4.8	5.2

Absence.

	A. Master 1997[75]		B. White 2001[70]		B. Hammond 2000[76]		B. Dyer 2000[77]		Ci. Kimel 1996[73]		Cii. Guinan 2004[74]		Ciii. Morton 2004*[71]		MCHI. Ponka 2004[83]	
	Inc.	Con	Inc	Con	Int	Con	Int	Con	Int	Con	Int	Con	Int	Con	Int	Con
Number of clusters	6	8	16	16	8	8	7	7	4	5	9	9	17			
Number of participating students	143	162	388	381	3075	3005	210	210	87	112	-	-	253	804		
Possible days of attendance	5172	5836	9615	9459	-	-	8292	8260	-	-	-	-	-	-	Results measured as the mean differences (in change in the	
Absence incidence	78	111	96	145	-	-	59	112	-	-	-	-	39	69		

	A. Master 1997[75]		B. White 2001[70]		B. Hammond 2000[76]		B. Dyer 2000[77]		Ci. Kimel 1996[73]		Cii. Guinan 2004[74]		Ciii. Morton 2004*[71]		MCHI. Ponka 2004[83]
Days absent	116.5	175	153	222	7441.5	9066	98	168	-	-	-	-	-	-	number of absences per month from baseline to intervention), between intervention and control groups.
Different students absent	58	66	74	88	-	-	48	94	-	-	-	-	-	-	
Days absent per student	2.01	2.64	2.1	2.5	2.42	3.02	2.04	1.79	-	-	-	-	-	-	
Percentage of students ill per day	-	-	-	-	-	-	-	-	1.8%	3.8%	-	-	-	-	
Number of episodes of absence per child per month	-	-	-	-	-	-	-	-	-	-	140	277	-	-	

*cross-over trial

Appendix 14 Relative risk calculations

Output from StatsDirect, comparison of two crude rates.

Master 1997[75] - Incidence rate comparison

	Exposure:		
Outcome:	**Exposed**	**Non-exposed**	**Total**
Cases	116.5	175	291.5
Person-time	5172	5836	11008

Exposed incidence rate = 0.022525
Non-exposed incidence rate = 0.029986

Rate difference = -0.007461
approximate 95% confidence interval = -0.013552 to -0.00137

chi-square = 5.764313 P = 0.0164

Rate ratio = 0.751181
exact 95% confidence interval = 0.58906 to 0.955

Conditional maximum likelihood estimate of rate ratio = 0.743707
Exact Fisher 95% confidence interval = 0.583155 to 0.945501
Exact Fisher one sided P = 0.0074, two sided P = 0.0137
Exact mid-P 95% confidence interval = 0.587204 to 0.939286
Exact mid-P one sided P = 0.0064, two sided P = 0.0128

White 2001[70] - Incidence rate comparison

	Exposure:		
Outcome:	**Exposed**	**Non-exposed**	**Total**
Cases	153	222	375
Person-time	9615	9459	19074

Exposed incidence rate = 0.015913
Non-exposed incidence rate = 0.02347

Rate difference = -0.007557
approximate 95% confidence interval = -0.011537 to -0.003577

chi-square = 13.850667 P = 0.0002

Rate ratio = 0.678007
exact 95% confidence interval = 0.548166 to 0.836817

Conditional maximum likelihood estimate of rate ratio = 0.678007
Exact Fisher 95% confidence interval = 0.548166 to 0.836817
Exact Fisher one sided P = 0.0001, two sided P = 0.0002
Exact mid-P 95% confidence interval = 0.551106 to 0.832517
Exact mid-P one sided P < 0.0001, two sided P = 0.0002

Hammond 2000[76] - Incidence rate comparison

	Exposure:		
Outcome:	**Exposed**	**Non-exposed**	**Total**
Cases	7441.5	9066	16507.5
Person-time	553500	540900	1094400

Exposed incidence rate = 0.013444
Non-exposed incidence rate = 0.016761

Rate difference = -0.003317
approximate 95% confidence interval = -0.003777 to -0.002856

chi-square = 199.48755 P < 0.0001

Rate ratio = 0.802129
exact 95% confidence interval = 0.777806 to 0.827193

Conditional maximum likelihood estimate of rate ratio = 0
Exact Fisher 95% confidence interval = 0 to 0
Exact Fisher one sided P < 0.0001, two sided P < 0.0001
Exact mid-P 95% confidence interval = 0 to 0
Exact mid-P one sided P < 0.0001, two sided P < 0.0001

Dyer 2000[77]- Incidence rate comparison

	Exposure:		
Outcome:	**Exposed**	**Non-exposed**	**Total**
Cases	98	168	266
Person-time	8292	8260	16552

Exposed incidence rate = 0.011819
Non-exposed incidence rate = 0.020339

Rate difference = -0.00852
approximate 95% confidence interval = -0.012383 to -0.004658

chi-square = 18.692779 P < 0.0001

Rate ratio = 0.581082
exact 95% confidence interval = 0.448231 to 0.749883

Conditional maximum likelihood estimate of rate ratio = 0.581082
Exact Fisher 95% confidence interval = 0.448231 to 0.749883
Exact Fisher one sided P < 0.0001, two sided P < 0.0001
Exact mid-P 95% confidence interval = 0.451767 to 0.744385
Exact mid-P one sided P < 0.0001, two sided P < 0.0001

Kimel 1996[73] Incidence rate comparison

	Exposure:		
Outcome:	Exposed	Non-exposed	Total
Cases	1.566	4.256	5.822
Person-time	87	112	199

Exposed incidence rate = 0.018
Non-exposed incidence rate = 0.038

Rate difference = -0.02
approximate 95% confidence interval = -0.067909 to 0.027909

chi-square = 0.669461 P = 0.4132

Rate ratio = 0.473684
exact 95% confidence interval = 0.028958 to 3.577251

Conditional maximum likelihood estimate of rate ratio = 0.643678
Exact Fisher 95% confidence interval = 0.058226 to 4.491292
Exact Fisher one sided P = 0.4676, two sided P = 0.7021
Exact mid-P 95% confidence interval = 0.082457 to 3.628264
Exact mid-P one sided P = 0.3237, two sided P = 0.6475

Appendix 15 Previous economic evaluations – study details

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
Aim	Extrapolation of a model based on an infection control programme in a preschool for children with Down's Syndrome. Aim to improve generalisability to general school settings.	To determine the effectiveness of a comprehensive handwashing program "Buddies Handwashing Program" on absenteeism in elementary grades (p218).
Conclusions	Results suggest that the reduction in the costs of illness more than offsets the cost of implementing the hygiene intervention. Potential societal savings of a less intensive ICEP were estimated at $32,500 annually. When extrapolated to the 3 million US children who are younger than 5 years and who attend a day care centre, the potential societal savings are estimated at $974 million annually, offsetting 70% of the excess costs associated with increased risk of illness in day care centres (Haskins 1989) (p7). **Points:** It is unclear where the figure of $325 came from – the cost quoted in Table 6 is $286 in the text is $348 and from my crude mean calculation from the data derived from Uhari ($188), Carabin ($387 [£251.94]), Kotch ($206) and Roberts ($335) was $279.	The data strongly suggest that a hand hygiene program that combines education and use of a hand sanitizer in the classroom can lower absenteeism and be cost effective (p217).
Country	USA	USA
Evaluation type	Cost benefit analysis	Cost benefit analsysis
Modelling employed	Yes	Minimal
Nature of modelling	Health state transition Markov decision analysis model that estimated annual expected costs for baseline (control/usual practice) and multi component hygiene intervention. Cost of intervention was compared with reduction in costs of illness (direct medical costs plus costs associated with lost parental working time using opportunity and replacement methods).	Some integration of effects from trial data and costs
Perspective	Societal (sensitivity analysis on household) (USA)	Not given
Intervention	Modelled less intensive version of the multi component hygiene intervention lasting for 1 year (termed "intervention year"): *site assessment, in-service educational training for teachers and aides*	**Education and hand sanitizer (p218):** Included review study.

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
	every 4 to 6 weeks, increased emphasis on handwashing, compliance monitoring (using an "on-site monitor"), excluded cleaning service (but this was to be done by the teachers i.e. washing and cleaning of the mouthed toys), reduced cleaning and disinfecting product use by 25%, decreased ICEP effectiveness by 25% (p4).	**Points:** "Cross contamination" i.e. influence of intervention group on control group and vice versa. Hence, cluster RCT would have been better. Was this monitored or attempted to be controlled in any way? It may be argued that the hand sanitizer was only available per classroom. Did other students from different classes also have access?
Comparator	Modelled control unchanged from original: *school's current infection control (IC) procedures were unchanged for 1 year, termed the "baseline year". This preceded the "intervention year" (p2).* **Points:** There was no description of what current hygiene interventions were in place.	Did not receive the intervention (p218). **Points:** Any existing infection control program?
Population	Modelled nonspecialised preschoolers from original unchanged except: decreased "baseline" rates of illness from Krilov's paper by 10% (p4). **Points:** No justification for the selected 10% decrease in "baseline" rates given.	Teachers of primary school students in Pennsylvania (p218). 5 schools with 2 test groups and 2 control groups each. However, there were only: 4 schools having 2 test groups and 2 control groups. 1 school having 1 test group and 1 control group.
Outcomes	Modelled from original unchanged except: decreased "baseline" rates of illness by 10%, reduced medical resource utilisation by 50%, decreased ICEP effectiveness by 25%. **Points:** Exactly how these reductions were calculated is unclear for example how was the ICEP effectiveness reduced and in which conditions (Table 4 p4) – was the total cost in the "intervention year" reduced by 25%? Which medical resources were decreased as this may influence the costs substantially e.g. use of antibiotics versus physician visits or hospitalisations.	Absenteeism was defined as the number of episodes of illness per child per month (p218). Illness was defined as an infectious process such as cold, flu and gastroenteritis. Absenteeism data was collected for 3 months (March – May) after initiation of program. **Points:** Length of time absent would have an effect on costs? 3 months adequate time frame? March – May flu season?

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
Time frame	2 years	3 months (March – May 2000)
Discounting	As costs were enumerated over 1 year, discounting costs were deemed unnecessary (p2).	Not considered
Funding	Reckitt Benckiser	GOJO Industries supplied educational materials and hand sanitizer
Results	**NB: most of these results unless specified were reported in the abstract of this article.** **Secondary analysis: less intensive ICEP in a nonspecialised preschool setting:** **Cost of illnesses:** “Baseline year”: mean cost of illness $962 “Intervention year”: mean cost of illness $614 Difference: 36% **Cost of IC/ICEP:** “Baseline year”: cost of IC $716 “Intervention year”: cost of ICEP $3087 **Cost savings?** Cost of illness savings $13224 (not considering cost of IC/ICEP), for 38 children Annual incremental cost (ICEP cost – IC cost) $2371 Estimated net annual savings of less intensive ICEP in nonspecialised preschool $10853 for 38 students, $286 per child **Sensitivity analyses: household perspective:** **Cost of illnesses:** “Baseline year”: mean annual costs of illness per child was $176	**Cost of illnesses:** **Intervention:** $7000 per quarter for 145 students **Control:** $13850 per quarter for 145 students **Cost of intervention/control:** **Intervention:** $7775 per quarter for 145 students **Control:** $0 **Cost savings?** $6075 per quarter for 145 students $24300 per annum for 145 students $167 per student per annum

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
	"Intervention year": mean annual costs of illness per child was $113 Difference: 36% (as above) **Cost of IC/ICEP:** As above **Cost savings?** Cost of illness savings $63 (not considering cost of IC/ICEP), per child Annual incremental cost (ICEP cost – IC cost) $2371 The authors suggested that the resulting cost-of-illness savings $63 per child per year seem to be sufficient to pay for the ICEP should the entire ICEP cost be passed on to parents through higher tuition payments (incremental program cost $2371 divided by 38 children in the day care centre = $62.39 per child per year) (p5, 6).	
Is there a generally well defined question?	Yes	Yes
Is there comprehensive description of alternatives?	No	No
Are all important and relevant costs and outcomes for each alternative identified?	This is based on the original model with some exceptions as stated above. It is unclear exactly how the costs of illness for "baseline year" were derived. It seems that it may have been calculated based on the 10% reduction in illness rate and 50% reduction in medical utilisation.	No, did not cost health service costs. No, they did not cost the videos and infrastructure required for this i.e. television etc.
Has clinical effectiveness been established?	Yes, it has been stated that ICEP is clinically effective and more details are given in the Krilov study used.	Yes, but study has some quality issues.
Are costs and outcomes measured accurately?	? this is unclear as full details are not given. In addition, without clear justifications for the modifications set out in the model, it is hard to judge whether these were valid.	Yes.
Are costs and outcomes valued credibly?	Yes, seems so. However, again, without clear justifications for the modifications set out in the model, it is hard to judge whether these were valid.	Don't know
Are costs and outcomes	No, does not seem so, although this study occurred over 2 years, 1st	No.

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
adjusted for differential timing?	year "baseline" and 2nd year "intervention".	
Is there an incremental analysis of costs and consequences?	Yes	Yes
Were sensitivity analyses conducted to investigate uncertainty in estimates of costs and consequences?	Yes	No
How far do study results include all issues of concern to users?	The authors have made quite good attempt to cover all aspects of cost that may be incurred by society as a whole. However, it did highlight the fact that it did not consider costs associated with secondary infections in parents, siblings or day care centre personnel nor savings with exercising IC practices in the home.	See concerns under "Cost (source)" below
Are the results generalisable to the setting of interest?	No, data were taken from USA and the pathways of care are not necessarily the same in the UK (e.g. diagnostic testing in children with pharyngitis Table 3). In addition, it is not known whether the IC was reflective of usual practice either in the USA or the UK. The model was also initially constructed on data collected on Down Syndrome individuals, a minimum of ¼ had cardiopulmonary disease. Although the authors did use 4 other studies to determine the range of cost savings, exactly whether these could be extrapolated to the West Midlands settings is unclear.	Correct age group but USA data, specifically Pennsylvania from middle-class and upper class private school students. Seasonal absenteeism was not determined.
Effectiveness (source)	Krilov 1996, (Uhari 1999, Carabin 1999, Kotch 1994, Roberts 2000 – although these were simply used to determine whether the cost savings were comparable, but were not the main source of effectiveness).	Guinan 2002
Effectiveness (data)		Derived from the study by Guinan 2002
Quality of life (source)	N/A	N/A
Quality of life (data)	N/A	N/A
Costs (source)	As in original model	Guinan 2002 Cost data associated with absenteeism was defined as the following (p218): Teacher time: 1 hour of teacher time per episode (for remedial work,

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
		take-home assignment) at an hourly rate of $50. Time was determined by averaging the estimates reported by each school for preparing assignments and remedial work. The hourly rate was determined on the basis of the substitute teacher salary rate for the county in which the test schools were located. School nurse time: one hour per in-service and 1 hour preparation time per class at $35. Although a school nurse was not part of this study, we factored in this cost since the school nurse would be responsible for the implementation of the program. Hand sanitizers: ¼ of the yearly cost for soap per child ($2 per year). Activity booklet and ambassador card: $0.50 per child. **Points:** ? intervention costs – only hand sanitizers and possibly school nurse's time factored in as the person responsible for implementation. However, they did not cost the videos and infrastructure required for this i.e. television etc. Did not consider any productivity losses with respect to parents who may have to stay at home to look after sick child (opportunity costs) or replacement costs for these. Any costs associated with the control group?
Cost year	1999 US $	Not stated
Base-case	N/A	N/A
Chance variation in base-case	N/A	N/A
Sensitivity analyses	As described above in **Results**	None
General points	Table 5, Fig 2, text: In the specialised setting, the cost of illnesses was $615. Also, in the non-specialised setting, the cost of illnesses was virtually identical at $614. Whereas, at baseline for the specialised setting, the cost of illnesses was $1235 compared to $962 in the non-specialised setting. Given that as stated by the authors that non-specialised populations tend to require less follow	

	Ackerman 2001 Less intensive ICEP in a non-specialised day care centre setting (3 papers in all, others are Duff 2000[88], Rubino 2002[87])	**Guinan 2002[74]**
	up care and hospitalisations, could this equivalent cost of $614/$615 indicate that the less intensive ICEP is highly ineffective, as a plausible explanation? Table 7, No breakdown of derivation of rates of illness figures i.e. for Uhari 1999, Carabin 1999, Kotch 1994, Roberts 2000.	

Appendix 16 Published cost survey details.

	Carabin 1999 [89]	**Lambert Lambert (2 papers) Initial data from 2005 publication, [17]costs from Lambert 2004[90]**
Aim of study	To describe both the direct & indirect costs of illness in a cohort of toddlers in day care.	To examine the epidemiology & burden of respiratory illness (resource use) during winter in urban children from temperate Australia.
Notes	Preliminary work before study period. From baseline questionnaire to 6 months (preceding randomisation)	
Country	Quebec, Canada.	Melbourne, Australia.
Evaluation type	Cost survey.	Cost survey.
Modelling employed	No	No
Nature of modelling	N/A	N/A
Perspective	Not given.	Societal.
Intervention	Standard care.	Standard care.
Comparator	N/A	N/A
Population	Children in day care centre, mean age 24.8 (SD 6.1), median 24 (20.3, 28.2).	Children between 1 and 6 yrs. (12 to 71 mths of age). Children under 2 yrs = 6.8% (8 children). Children with risk factors for resp infection were excluded.
Outcomes	Cold (URTI), diarrhoea, vomiting, illness related absence.	Influenza like illness (ILI), based on definitions by Belshe 1998. Number & duration of episodes. Burden of ILI.
Time frame	1st Sept 1996 to 1st March 1997 (6 mths).	July 2001 and December 2001.
Discounting		N/A costs over a single yr.
Direct Costs	• Medication (prescribed & OTC). • Visit to a physician.	• Medication (prescribed & OTC). • Visits to a physician. • Diagnostic tests.
Indirect Costs	• Cost of an employed parent missing work to care for a child – 2 methods, replacement cost and opportunity cost.	(For influenza season). • Total time providing care

	Carabin 1999 [89]	Lambert Lambert (2 papers) Initial data from 2005 publication, [17] costs from Lambert 2004 [90]
	• Cost of care provided by a family member (excluding parents), replacement costs (hrly wage x 8 hrs). • Cost of care provided by a babysitter (hrly wage x 8 hrs).	• Travel. • Time seeking health care.
Funding	Rhône Poulenc Rorer Canada Ltd.	CSL Ltd. (unknown as to what this is)

Results	**Carabin 1999 [89]**	**Lambert Lambert (2 papers) Initial data from 2005 publication, [17] costs from Lambert 2004 [90]**
No. in study	273 study children.	122 children, 80 households. (4 children, 2 households lost to follow up).
No. illnesses	Average % with a cold, diarrhoea, or vomiting were 23.4% (SD 17), 2.3% (SD 3.6) & 0.9% (SD 1.4) respectively.	205 ILI episodes in 477.3 child mths between 1st July and 1st Dec 2001. Influenza season 15th July to 6th Oct 2001 there were 137 ILI episodes in 260.4 child mths.
No. of absences	Incidence rate of URTI = 502 days absent (out of a potential 18,551 days), giving the proportion of absence as 2.7%.	N/A
Direct costs – medication	**Total medication** = $49.10 (SD $51.34) per child/per 6mths (adjusted for no. of days follow up per period). **OTC** = $12.44 (SD 14.26) per child/per 6mths (adjusted). **Prescription** = $35.03 (SD 47.45) per child/per 6mths (adjusted).	**OTC** = Aus$2,617.40 (%ILI cost = 0.7%) **Antibiotics** =Aus$ 579.47 (%ILI cost = 1.2%) **Other prescriptions** = Aus$ 336.92 (%ILI cost = 0.7%)
Direct costs – consultation with physician	**Total** = $49.10 (SD 51.34) per child/per 6 mths (adjusted).	**GP visits** = Aus$255.43 + Aus$2,174.94 (%ILI cost = 5%) **Other healthcare providers = Aus$156.42 + Aus$115.00 (%ILI cost = 0.2%)** **Hospital A & E visit** (no admission) = Aus$ = 160.00 (% ILI cost = 0.3%)
Indirect costs -	**Baby sitter** = $11.59 (SD $49.16) per child/per 6mths (adjusted) **Family member** = $35.19 (SD $94.62) per child/per 6mths (adjusted). **Missed work (replacement cost)** = $63.43 (SD $ 101.30) per child/per 6mths (adjusted). **Missed work (opportunity cost)** = $125.35 (SD $226.65) per child/per 6mths (adjusted.	Carer costs **Time away from work** (pay lost) = Aus$1,604.74 (%ILI cost = 3.3%) **Time away from work** (no pay lost) = Aus$3,609.03 (%ILI cost 7.4%) **Time away from usual activities** = Aus$34, 212.06 (%ILI cost 70.3%) Travel costs Car = Aus$ 209.96 (%ILI cost = 0.4%) Parking = Aus$ 13.00 (%ILI cost = 0.0%)

Results	Carabin 1999 [89]	Lambert Lambert (2 papers) Initial data from 2005 publication, [17] costs from Lambert 2004 [90]
		Paid childcare for other children = Aus$ 133.00 (% ILI cost = 0.3%)
Total Costs	**Using replacement cost** = $206.77 (SD $217.30) per child/per 6mths. **Using opportunity cost** = $260.96 (SD $302.00) per child/per 6 mths.	**Total costs** = Aus$48,657.25 **Total cost per ILI** = Aus$240.88
Costs (source)	Replacement costs: hrly wage of untrained educators per region Opportunity costs: hrly wage of full time workers by gender & education level (based on Jean 1996)	Various - See ref Lambert 2004 [90] for details.
Cost year	1997	2001
Cost units	USA dollars (Feb 2006 USA $ = £1.76)	Presume Australian dollars. (Feb 2006 Aus $ = £2.35)
Base-case		
Chance variation in base-case		
Sensitivity analyses		

Quality assessment.	Carabin 1999 [89]	Lambert Lambert (2 papers) Initial data from 2005 publication [17], costs from Lambert 2004 [90]
Is there a generally well defined question?	Yes	Yes
Is there comprehensive description of alternatives?	Yes	
Are all important and relevant costs and outcomes for each alternative identified?	No – missing costs for alternative treatment pathways such as telephone advice e.g. NHS direct, walk in clinics, emergency care. Costs such as missed schooling (whether sick and attending or absent) not calculated. Costs to the community not calculated e.g. spread of infection to parents, siblings etc.	No – missing alternative treatment pathways such as telephone advice e.g. NHS direct, walk in clinics. No costs for missed schooling. Costs such as spread of infection not included. But – more wide ranging costs than Carabin. Time spent seeking health care – may have double counted this time with time provided by the carer.
Has clinical effectiveness been established?	N/A	N/A
Are costs and outcomes measured accurately?	Values were imputed for 20.9% of OTC and 16.7% of prescription drugs as parents failed to note the actual cost.	Costing information available for 89% of illnesses. Illness episodes without burden information reported were more likely to be shorter in duration 2.5 days versus 5 days, and less likely to have fever or ear infection.

Are costs and outcomes valued credibly?	Yes	No clear definition for "time away from usual activities". This accounts for 70.3% of the costs, which seems a very high amount.
Are costs and outcomes adjusted for differential timing?	Unsure	Unsure.
Is there an incremental analysis of costs and consequences?	N/A	N/A
Were sensitivity analyses conducted to investigate uncertainty in estimates of costs and consequences?	N/A	N/A
How far do study results include all issues of concern to users?		
Are the results generalisable to the setting of interest?	The age groups include children younger than 2 yrs therefore may not be relevant to the review. Younger children are more likely to be taken to see a physician for URTI[12]. No mention of hygiene practices therefore it is unknown whether the setting would equate to simple handwashing techniques or more intensive interventions.	Eight children in the study are less than 2 yrs old. No mention of hygiene practices therefore unknown if the setting would equate to the interventions in the studies in the review.

Appendix 17 Costs needed for model.

INTERVENTION

	Elements making up cost		Source of data	Estimated cost £
SCHEDULED HANDWASHING	Water costs	Water supply		
		Water heating		
	Soap	Soap supply	Wendy Jeffreys (Healthy Schools Co-ordinator Solihul) – 'Soapy Soap' Note: "number of sinks determined the number of soap dispensers".	Full price £35.47 per 6 litres. Discount price £27.37 per 6 litres. (approx 1,400 shots)
		? Moisturizer supply		
	Drying facilities	Electric dryer – One off installation cost + maintenance + electricity		
		Linen roller towels – laundry costs		
		Paper towels – disposable (buying and disposal costs).		
	Facility management	? Installation of facilities, e.g. upgrade existing facilities, install new facilities e.g. sinks in classrooms.		
		Maintenance of facilities – cleaning, prevention of vandalism.		
	Time	Teacher time – supervise handwashing, when scheduled it could use up teaching time. Student time – effective handwashing takes around 1 minute, could have a queue situation.		
	Set up costs	Teacher training, child instruction – could involve educational materials.		

	Elements making up cost		Source of data	Estimated cost £
HAND SANITIZERS	Hand sanitizer	Cost of product		
		Cost of maintenance		
		Cost of installation		
		Cost of storage – possible fire hazard		
		Cost of additional hand products e.g. moisturizers.		
		Total costs	Guinan 2002[74] estimated that in 2000 the cost hand sanitizer would be $2 per child per year.	[£1.28] per child per year (seems very low)

CONTROL

	Elements making up cost		Source of data	Estimated cost £
CONTROL - STANDARD HANDWASHING PROVISION	Water costs	Water supply		
		Water heating?		
	Soap	Soap supply		
		? moisturizer supply		
	Drying facilities	Electric dryer		
		Linen roller towels		
		Paper towels.		
	Facility management	Maintenance of facilities – cleaning, prevention of vandalism.		
	Time	Teacher time. Student time.		

COST OF INFECTION (INCLUDING AND EXCLUDING ABSENCE FROM SCHOOL OR DAY CARE CENTRE)

	Elements making up cost		Source of data	Estimated cost £
Direct costs	Medical costs	NHS direct consultation	Cost for all ages per call = £15.11. HPA burden of disease report[10]	
		GP visit	a). Surgery consultation lasting 10 minutes, including direct care staff costs, with qualification costs (any disease). b). Average costs incurred by patient when attending a GP surgery (any disease). Curtis & Netten 2005[98]	a). £24 b). £7.60
		Visit to hospital	a). A&E (any disease) b). Paediatrics. (any disease) Curtis & Netten 2005[98]	a). Cost per first attendance range £75 to £118. National average £110 b). Cost per first attendance range £158 to £262. National average £206. ? is this per day.
		Diagnostic tests Need to speak to a paediatrician or GP.	Lambert 2004[90]: (ILI)Aus$5. (recorded as a chest x-ray therefore could we get the cost of chest x ray. Other tests of diarrhoea could be FOB, fluid and electrolyte blood tests.	[£2.34] (seems a very low amount for a chest x-ray)
		Over the counter medication	Lambert 2004[90]: (ILI) OTC/natural medicines = Aus$10.72 units (2001 prices).	[£5.03]
Indirect costs	Societal costs – child absent from school	Teacher time – cost of remedial work, take home assignments	Guinan 2002[74]: 1 hour of teacher time per episode at an hourly rate of $50 (USA 2000)	[£31.90]
		Parental absence from work	Lambert 2004[90] gives costs for this, but got them from weekly earnings ect – perhaps we could find some GB data in this area.	
		Baby sitter time	As above.	
		Time taken seeking health care	Included in GP costs.	

8 REFERENCES

1 Goldmann DA. Transmission of viral respiratory infections in the home. *Pediatr Infect Dis J* 2000; **19**(10 Suppl):S97-102.
2 Cleary,V, Slaughter,R, Heathcock,R. An infection control programme in primary schools and wider public health impact. *British Journal of Infection Control* **4**[5], 11-16.2003
3 PRODIGY Guidance - Common Cold. URL: www.prodigy.nhs.uk/guidance [accessed 21-2-06]
4 BMA association. Infection control. 1st ed. London: Edward Arnold; 1989.
5 Nystad W, Skrondal A, Magnus P. Day care attendance, recurrent respiratory tract infections and asthma. *Int J Epidemiol* 1999; **28**(5):882-887.
6 Angelakou V, Bitsori M, Galanakis E. Asthma and early childhood infectious disease. Infection is trigger rather than cause. *BMJ* 2001; **323**(7305):164.
7 Frenck Jr,RW, Glezen,WP. Respiratory tract infections in children in day care. *Seminars in Pediatric Infectious Diseases* **1**[2], 234-244.1990
8 Pickering LK, Evans DG, DuPont HL, Vollet JJ, III, Evans DJ, Jr. Diarrhea caused by Shigella, rotavirus, and Giardia in day-care centers: prospective study. *J Pediatr* 1981; **99**(1):51-56.
9 Annonymous. Your Keyboard has More Germs than your Loo Seat. URL: www.unotron.com/US/newsarticles [accessed 25-1-06]
10 Health Protection Agency,U. Health Protection in the 21st Century - Understanding the Burden of Disease; preparing for the future. URL: www.hpa.org.uk/publications [accessed 3-2-06]
11 Benenson AS. Control of Communicable Diseases Manual. 16th ed. Washington: American Public Health Association; 1995.
12 Saunders NR, Tennis O, Jacobson S, Gans M, Dick PT. Parents' responses to symptoms of respiratory tract infection in their children. *CMAJ* 2003; **168**(1):25-30.
13 Department for Education and Skills (DfES). Pupil Absence in Schools in England 2004/05 (Revised). URL: www.dfes.gov.uk/rsgateway/DB/SFR/ [accessed 27-2-06].
14 Blyth E, Milner J. Improving School Attendance. 1st ed. London: Routledge; 1999.
15 Haskins R, Kotch J. Day care and illness: evidence, cost, and public policy. *Pediatrics* 1986; **77**(6 Pt 2):951-982.
16 Bell DM, Gleiber DW, Mercer AA, Phifer R, Guinter RH, Cohen AJ, *et al*. Illness associated with child day care: a study of incidence and cost. *Am J Public Health* 1989; **79**(4):479-484.
17 Lambert SB, O'Grady KF, Gabriel SH, Nolan TM. Respiratory illness during winter: a cohort study of urban children from temperate Australia. *J Paediatr Child Health* 2005; **41**(3):125-129.
18 Joseph C, Noah N, White J, Hoskins T. A review of outbreaks of infectious disease in schools in England and Wales 1979-88. *Epidemiol Infect* 1990; **105**(2):419-434.
19 Morgan P, Gitchell J, Stanker P, Ljunghag M. Assessment of upper respiratory infections in the school-age child. *Nurse Pract* 1984; **9**(1):48-49.
20 Mottonen M, Uhari M. Absences for sickness among children in day care. *Acta Paediatr* 1992; **81**(11):929-932.
21 Klein JO. Infectious diseases and day care. *Rev Infect Dis* 1986; **8**(4):521-526.
22 Petersen NJ, Bressler GK. Design and modification of the day care environment. *Rev Infect Dis* 1986; **8**(4):618-621.
23 Vihma L. Virus isolations from children with acute respiratory illness. A comparison of a family study group and a group of nursery infants. *Acta Paediatr Scand* 1967;Suppl.
24 Kaltenthaler EC, Elsworth AM, Schweiger MS, Mara DD, Braunholtz DA. Faecal contamination on children's hands and environmental surfaces in primary schools in Leeds. *Epidemiol Infect* 1995; **115**(3):527-534.
25 Pickering LK, Bartlett AV, Woodward WE. Acute infectious diarrhea among children in day care: epidemiology and control. *Rev Infect Dis* 1986; **8**(4):539-547.
26 Colombet G, Croize J, Pavese P, Chanteperdrix V, Stahl JP. Screening bacterial hand carriage in schools. A tool for hygiene education. *Medecine et Maladies Infectieuses* 2003; **. 33**(6):01.
27 Fleming DW, Cochi SL, Hightower AW, Broome CV. Childhood upper respiratory tract infections: to what degree is incidence affected by day-care attendance? *Pediatrics* 1987; **79**(1):55-60.

28 Uhari M, Mantysaari K, Niemela M. A meta-analytic review of the risk factors for acute otitis media. *Clin Infect Dis* 1996; **22**(6):1079-1083.
29 Denny FW, Collier AM, Henderson FW. Acute respiratory infections in day care. *Rev Infect Dis* 1986; **8**(4):527-532.
30 Doyle AB. Incidence of illness in early group and family day-care. *Pediatrics* 1976; **58**(4):607-613.
31 Anderson LJ, Parker RA, Strikas RA, Farrar JA, Gangarosa EJ, Keyserling HL, *et al*. Day-care center attendance and hospitalization for lower respiratory tract illness. *Pediatrics* 1988; **82**(3):300-308.
32 Johnston SL, Pattemore PK, Sanderson G, Smith S, Campbell MJ, Josephs LK, *et al*. The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. *Am J Respir Crit Care Med* 1996; **154**(3 Pt 1):654-660.
33 Hernández SF, Morales HR, Cuevas RP, Gallardo HG. The day care center as a risk factor for acute respiratory infections. *Archives of Medical Research* 1999; **30**:216-223.
34 Petersson C, Hakansson A. A retrospective study of respiratory tract infections among children in different forms of day care. *Scand J Prim Health Care* 1990; **8**(2):119-122.
35 Nafstad P, Hagen JA, Oie L, Magnus P, Jaakkola JJ. Day care centers and respiratory health. *Pediatrics* 1999; **103**(4 Pt 1):753-758.
36 Holberg CJ, Wright AL, Martinez FD, Morgan WJ, Taussig LM. Child day care, smoking by caregivers, and lower respiratory tract illness in the first 3 years of life. Group Health Medical Associates. *Pediatrics* 1993; **91**(5):885-892.
37 Lunn JE, Knowelden J, Handyside AJ. Patterns of respiratory illness in Sheffield infant schoolchildren. *Br J Prev Soc Med* 1967; **21**(1):7-16.
38 Uldall P. Forms of care and children's infections. 1. Occurrence and causal factors. *Ugeskr Laeger* 1990; **152**(33):2345-2348.
39 Kvaerner KJ, Nafstad P, Jaakkola JJ. Upper respiratory morbidity in preschool children: a cross-sectional study. *Arch Otolaryngol Head Neck Surg* 2000; **126**(10):1201-1206.
40 Taskinen T, Hyvarinen A, Meklin T, Husman T, Nevalainen A, Korppi M. Asthma and respiratory infections in school children with special reference to moisture and mold problems in the school. *Acta Paediatr* 1999; **88**(12):1373-1379.
41 Rylander R, Megevand Y. Environmental risk factors for respiratory infections. *Arch Environ Health* 2000; **55**(5):300-303.
42 Nafstad P, Hagen JA, Botten G, Jaakkola JJ. Lower respiratory tract infections among Norwegian infants with siblings in day care. *Am J Public Health* 1996; **86**(10):1456-1459.
43 Monto AS. Studies of the community and family: acute respiratory illness and infection. *Epidemiol Rev* 1994; **16**(2):351-373.
44 Sterne GG, Hinman A, Schmid S. Potential health benefits of child day care attendance. *Rev Infect Dis* 1986; **8**(4):660-662.
45 Mattey EA. Teach us body sense (TUBS): a health education program for primary students. *Pediatr Nurs* 1996; **22**(6):545-551.
46 Endericks,T. Health Protection Agency - Board Meeting Thusday 23 September 2003. Enclosure 04/105. URL: www.hpa.org.uk/hpa/board_meetings/docs_ 2004/040923/child_health_prog.pdf [accessed 27-1-06]
47 Curtis V, Biran A, Deverell K, Hughes C, Bellamy K, Drasar B. Hygiene in the home: relating bugs and behaviour. *Soc Sci Med* 2003; **57**(4):657-672.
48 Food Standards Agency. Largest ever survey of catering staff shows that one in three do not wash their hands after visiting the lavatory.
49 Hand washing. *BMJ* 1999; **318**(7185):686.
50 Jordan R, Connock M, Albon E, Fry-Smith A, Olowokure B, Hawker J, *et al*. Universal vaccination of children against influenza: are there indirect benefits to the community? A systematic review of the evidence. *Vaccine* 2006; **24**(8):1047-1062.
51 Connock M, Jordan R, Fry-Smith A, Chen Y-F, Hawker J, Albon E, *et al*. Influenza vaccination of children and household contacts for the indirect protection of others: A systematic review of clinical and cost effectiveness. *DPHE* 2005; **Report Number 53**.
52 Collins Gem. English Dictionary. New Edition ed. Harper Collins; 2000.
53 Department of Health. Guidance on Infection Control in Schools and Nurseries. URL: www.wiredforhealth.gov.uk/PDF/infect_poster.pdf [accessed 2-2-06]
54 Centers for Disease Control and Prevention. Guideline for Hand Hygiene in Health-Care Settings. *Morbidity and Mortality Weekly Report.* **51**[RR-16].2002

55 NHS Estates. NHS Estates Alert.Gateway Ref: 5084. URL: www.nhsestates.gov.uk [accessed 3-2-06]
56 WHO. WHO Guidlines for Hand Hygiene in Health Care Settings. Geneva: 2004. Report No.:
57 Ibrahim,T, Smith,M. The Dangers of wall-mounted hand gel dispensers. *Journal of Hospital Infection* **54**[1], 82.2003
58 Lee GM, Salomon JA, Friedman JF, Hibberd PL, Ross-Degnan D, Zasloff E, *et al*. Illness transmission in the home: a possible role for alcohol-based hand gels. *Pediatrics* 2005; **115**(4):852-860.
59 Bog Standard - Better toilets for pupils. URL: WWW.bog-standard.org [accessed 23-1-06]
60 Children's Commissioner for Wales. Lifting the lid on the nations school toilets. *www childcomwales org uk (accessed 23-1-06)* 2004.
61 Department for Education and Skills (DfES). Qualifications and Curriculum Authority. URL: www.qca.org.uk [accessed 27-2-06]
62 Local Healthy Schools Programme Contacts: West Midlands Region. URL: www.1hsp.org [accessed 25-1-06]
63 Curtis V, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *The Lancet Infectious Diseases* 2003; **3**(5):275-281.
64 Meadows E, Le Saux N. A systematic review of the effectiveness of antimicrobial rinse-free hand sanitizers for prevention of illness-related absenteeism in elementary school children. *BMC Public Health* 2004; **4**(1):50.
65 Ehiri,JE, Ejere,HOD. Hand washing for Preventing Diarrhoea (Protocol). *The Cochrane Database of Systematic Reviews.* **Issue 2**.2003
66 National Patient Safety Agency. The Economic Case - Implementing near-patient alcohol handrub in your trust. URL: www.npsa.nhs.uk/site/media/documents/674_full_economic_case_pdf [accessed 7-3-06]
67 Higgins,JPT, Green.S. Cochrane Handbook for Systematic Revies of Interventions 4.2.5 (updated Many 2005).
68 Kirkwood BR, Sterne AC. Essential Medical Statistics. 2nd Edition ed. Oxford: Blackwell Science; 2003.
69 Donner A, Klar N. Design and analysis of cluster randomization trials in health research. 1st ed. New York: Oxford University Press; 2000.
70 White CG, Shinder FS, Shinder AL, Dyer DL. Reduction of illness absenteeism in elementary schools using an alcohol-free instant hand sanitizer. *J SCH NURS* 1923; **2001 Oct; 17**(5):258-265.
71 Morton JL, Schultz AA. Healthy Hands: Use of alcohol gel as an adjunct to handwashing in elementary school children. *J SCH NURS* 2004; **20**(3):161-167.
72 Niffenegger JP. Proper handwashing promotes wellness in child care. *J Pediatr Health Care* 1997; **11**(1):26-31.
73 Kimel LS. Handwashing education can decrease illness absenteeism. *J SCH NURS* 1996; **12**(2):14-6, 18.
74 Guinan M, McGuckin M, Ali Y. The effect of a comprehensive handwashing program on absenteeism in elementary schools. *AM J INFECT CONTROL* 1912; **2002 Jun; 30**(4):217-220.
75 Master D, Hess Longe SH, Dickson H. Scheduled hand washing in an elementary school population. *Family Medicine* 1997; **29**(5):336-339.
76 Hammond B, Ali Y, Fendler E, Dolan M, Donovan S. Effect of hand sanitizer use on elementary school absenteeism. *AM J INFECT CONTROL* 2000; **28**(5):340-346.
77 Dyer DL, Shinder A, Shinder F. Alcohol-free instant hand sanitizer reduces elementary school illness absenteeism. *Family Medicine* 2000; **32**(9):633-638.
78 US Office of Education. Structure of Education in the US.
79 Kotch JB, Weigle KA, Weber DJ, Clifford RM, Harms TO, Loda FA, *et al*. Evaluation of an hygienic intervention in child day-care centers. *Pediatrics* 1994; **. 94**(6 **II**).
80 Uhari M, Mottonen M. An open randomized controlled trial of infection prevention in child day-care centers. *Pediatric Infectious Disease Journal* 1999; **. 18**(8).
81 Roberts L, Jorm L, Patel M, Smith W, Douglas RM, McGilchrist C. Effect of infection control measures on the frequency of diarrheal episodes in child care: A randomized, controlled trial. *Pediatrics* 2000; **105**(4 **I**).

82 Roberts L, Smith W, Jorm L, Patel M, Douglas RM, McGilchrist C. Effect of infection control measures on the frequency of upper respiratory infection in child care: a randomized, controlled trial. *Pediatrics* 2000; **105**(4 Pt 1):738-742.
83 Ponka A, Poussa T, Laosmaa M. The effect of enhanced hygiene practices on absences due to infectious diseases among children in day care centers in Helsinki. *Infection* 2004; **32**(1):2-7.
84 Morton JL, Schultz AA. Healthy hands: use of alcohol gel as an adjunct to handwashing in elementary school children. *J SCH NURS* 1916; **2004 Jun; 20**(3):161-167.
85 Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. Second Edition ed. Oxford: Oxford University Press; 1986.
86 Ackerman SJ, Duff SB, Dennehy PH, Mafilios MS, Krilov LR. Economic impact of an infection control education program in a specialized preschool setting. *Pediatrics* 2001; **108**(6):E102.
87 Rubino JR. Economic impact of a healthy school environment. *J SCH NURS* 2002; **Suppl**:27-30.
88 Duff SB, Mafilios MS, Ackerman SJ. Economic evaluation of infection control practices in day care and the home: methodologic challenges and proposed solutions. *Pediatr Infect Dis J* 2000; **19**(10 Suppl):S125-S128.
89 Carabin H, Gyorkos TW, Soto JC, Penrod J, Joseph L, Collet JP. Estimation of direct and indirect costs because of common infections in toddlers attending day care centers. *Pediatrics* 1999; **103**(3):556-564.
90 Lambert S, O'Grady KA, Gabriel S, Carter R, Nolan T. The cost of seasonal respiratory illnesses in Australian children: the dominance of patient and family costs and implications for vaccine use. *Commun Dis Intell* 2004; **28**(4):510-516.
91 Murray DM, Short BJ. Intraclass correlation among measures related to tobacco use by adolescents: estimates, correlates, and applications in intervention studies. *Addict Behav* 1997; **22**(1):1-12.
92 Campbell MK, Elbourne DR, Altman DG. The CONSORT statement for cluster randomised trials. *Med Clin (Barc)* 2005; **125 Suppl 1**:28-31.
93 Chuang JH, Hripcsak G, Heitjan DF. Design and analysis of controlled trials in naturally clustered environments: implications for medical informatics. *J Am Med Inform Assoc* 2002; **9**(3):230-238.
94 Kerry SM, Bland JM. Analysis of a trial randomised in clusters. *BMJ* 1998; **316**(7124):54.
95 Piaggio G, Carroli G, Villar J, Pinol A, Bakketeig L, Lumbiganon P, *et al*. Methodological considerations on the design and analysis of an equivalence stratified cluster randomization trial. *Stat Med* 2001; **20**(3):401-416.
96 Klar N, Donner A. Current and future challenges in the design and analysis of cluster randomization trials. *Stat Med* 2001; **20**(24):3729-3740.
97 Kerry SM, Bland JM. The intracluster correlation coefficient in cluster randomisation. *BMJ* 1998; **316**(7142):1455.
98 Curtis,L,Netten,A. Unit Costs of Health & Social Care. University of Kent: PSSRU; 2005. Report No.: www.pssru.ac.uk [accessed 3-4-06].

UNIVERSITY OF
BIRMINGHAM
Edgbaston, Birmingham,
B15 2TT, United Kingdom

ISBN No: 07044 26102

www.bham.ac.uk

Price: £15.00