NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Public Health & Social Care Centre

Supplementary evidence review – patient/public education antimicrobial resistance and infection prevention interventions with prescribing rates and incidence of infection as outcome measures

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Contents

Acknowledgements

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Introduction

The RAND evidence review for the 'Antimicrobial stewardship: Changing risk-related behaviours in the general population' guideline was discussed in the Antimicrobial stewardship PHAC meeting on 12th May 2015. The Committee discussed the exclusion of studies that only measured prescribing rates as an outcome. The rationale for excluding these studies was that prescribing is a behaviour that is under the control of a prescriber, not the patient. Without any direct measure of patients' knowledge or behaviour (for example changes in consultation rates) it was felt that it is not possible to determine whether changes in prescribing are caused by changes in patients' or prescribers' behaviour. However, the Committee felt that if an intervention was solely targeting patients or the general public, that prescribing rates may be a reasonable outcome measure. This is because changes in patient behaviour may be affecting doctors' prescribing habits (for example a patient deciding not to ask a GP for antibiotics or consulting a doctor about cold or flu symptoms, may in turn lead to reductions in prescribing). In response to these discussions the NICE team agreed to screen the list of studies excluded at full paper stage from the evidence review and to review any patient/public education-only studies that were excluded on the basis that they reported prescribing rates (and no direct measures of patient knowledge or behaviour). On screening the excluded paper list the NICE team felt that papers excluded on the basis of reporting incidence of infection should also be included as changes to incidence of infection following an intervention may well be due to changes in behaviour. It had been previously agreed with the review team (RAND) at full paper stage that these papers did not need to be included in the review due to the volume of included papers.

Given that this is a rapid supplementary review only evidence statements, quality assessment tables and evidence tables have been provided in this report (i.e. only a brief methods section and no study summaries, synthesis or discussion).

Methods

Two reviewers went through all the titles and abstracts of the papers excluded at full paper stage from the RAND evidence review on the basis of reporting prescribing rates (n=13) or incidence of infection (n=5) (see Appendix A). Each reviewer independently decided whether a paper should be included or not on the basis that it reported prescribing rates and/or incidence of infection and was relevant to the key research questions set out in the Scope:

Question 1: Which educational interventions are effective and cost effective in changing the public's behaviour to ensure they only ask for antimicrobials when appropriate and use them correctly?

Question 2: Which educational interventions are effective and cost effective in changing the public's behaviour to prevent infection and reduce the spread of antimicrobial resistance?

At the end of the process any papers where there was disagreement or uncertainty about inclusion were discussed between them.

In order to ensure quality assessment was consistent with the RAND evidence review, RAND agreed to undertake the quality assessment of all included papers (see Table 1). In addition, they provided the data extraction, study summaries and draft evidence statement text for two included papers (Little et al. *in press*[1] and Francis et al. 2009). All other work was undertaken by the NICE team.

Results

Four papers were identified from the excluded list of papers in the RAND review that met our inclusion criteria of patient/public education-only interventions with prescribing rates as an outcome. One other paper that is included in the RAND review (Francis et al. 2009) which reported on outcomes other than prescribing rate was also included to ensure that the ensuing evidence statements were representative of studies assessing the effect of patient education on prescribing rates. All five included studies targeted patient populations and focussed on respiratory illnesses.

There were also four papers identified from the excluded list of papers in the RAND review that reported on incidence of respiratory or gastrointestinal illnesses following an infection prevention intervention. One relevant *in press* paper (Little et al.) that had been provided by a committee member was also included. All five studies included education on hand hygiene.

Evidence statements

Research question 1

Patient-targeted education interventions with antibiotic prescribing as main outcome

Evidence statement 1 Parental education interventions targeting antibiotic prescribing for children's respiratory tract infections in primary care

There is inconsistent evidence from four studies (RCT (++)[1],cluster RCT (+)[2], non-RCT (+)[3] and a before-and-after study (+)[4]) concerning whether parental education interventions lead to a reduction in prescribing antibiotics for children's respiratory tract infections within primary care. All three US studies[1,3,4] found no effect, while the one UK study[2] found a significant decrease in antibiotic prescribing following a patient education intervention. Interventions all involved written materials but differed in format, content, additional intervention components and mode of delivery. Baseline prescribing levels also differed between studies.

[1] Published in The Lancet, Online 06 August 2015; DOI: http://dx.doi.org/10.1016/S0140-6736(15)60127-1

One RCT[1] (++) (US; n=247 control, n=252 intervention) found no significant difference in the mean number of prescribed antibiotics for upper respiratory tract infections symptoms between the intervention (parent received a pamphlet and videotape on the judicious use of antibiotics) and control (parent received a brochure on injury prevention) in children younger than 24 months. The number of antibiotic prescriptions per patient: 2.2 $\pm$ 2.6 vs 2.5 $\pm$ 2.9 in the intervention vs control respectively over 12 month study period; *P*=0.23.

One cluster-RCT[2] (+) (England and Wales; n=31 control practices, n=30 intervention practices) assessed whether a patient education booklet for parents of children (aged 6 months to 14 years) presenting with acute respiratory tract infections, delivered by clinicians trained to use it during consultations and given as a take-home resource, led to a reduction in antibiotic prescribing. The patient education booklet provided information on prognosis, treatment options and reasons for re-consultation. The intervention led to significant reductions in self-reported antibiotic prescription rates (55.3% in intervention vs. 76.4% in control; aOR=0.29 [95%CI: 0.14 to 0.60]).

One non-RCT[3] (+) (US; n=362 local control practices and n=65 distant control practices, n=7 intervention practices) assessed the addition of patient education to an existing healthcare professional targeted intervention on reducing antibiotic prescribing for children with pharyngitis (sore throat) aged from 0 to 17 years old. The patient education consisted of posting 'Be S.M.A.R.T. about antibiotics campaign materials to households, plus examination room posters, waiting room posters and leaflets. There was no effect of the patient education intervention on antibiotic prescribing: adjusted antibiotic prescription rates pre- and post-intervention: 38% to 39 % at the distant control practices, 39% to 37% at local control practices, and from 34% to 30% at the intervention practices (*P*=0.18 and *P*=0.48 for intervention practices compared with distant and local control practices, respectively).

One BA study[4] (+) (US; n=540 historic controls, n=180 intervention) found that waiting room posters placed in paediatric practices on 'a parent's guide to help understanding colds and viruses' had no effect on antibiotic prescribing for upper respiratory tract infections in children aged 6 months to 10 years old. The proportion of respiratory illness visits resulting in antibiotic prescriptions was 44.3% before the intervention and 48.3% after (*P*=0.79).

[1]Taylor et al. 2005 (++)

[2]Francis et al 2009 (+)

[3]Gonzales et al. 2005 (+)

[4]Ashe et al. 2006 (+)

The evidence is only partially applicable to the UK patient population as the majority of studies were conducted in the US.

Evidence statement 2 Education interventions targeting antibiotic prescribing for adults' respiratory tract infections in primary care

There is inconsistent evidence from two US non-RCT studies (+)[1,2] concerning whether education interventions lead to a reduction in prescribing antibiotics for adults' respiratory tract infections within primary care.

One non-RCT[1] (+) (n=362 local control practices and n=65 distant control practices, n=7 intervention practices) assessed the addition of patient education to an existing healthcare professional targeted intervention on reducing antibiotic prescribing for adults with acute bronchitis aged from 18 to 64 years old. The patient education consisted of posting 'Be S.M.A.R.T. about antibiotics campaign materials to households, plus examination room posters, waiting room posters and leaflets. There was a significant decrease in antibiotic prescribing following the intervention: adjusted antibiotic prescription rates pre- and post-intervention: 50% to 44% at the distant control practices, 55% to 45% at local control practices, and from 60% to 36% at the intervention practices (*P*<0.002 and *P*=0.006 for intervention practices compared with distant and local control practices, respectively).

One non-RCT[1] (+) (n=51 control practices, n=4 intervention practices) assessed the same intervention as that described above[1], but with adults aged 65 to 85 years old with acute respiratory tract infections (ARIs). The educational intervention was not effective at reducing antibiotic prescription rates for ARIs: prescription rate decreased from 51% to 49% at control practices and from 45% to 40% at intervention practices (*P*=0.79 after adjusting for patient age, chronic obstructive pulmonary disease, specific ARI diagnosis, and practice-level clustering).

[1]Gonzales et al. 2005 (+)

[2]Gonzales et al. 2004 (+)

The evidence is only partially applicable to the UK patient population as both studies were conducted in the US.

Research question 2

Hand hygiene interventions measuring the incidence of infections

Evidence statement 1 Hand hygiene interventions delivered in day/child care centre populations to reduce the incidence or transmission of infections

There is moderate evidence from 3 studies (One non RCT[1] (+) one cluster RCT (++[2]) and one non-RCT(-[3])) that hand hygiene interventions targeting day/child care

centre staff and/or children and/or their parents do not reduce the incidence of getting a respiratory or gastrointestinal illness but may reduce the onward transmission of a gastrointestinal illness to others.

One non-randomised study[1] (+) (Iceland; n=30 day care centres, 2,349 children aged 2 to 6 years old) found no difference in the incidence of febrile, respiratory, or gastrointestinal illnesses in day care centres involved in a hand and environmental hygiene intervention (n =15) compared to control day care centres (n = 15). Crude and adjusted incidence rate ratios of the illnesses were not significantly different for any of the illnesses between baseline and intervention period. The intervention lasted for 1.5 years and consisted of regular hygiene education to staff and children; staff also received hand washing training, instruction on use of gloves, use of disposable nose wipes for children and washing of toys, furniture, floors, doorknobs, and toilets. Self-reported compliance with the hygiene intervention was high.

One cluster RCT[2] (++) (US; n=292 families with children aged 6 months to 5 years old attending 26 child care centres) assessed the effectiveness of a hand hygiene intervention in which families were provided with hand sanitizers and biweekly hand-hygiene educational materials for 5 months; control families received materials on good nutrition. The intervention did not change the incidence of getting an illness in the first place (primary illness incidence rate measured as number of primary illnesses per susceptible person-month for intervention vs control for gastro-intestinal illnesses: 0.06 vs 0.05; for respiratory illnesses: 0.37 vs 0.37). The intervention did significantly lower the onward transmission of gastrointestinal illnesses from one family member to another when compared to control families (IRR:0.41; 95% CI: 0.19–0.90; p=0.03). It did not reduce the onward transmission of respiratory illnesses (IRR: 0.97; 95% CI: 0.72-1.30; p=0.83).

One non-RCT[3] (-) (Sweden; n=6 day care centres with 292 children aged 1 to 5 years old) found that a hygiene education intervention did not have an effect on parent-reported sickness absence (10.5±8.6 days vs 11.2±7.4 days in intervention vs control respectively), incidence of respiratory illnesses (55.9% vs 61.6%) or gastroenteritis (17.7% vs 13.9%), doctor's consultations (47% vs 59%) or antibiotic prescriptions (38% vs 42% given antibiotics) in children. The intervention consisted of providing guidelines to staff on how to handle infections in children and reduce infection in day-care centres, providing liquid soap and paper towels (instead of terry towels and bars of soap); information posters were placed near entrances and parents were provided with verbal information in to meetings on infectious diseases and their spread, use of antibiotics and risk of antimicrobial resistance. Control day care centres received no intervention.

[1]Gudnason et al. 2013 (+)

[2]Sandora et al. 2005 (++)

[3]Hedin et al. 2006 (-)

The evidence is only partially applicable to the UK child and day care centre populations as none of the studies were undertaken in the UK – studies were undertaken in Iceland, Sweden and the US.

IRR: incidence rate ratio

Evidence statement 2 Hand hygiene interventions delivered in schools

There is weak evidence from one US non-RCT[1] (-) that regular hand hygiene education delivered in schools in combination with the provision of hand sanitizers and information posters (intervention) compared to the provision of hand sanitizers and information posters alone (control) may reduce the incidence of illnesses when contagious illnesses are at a high level. The study (n=773 students aged 6 to 14 years allocated to intervention or control by classroom in two schools) reported that the percentage of respiratory and gastrointestinal illness-related absent days was significantly lower in the intervention group compared to the control group during flu season (October to December: 1.15% vs 1.57% respectively; *P*<0.001) but not across the whole academic year (October to May: 1.23% vs 1.26% respectively; *P*=NR).

[1]Lau et al. 2012 (-)

The evidence is only partially applicable to the UK as the study was conducted in the US.

Evidence statement 3 Web-based hand hygiene interventions aimed at adults

There is moderate evidence from one RCT[1] (++) (UK; n=20,066) that a bespoke web-based intervention reduces the incidence of respiratory illnesses. The intervention included prompt emails sent once a month to encourage participants to use the sessions, and to maintain hand washing. It was aimed at adults registered on participating GPs list. The intervention successfully reduced episodes of respiratory infections (p<0.0001), the total number of days of infection (p<0.001), transmission to other household members (p<0.001) and led to shorter duration of illness (p<0.001) in the 16 weeks following randomisation. The intervention also resulted in fewer consultations with either a GP or contact with health services for respiratory infection type symptoms at both 16 weeks (p=0.014) and 12 months (p=0.001) post intervention and a reduction in the number of antibiotic prescriptions at both 16 weeks (p=0.002) and 12 months (p<0.001).

[1]Little et al. *in press* (++)

The evidence is directly applicable to the UK adult population.

Table 1 Quality Assessment of Included Studies

Reference	Design	Population			Method of allocation to intervention/comparison										Outcomes						Analyses						Summary	
		1.1	1.2	1.3	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	2.10	3.1	3.2	3.3	3.4	3.5	3.6	4.1	4.2	4.3	4.4	4.5	4.6	5.1	5.2
Ashe et al. 2006	BA	(++)	(+)	(++)	NA	(++)	NA	NA	(+)	NA	NA	(++)	(++)	(++)	(++)	(++)	NA	NA	NA	(+)	NR	(++)	(++)	(+)	(++)	(+)	(+)	(++)
Francis et al. 2009	Cluster RCT	(++)	(++)	(++)	(++)	(+)	NR	(-)	(++)	NR	NR	(+)	(++)	(++)	(+)	(++)	NA	NA	(++)	(+)	NR	(+)	(++)	(++)	(+)	(++)	(+)	(++)
Gonzales et al. 2004	Non-RCT	(++)	(+)	(++)	NR	(++)	NR	NA	(++)	NR	NR	NA	(++)	(++)	(++)	(++)	NA	NA	(++)	(+)	(+)	NA	(++)	(+)	(++)	(+)	(+)	(++)
Gonzales et al. 2005 (includes data from 2004)	Non-RCT	(++)	(+)	(++)	NR	(++)	NR	NA	(++)	NR	NR	NA	(++)	(++)	(++)	(++)	NA	NA	(++)	(+)	(++)	NA	(++)	(+)	(++)	(+)	(+)	(++)
Gudnason et al. 2013	Non-Randomised study	(++)	(++)	(++)	NR	(++)	NR	NA	(++)	NR	NR	NA	(++)	(++)	(++)	(++)	NA	NA	(++)	(++)	(+)	NA	(+)	(++)	(++)	(++)	(+)	(++)
Hedin et al. 2006	non-RCT	(++)	(+)	(+)	(+)	(+)	NR	NA	(+)	NR	NR	(+)	(++)	(++)	(++)	(+)	NA	NA	(++)	(++)	(-)	NA	(+)	(++)	(-)	(+)	(-)	(+)
Lau et al. 2012	non-RCT	(++)	(+)	(+)	(+)	(++)	NA	NA	(+)	NR	NR	(+)	(++)	(++)	(+)	(++)	NA	NA	(++)	(++)	NR	NA	(+)	(+)	(-)	(+)	(-)	(+)
Little et al. (*in press*)	RCT	(++)	(++)	(++)	(++)	(++)	(++)	NA	(+)	NR	NR	(+)	(++)	(++)	(+)	(++)	NA	NA	(++)	(++)	(++)	(++)	(++)	(++)	(++)	(++)	(++)	(++)
Sandora et al. 2005	Cluster RCT	(++)	(+)	(++)	(++)	(+)	(++)	NA	(+)	NR	NR	(+)	(++)	(++)	(+)	(++)	NA	NA	(++)	(++)	(++)	(++)	(++)	(++)	(++)	(++)	(++)	(++)
Taylor et al. 2005	RCT	(++)	(+)	(++)	(++)	(++)	(++)	NA	(+)	NR	NR	(++)	(++)	(++)	(++)	(++)	NA	NA	(++)	(++)	(++)	(++)	(++)	(+)	(++)	(++)	(++)	(++)

Shaded cells are criteria that are key to the overall quality assessment of the RCTs

Key to questions:

Population

1.1 Is the source population or source area well described? (RAND Europe note: The 'population' could be at the community level or have been more specific (e.g. such as parents of children in a day care centres). The authors had to describe the population in enough detail so that it would be possible to replicate the study).

1.2 Is the eligible population or area representative of the source population or area? (RAND Europe note: To answer this question, we considered the method of recruitment reported by the study authors: Is it likely to have missed important demographic groups? Were all eligible participants enrolled? Did study authors choose a sub-selection of 1.1 for inclusion?).

1.3 Do the selected participants or areas represent the eligible population or area? (RAND Europe note: This was difficult to assess in many of the pre-post papers reviewed as the selected participants were the same as the source population (e.g. if the authors included parents of children attending a day care centre in a particular region of the US). In this example, the source population was narrow (i.e. parents of children in day care centres), and as such, the selected participants are the same as the source population. For RCTs, this criteria was judged as adequate if clear inclusion/exclusion criteria were reported in the study, and if there were no other sources of bias (for example, a source of bias would be if there was a difference between samples who agreed to participate, and those who did not agree to participate).

Method of Allocation

2.1 Was selection bias minimised? (RAND Europe note: For RCTs, we considered this adequate if the method of randomisation was reported in detail, and the authors used an appropriate methodology (e.g. random numbers tables).

2.2 Were interventions (and comparisons) well described and appropriate? (RAND Europe note: For most of the studies, we considered that the interventions and comparisons were appropriate, so that we focused on whether or not they were well described).

2.3 Was the allocation concealed?

2.4 Were participants and/or investigators blind to exposure and comparison?

2.5 Was the exposure to the intervention and comparison adequate? (RAND Europe note: We considered that educational interventions that were person-delivered (e.g. by a teacher or a GP would be adequate because it is likely that the participant received [and understood] the intervention (++); in contrast, educational interventions delivered through posters or mass media do not guarantee exposure. Those studies that reported high levels of exposure were rated as '+', whereas those who did not provide an estimate of exposure, or reported a low degree of exposure, where rated as '-')

2.6 Was contamination acceptably low?

2.7 Were other interventions similar in both groups?

2.8 Were all participants accounted for at study conclusion? (RAND Europe note: We considered a loss to follow-up greater than 20% as '-').

2.9 Did the setting reflect usual UK practice? (RAND Europe note: most of the types of interventions evaluated in this review (e.g. leaflets, posters, teaching, etc. given in a community or primary care setting.) were considered to be applicable to the UK).

2.10 Did the intervention or control comparison reflect usual UK practice?

Outcomes:

3.1 Were outcome measures reliable? (RAND Europe note: As this review focuses on behaviour and attitude, etc. most of the measures were self-reported. Measures that used a validated questionnaire and/or were observed were rated ad '++'; those that used a self-reported questionnaire were rated as '+', unless any obvious source of bias was detected).

3.2 Were all outcome measurements complete?

3.3 Were all important outcomes assessed? (RAND Europe note: As no harms were applicable/evaluated in this review, we did not consider this criterion to be relevant to our overall assessment of study quality)

3.4 Were outcomes relevant? (RAND Europe note: As we did include studies that evaluated surrogate outcome measures, we did not consider this criterion to be relevant to our overall assessment of study quality)

3.5 Were there similar follow-up times in exposure and comparison groups?

3.6 Was follow-up time meaningful? (RAND Europe note: Most studies had a short-term follow up; studies that reported outcomes immediately following intervention were rated as '-; Those with longer term follow-up were rated at '+' or '++' (>6 weeks).

Analyses

4.1 Were exposure and comparison groups similar at baseline? If not, were these adjusted?

4.2 Was Intention to Treat (ITT) analysis conducted?

4.3 Was the study sufficiently powered to detect an intervention effect (if one exists)? (RAND Europe note: If the authors reported power calculation using 0.8 and met that calculation, the study was rated as '++';If no power calculation was presented, but the sample size was relatively large (>200 individuals), the study was rated as '+'; If no power calculated was reported, and if the sample size was small, the study was rated as '-')

4.4 Were the estimates of effect size given or calculable?

4.5 Were the analytical methods appropriate (RAND Europe note: For this criterion, we also assessed whether or not important confounders controlled for in the analysis or if the authors provided reasons for not controlling for confounders).

4.6 Was the precision of intervention effects given or calculable? Were they meaningful?

Summary

5.1 Are the study results internally valid? (i.e. unbiased) (RAND Europe note: In order for RCTs to get a '++' rating, the trials must have reported adequate (i.e. a rating of '++') randomisation and allocation processes, used intention-to-treat (ITT) analysis, have controlled for confounding factors in the analysis, and had an adequate sample size. If most of

these criteria were given a '+' rating, the study was given an overall rating of '+'; if one or more of these criteria were not met (i.e. given a '-' rating), the study was given a '-'; In order for non-randomised or before-and-after studies to get a ++ rating, all criteria had to be adequately addressed (i.e. all of the individual criteria were scored as '++'); for a '+' rating, the majority criteria ratings had to be '+' or '++', (with no '-'); a study was given a '-' if there were one or more criteria were rated as '-')

5.2 Are the study results generalisable to the source population? (i.e. externally valid) (RAND Europe note: To evaluate external validity, we made a judgement regarding whether or not the findings of the study were generalizable beyond the confines of the study itself to the source population).

Evidence Tables

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
Author(s): Ashe et al **Year: 2005** **Citation: Educational Posters to Reduce Antibiotic Use** **Country of study: New York; USA** **Aim of study: Examined the effectiveness of a waiting room poster in reducing excessive antibiotic use in clinical practice.** **Study design: before and after Authors classified as a non-randomized control trial (historical control)** **Method of allocation: Random sampling was used to select 60 patient visits from each practice during each month of the study.** **Quality assessment: Internal (+); External (++)**	**Source population(s):** children between the ages of 6 months and 10 years at the time of a visit to diagnose and treat symptoms of respiratory illness - 7 of 10 clinicians across 3 sites volunteered to participate in the study **Overall sample size at start of study:** 720 patients **Number analysed at end of study: 720** **Inclusion/exclusion criteria:** The child was between 6 months and 10 years old at time of the visit; purpose of the visit was to diagnose and treat an acute illness; child or guardian reported symptoms of respiratory illness, **Participant characteristics:** Mean age: 4.2 years Gender: 369 boys (51.3%) and 351 girls (48.8%) **Race/ethnicity:** practices serve a patient population that is 80% White, 10% Latino, 5% Asian, and 5% African-American **Other:** **Are groups similar at**	**Description:** Intervention 3 sites- 1-month trial of an educational poster was carried out at three sites. Posters were placed in the reception area of each practice on December 1, 2001**.** **Sample sizes at baseline**: unclear as done by sites (n=3) outcomes outline 180 patients	**Description: control –** historical control same 3 sites but records of ABx prescriptions reviewed 1 month previously as a historical trial (November 2000, December 2000 and November 2001) **Setting:** same 3 sites **Sample sizes at baseline:** unclear as done by sites (n=3) outcomes outline 540 patients	**Outcomes evaluated:** Antibiotic prescriptions for children with respiratory illnesses seen during the poster month were compared with prescriptions written during three 1-month historical control periods. The proportion of visits that resulted in a prescription for an antibiotic **Length of follow-up:** 1-month **Method of analysis:** Multiple logistic regression analysis was used to compare the intervention and control months with respect to the percentage of visits resulting in a prescription for an antibiotic.	Public education in the form of a waiting room poster was not sufficient to decrease antibiotic prescriptions - 326 of the 720 patients (45.2%) enrolled in the study were treated with an antibiotic. Multiple logistic regression analysis revealed no statistically significant difference in the proportion of visits resulting in an antibiotic prescription among the 4 study months (P=.79). The proportion of respiratory illness visits resulting in antibiotic prescriptions was 44.3% before the intervention and 48.3% after indicating that the educational poster had no effect on antibiotic use Table a: Percent of visits for respiratory illnesses that resulted in an antibiotic prescription during each of the four study months **November** 2000 81/180*(45.0%) (C) 2001 64/180 (35.6%) (C) **December** 2000 94/180 (52.2%) (C) **2001 87/180 (48.3%) (I)**	**Loss to follow-up?: NR/**Unclear – but as done by sites and 60 random prescriptions selected per site (intervention and historical control)it would appear no loss to follow up (?) **Study sufficiently powered?: yes -** Power calculations determined that a sample of 60 visits for respiratory illnesses in each practice during the 1-month trial and during each control month would be sufficient to detect a difference of 15 percentage points in the proportion of visits resulting in an antibiotic prescription with 80% power and a significance level of 0.05. **Limitations identified by author:** Do not know whether parents noticed the poster or understood the information Tailoring of information and the poster itself not undertaken/investigated **Limitations identified by review team:** study details are limited in terms of control and intervention site details and exposures **Evidence gaps and/or recommendations for future research identified by study authors: Not reported** **Source of funding: Not reported.** **Additional comments: None**

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
	baseline?: undertaken by site with historical control – judging by demographics provided similar					
Author(s): Francis et al. **Year:** 2009 **Citation:** Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial. BMJ 2009;339:b2885. **Country of study:** England and Wales **Aim of study:** To evaluate the effect of an information booklet used as a consultation aid on reconsultation and prescribing rates. **Study design:** Cluster- RCT **Method of allocation:** Block randomisation **Quality assessment:** Internal (+); External (++)	**Source population(s):** Children (aged 6 months to 14 years) presenting to primary care with an acute respiratory tract infection **Overall sample size at start of study:** 83 practices (558 children) **Number analysed at end of study:** 61 practices (528 children) **Inclusion/exclusion criteria:** Children presenting with asthma and serious ongoing medical conditions were excluded. **Practice characteristics intervention vs. control:** **List size:** 6750 vs. 6800 **% above average prescribing:** 30% vs. 32.3% **% in England:** 46.7% vs. 35.5% **Participating clinicians:** **% nurse:** 9.1% vs. 20.8% **Participant characteristics:** **Mean age:** 5.1 yrs vs. 5.3 years **Gender (male):** 45.3% vs. 53.5% **Race/ethnicity:** nr **SES:** nr **Other:** % with symptoms; cough 63.4% vs. 58.8%, earache 27.1% vs. 24.3%, runny nose 31.1% vs. 34.2%, sore throat 32.6% vs. 39.4%, fever 37.7% vs. 38.4%, looks unwell 13.2%	**Description:** Clinicians were trained in the use of an interactive booklet on respiratory tract infections, and used the booklet during consultations with participants to facilitate discussion of parent's main concerns, asking about their expectations, prognosis, treatment options and reasons they should re-consult. The 8-page booklet was given to parents at end of consultation. Details on the content of the booklet are described elsewhere. **Setting**: General Practices **Sample sizes at baseline:** 30 practices (274 patients)	**Description:** Consultation following standard practice **Setting**: General Practice **Sample sizes at baseline:** 31 practices (284 patients)	**Outcomes evaluated**: Self-reported via. Telephone questionnaire. 1) Proportion of children who attended a face-to-face consultation about the same illness. 2) Antibiotic prescribing 3) Antibiotic consumption 4) Future consultation intentions 5) Parental satisfaction, reassurance and enablement. **Length of follow-up:** 2 weeks **Method of analysis:** Intercept logistic regression model (two models; adjusted for practice or patient level) of primary outcomes, controlled for practice size, practice prescribing status, country, age, duration of illness, and variables found to be significant in univariate analysis. Interaction factors included to look for subgroup effects.	1) Re-consultation rates intervention vs. control: 12.9% vs. 16.2%; absolute risk reduction 3.3% (95%CI -2.7% to 9.3%) p=0.29; aOR 0.75 (95%CI 0.41 to 1.38) When consultation rates included both primary care and emergency department: aOR 0.85 (95%CI 0.48 to 1.51) or telephone consultations and face-to-face consultations: aOR 0.81 (95%CI 0.47 to 1.42) 2) Antibiotic prescribed at consultation: 19.5% vs. 40.8%; absolute risk reduction 21.3% (95%CI 13.7% to 28.9%) p<0.001; aOR 0.29 (95%CI 0.14 to 0.60) Immediate use: aOR 0.26 (95%CI 0.11 to 0.62) Any time in two-week follow up: aOR 0.31 (95%CI 0.16 to 0.62) 3) Antibiotic consumption: absolute reduction in risk 20.6% (95%CI 12.7% to 28.5%) p<0.001 4) Intention to consult if child had similar illness: 55.3% vs. 76.4%; absolute risk reduction 21.1% (95%CI 13.1% to 29.2%) p<0.001; aOR 0.34 (95%CI 0.20 to 0.57) 5) Parent satisfaction: 90.2% vs. 93.5%; aOR 0.64 (95%CI 0.33 to 1.22), reassurance: 72.0% vs. 75.3%; aOR 0.84 (95%CI 0.57 to 1.25), enablement 40.2% vs. 35.9%; aOR 1.20 (95%CI 0.84 to 1.25)	**Loss to follow-up?:** 94.6% (93.4% intervention, 95.8% control) **Study sufficiently powered?:** Sample size calculation based on 80% power and 5% significance level, with an intra-cluster coefficient of 0.04, and allowed for more than 10% loss to follow up. **Limitations identified by author:** Neither clinicians nor parents were blinded to aims of study. Clinicians in the control might have altered their behaviour as a consequence of participating in the study. Did not measure treatment fidelity, suboptimal fidelity of intervention delivery is likely to have diluted the treatment effect. **Limitations identified by review team:** Study does not measure change in parents' awareness/knowledge. Potentially the intervention is having more of an impact on physician behaviour than parents' behaviour given that led to reduction in prescribing rates but not re-consultation rates. **Evidence gaps and/or recommendations for future research identified by study authors:** Not possible to determine which aspect of the intervention was important; training programme or interactive use of booklet. Authors are exploring these issues in an ongoing study. **Source of funding:** Health Services fellowship funded by the Medical research Council and the Welsh Assembly Government. Development of the training website was funded by an educational grant from Pfizer.

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
	vs. 16.9% **Are groups similar at baseline?:** p=NR					**Additional comments:** Authors comment that the booklet and online training could be produced and distributed fairly cheaply.
Author(s): Gonzales et al **Year:** 2004 **Citation:** Antibiotic Treatment of Acute Respiratory Tract Infections in the Elderly: Effect of a Multidimensional Educational Intervention - J Am Geriatr Soc 52:39–45, 2004. **Country of study: Denver metropolitan area Colorado, USA** **Aim of study:** To measure and improve antibiotic use for acute respiratory tract infections (ARIs) in the elderly **Study design:** Prospective, nonrandomized controlled trial **Method of allocation:** Office practices located in a pre-specified geographical area in the Denver metropolitan area were invited to participate.	**Source population(s):** adult and elderly (65-85 years) patients with ARIs (and Physicians) at 6 commercial Medicare managed care organization (MCO's)+ 2 additional MCO's outside the geographical area; **Overall sample size at start of study:** 51 control sites and 4 intervention sites 4270 total patient visits - 2160 visits (ARI during the baseline period) **Number analysed at end of study: 51 control sites and 4 intervention sites -** 4270 total patient visits**;** 2110 visits during the study period (ARI) **Inclusion/exclusion criteria:** Practices needed to have 20 or more patient visits for ARIs present in administrative claims data from at least one of the MCOs participating in the Joint Data Project during the baseline observation period of November 1, 2000, through February 28, 2001; practices were required to provide a mailing and telephone list of regular clinic patients (defined as any individual adult having at least two office visits based on the	**Description: physician and patient intervention** - patient educational intervention was added to an ongoing physician-centered quality improvement project: **Ongoing Physician project:** primary care physicians who provided care to at least five adults (aged ≥18) with bronchitis during November–February receive a prescribing profile depicting the proportion of bronchitis patients receiving antibiotic treatment, of antibiotics belonging to a narrow-spectrum group prescribed, and of antibiotics prescribed that are ineffective against proven bacterial causes of uncomplicated acute bronchitis. **Patient educational material:** Appropriate antibiotic use and antibiotic Resistance educational materials were mailed to intervention practice households ("Be	**Description: physician centered intervention** Physician based material only **Setting:** **Sample sizes at baseline:**	**Outcomes evaluated:** Antibiotic prescription rates, based on administrative office visit and pharmacy data, for total and condition-specific ARIs. **Length of follow-up:** November 2001 and February 2002 – 4 months **Method of analysis:** Chi-square and multivariate logistic regression analyses were performed to examine unadjusted and adjusted associations between patient characteristics and antibiotic prescription rates Change in antibiotic prescription rates of intervention and control practices from baseline to study periods were compared using the PROC MIXED procedure in SAS statistical software	**Office Visit and Antibiotic Prescription Rates:** At control (n=51) and intervention (n=4) office practices located within the Denver metropolitan area, there were 2,160 incident office visits for ARIs between November 2000 and February 2001 by Medicare MCO enrollees All four practices receiving the household- and office-based intervention had ARI antibiotic prescription rates below the median Wide variation in antibiotic prescription rates for ARIs across unique practices, ranging from 21% to 88% (median554%). Antibiotic prescription rates varied little by patient age, sex, and underlying chronic lung disease. Prescription rates varied by diagnosis: sinusitis (69%), bronchitis (59%), pharyngitis (50%), and nonspecific upper respiratory tract infection (26%). **Intervention effects:** Total ARI visits increased from 17 visits per member per 4-month winter period (PMPW) during the baseline period to 22 visits PMPW (a 29% increase) during the study period among Medicare MCO enrollees associated with the intervention practices. The proportion of total ARI visits associated with an antibiotic	**Loss to follow-up?:** NA **Study sufficiently powered?:** The sample size in this study was sufficient to detect a 20% decrease in antibiotic prescription rates for ARIs, assuming no change in prescription rates at the control practices **Limitations identified by author:.** **Significant differences detected in outcomes were likely conservative due to limitations in the study design:** **Limitations identified by review team:** Only 2 of the identified 6 practices met the inclusion criteria which required the recruitment of 2 additional practices outside the geographical area. Member enrollment data for specific control practices were not available The present study found no relationship between antibiotic use for ARIs and return visit rates, but lack of ED and hospitalization data and of a longer baseline period limit this result. limitations of using administrative data to measure antibiotic prescribing behavior - administrative pharmacy data fail to detect antibiotics given to patients in the office as samples, antibiotic prescriptions that patients decide not to fill, and antibiotic

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
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Office practices in the surrounding Denver metropolitan area that met intervention eligibility criteria described below served as controls. **Quality assessment: Internal (+); External (++)**	clinic's visit records) during the preceding 12 months and to review and approve final educational materials to be used in the intervention **Participant characteristics:** **Mean age: NR (Range 65-85y)** **Gender:** control (n =51) baseline - 755 Male/1250 Female@ – 728 M/ 1196 F @followup; Intervention (n = 4) 64 m/91 f @baseline – 72 m/114 f @follow up **Race/ethnicity: NR** **Other:** total ARI; Chronic lung disease and ARI diagnosis **Are groups similar at baseline?:** Yes(P-**NR**)	S.M.A.R.T. about Antibiotics'' Campaign, CDC brochures on antibiotic resistance, a refrigerator magnet, and a reference card providing easy-to-read facts about symptoms and treatments for ARIs). Waiting and examination room posters were provided to intervention office practices (CDC posters and patient reference cards) **Sample sizes at baseline:**			prescription was modestly different between control and intervention practices during the baseline period (control = 51% and intervention = 45%; Chi2 test, P=.16) During the study period, the overall antibiotic prescription rate for ARIs decreased from 51% to 49% at the control practices and from 45% to 40% at the intervention practices - This difference was not significantly different between groups after adjusting for patient age, COPD, specific ARI diagnosis, and practice-level clustering (P=.79) The educational intervention was not associated with greater reduction in antibiotic prescription rates for total or condition-specific ARIs beyond a modest secular trend(P=.79).	treatment rendered in an alternative facility such as the ED or hospital In addition, because pharmacy data were merged with office visit data, telephone, facsimile, and Internet-based antibiotic treatment of ARIs that were not associated with an office visit could not be accounted for. **Evidence gaps and/or recommendations for future research identified by study authors:** Future studies that examine the effect of additional patient factors (e.g., patient expectations), illness factors (e.g., illness manifestations), physician factors (e.g., years in practice), and practice characteristics (e.g., available support staff) that were not available for the current study might help to better quantify to what extent individual practice style or culture influences antibiotic prescribing behavior. Impact of quality improvement programs addressing ARI management? **Source of funding: Not reported.** **Additional comments: None**
Author(s): Gonzales et al **Year: 2005** **Citation:** The ''Minimizing Antibiotic Resistance in Colorado'' Project: Impact of Patient Education in Improving Antibiotic Use	**Source population(s):** children with pharyngitis and adults with acute bronchitis **Overall sample size at start of study:** 5 practices in geographical area, 2 outside the area; Local control practices 362 office practices in the surrounding area; Distant	**Description: intervention primary care** physicians mailed individual prescribing profiles depicting: (1) the proportion of adult bronchitis patients receiving antibiotic treatment (2) the proportion of erythromycin, doxycycline,	**Description: control** Primary care intervention only (Physicians mailed individual prescribing profiles) **Setting: *see population column*** **Sample sizes at baseline: *see population column***	**Outcomes evaluated:** Office visits and antibiotic prescriptions for ARIs were identified using administrative claims data and were the units of analysis **Length of follow-up:** 1 year (winter 2000 – winter 2001)	**Pediatric Pharyngitis:** **There is no significant change (p>.05) between sites after controlling for patient age, gender, physician specialty, and clustering by office practice, physician, and managed care organization** Groups showed similar distributions of patient age, gender, and physician specialty The proportion of visits managed by physicians who were mailed	**Loss to follow-up?** NA **Study sufficiently powered?:** sample size in this study was designed, a priori, to be sufficient to detect an approximate 10 percent decrease in antibiotic prescription rates for pharyngitis or bronchitis with 80 percent power and 95 percent confidence, assuming no change in prescription rates at the control practices

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
in Private Office Practices **- HSR: Health Services Research 40:1 (February 2005)** **Country of study:** Colorado USA **Aim of study:** To assess the marginal impact of patient education on antibiotic prescribing to children with pharyngitis and adults with acute bronchitis in private office practices **Study design:** nonrandomized controlled trial **Method of allocation:** Office practices located in a pre-specified geographical area in the Denver metropolitan area were invited to participate as intervention practices **Quality assessment: Internal (+); External (++)**	controls – 65 practices 60 miles away **Pediatric population -** @baseline: distant controls - 53 practices, 113 Providers with 1152 patient visits; Local controls - 288 practices, 655 providers with 8575 patient visits; intervention – 6 practices, 25 providers with 401 patient visits @study period: distant controls – practice 47, providers 86 with patient visits 996; local control – 234 practices, 475 providers with 8234 patient visits; intervention 5 practices, 17 providers with 356 patient visits **Adult population** @baseline: distant controls - 59 practices, 117 Providers with 763 patient visits; Local controls - 297 practices, 693 providers with 5575 patient visits; intervention – 6 practices, 26 providers with 220 patient visits **Number analysed at end of study:** @study period: distant controls – practice 52, providers 91 with patient visits 656; local control – 248 practices, 505 providers with 4239 patient visits; intervention 6 practices, 19 providers with 167 patient visits	tetracycline belonging to a first-line group (3)proportion of these antibiotics that are ineffective against proven bacterial causes of uncomplicated acute bronchitis Physicians providing care to children with pharyngitis were mailed profiles depicting: (1) the proportion of all pharyngitis patients having a group A streptococcus identification test performed; (2) the proportion of pharyngitis patients not receiving a group A streptococcal identification test who were treated with antibiotics (3) the proportion of penicillin, amoxicillin, erythromycin belonging to a first-line group. **Patient Educational intervention:** Household- and office-based patient education materials - campaign packets were mailed to households identified by the participating practices - consisted of a bilingual introductory letter explaining the ‘‘Be		**Method of analysis:** crude differences in patient characteristics across practice groups assessed using Chi2- and t-tests Change in the proportion of office visits for pediatric pharyngitis or adult bronchitis treated with antibiotics during baseline to study periods was compared among intervention, local control, and distant control practices using mixed-effects models	individual pediatric pharyngitis prescribing profiles increased equally within each study group, from 70 percent in the baseline period to about 90 percent during the study period. Adjusted antibiotic prescription rates during baseline and study periods increased from 38% to 39% for children at the distant control practices, decreased from 39% to 37% for children at the local control practices, and decreased from 34% to 30% for children at the intervention practices - p=.18 and p=.48 for intervention practice compared with distant and local control practices, respectively Increased age corresponded with decreased antibiotic prescribing; p<.001 **Adult Bronchitis** Adjusted antibiotic prescription rates decreased from 50% to 44% for adult bronchitis at the distant control practices, from 55% to 45% percent at the local control practices, and from 60% to 36% at the intervention practices (p<.002 and p=.006 compared with distant and local control practices, respectively) During the baseline period, fewer office visits at distant control practices (51%) were managed by physicians who were mailed individual adult bronchitis prescribing profiles compared with intervention practices (69%). However, during the study period the differences between practice sites (81–88%) decreased, but remained significantly different (p=.001).	**Limitations identified by author:** Study cannot quantify the degree to which this effect results from a synergy between physician and patient education, or whether the patient education alone would have resulted in the same effect Administrative pharmacy data fail to detect antibiotics given to patients in the office as samples, antibiotic prescriptions that patients decide not to fill, and antibiotic treatment rendered in an alternative facility such as the emergency department or hospital Merged pharmacy data with office visit data, fails to account for telephone, facsimile, and Internet-based antibiotic prescribing for ARIs, which were not associated with an office visit. selection bias - practices that agreed to participate in the ‘‘Be S.M.A.R.T. about Antibiotics’’ campaign may represent a group of practices more willing to modify their prescribing behaviors than the comparison practices **Limitations identified by review team:** **Evidence gaps and/or recommendations for future research identified by study authors: Not reported** **Source of funding: Not reported.** **Additional comments:** **Costs -** cost-accounting approach to determine replication costs of the household- and office-based

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
	Inclusion/exclusion criteria: Practices eligible for the intervention were required to have 20 or more patient visits for ARIs present in administrative claims data when aggregated across the MCOs participating in the Colorado Medical Society Joint Data Project during the baseline observation period of November 1, 2000–February 28, 2001 **Participant characteristics:** **Mean age: NR** – range 0-17 (pediatrics); 18-64 (adults) Gender: % female (range) 51-55% distant control; 52-53% local control; 54-55% intervention (Pediatrics) 62% distant control; 57-61% local control; 54-60% intervention (adults) **Race/ethnicity: NR** **Other:** **Are groups similar at baseline?: Yes - (P -NR)**	S.M.A.R.T. about Antibiotics'' campaign, CDC brochures on antibiotic resistance, a refrigerator magnet, and a reference card. Office-based materials - waiting room materials (CDC posters and patient reference cards) and examination room posters **Sample sizes at baseline: *see population column***				intervention. The total cost to conduct the household intervention was $1.64 per household in 2001 dollars for 37,375 households. The materials cost for office practices was approximately $350 per practice
Author(s): GUDNASON et al **Year:** 2013 **Citation:** Does hygiene intervention at day care centres reduce infectious illnesses in children? An intervention cohort study - Scandinavian	**Source population(s):** 30 Day Care Centres (**DCC's**) in 2 suburban communities (Hafnarfjordur and Kopavogur) located in the greater Reykjavik area in Iceland **Overall sample size at start of study: 2349 children**	**Description: hygiene intervention focused on both hand and environmental hygiene:** **(1)** Education on the transmission of microbes and the importance of environmental and hand hygiene was provided by the study	**Description: control** no intervention was carried out at the DCCs and hygiene was carried out in a non-standardized routine manner as decided by the staff. **Setting:** DCC's **Sample sizes at**	**Outcomes evaluated:** (1) retrospective information on the number of febrile, respiratory, and gastrointestinal illnesses (outcome variables) was registered at 6-month intervals by the parents as the number of	**Compliance with the hygiene intervention**: No difference was seen in the use of disinfectant, paper towels, liquid soap, or gloves between the intervention and non-intervention DCCs during the baseline period. During the intervention period on the use of disinfectant at the intervention DCCs increased 5-fold compared with the use during	**Loss to follow-up?:** There was a yearly dropout of older children leaving the DCCs and new entrance of young children. Some children stayed in the study for all 5 seasons while others stayed for 1, 2, 3, or 4 seasons **Study sufficiently powered?: NR** **Limitations identified by author:** DCCs is the monitoring of compliance

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
Journal of Infectious Diseases, 2013; 45: 397–403 **Country of study:** Iceland **Aim of study:** describe the effects of a hygiene intervention cohort trial at day care centres (**DCCs**) on the rates of febrile, respiratory, and gastrointestinal illnesses in preschool children **Study design: non randomised study** (Study authors classified as an **"**intervention Cohort study") **Method of allocation:** selection of DCCs for the intervention was based on their willingness to comply with the intervention protocol **Quality assessment: Internal (+); External (++)**	**Number analysed at end of study:** information was obtained once from 708 (30%), twice from 654 (28%), 3 times from 503 (21%), 4 times from 282 (12%), and 5 times from 202 (9%) - 5663 questionnaires were returned, comprising 2832 person-y **Inclusion criteria:** Preschool children in Iceland attend DCCs from approximately 2 to 6 years of age **exclusion criteria:** younger children attend private home day care and were not included in this study **Participant characteristics: Parents; Children attending DDC's (2-6 years of age); staff at DCC's** **Mean age:** 3.8y (C)/3.8(I) @ baseline; 3.8y(I)/3.9y(C)@ follow up **Gender:** 53% (I)/52%(C) (Boys @ baseline) ; 53%(I)/52% (C) boys@follow up **Race/ethnicity: NR** **Other: NR** **Are groups similar at baseline?:** Yes – same communities, same SES spread, same setting (P – NR)	nurse monthly during the intervention period, for both the staff and the children. **(2)** Only liquid soap was used for hand washing. **(3)** Staff were encouraged to wash their hands in the morning and afternoon when entering and leaving the DCCs, before eating, after toileting, after changing diapers (staff), and after nose wiping. **(4)** The staff and children were encouraged to use hand disinfectant (DAX Alcogel 85 ® ; 85% ethanol) after hand washing and instead of hand washing when hand washing was not possible. **(5)** Staff were instructed to use gloves when changing diapers and cleaning children after toileting**.** **(6)** Staff were encouraged to use disposable nose wipes for children**.** **(7)** Toys were washed and cleaned with soap at least once a month. If toys could not be washed they were taken out of use for at least 4 days each month.	**baseline:** 15 DCC's -	illness episodes during the previous 6 months; (2) retrospective information on potential risk factors (predictor variables) was collected at the time of enrolment and at 6-month intervals throughout the study from the parents and the staff at the DCCs. The use of all hygiene products was monitored throughout the study at both the intervention and non-intervention DCCs. Compliance with the hygiene intervention was assessed by comparing the use of liquid soap, disinfectants, gloves, and paper towels at the intervention and non-intervention DCCs before and after the introduction of the hygiene intervention. an anonymous survey - Staff compliance with the hygiene protocols and attitude towards the hygiene intervention in general **Length of follow-up:** October 2000 and ended in March 2003	the baseline period, the use of paper towels increased 8-fold, the use of liquid soap 1.1-fold, and the use of gloves 1.2-fold. No change in the use of these items was seen at the non-intervention DCCs during the intervention period compared with the baseline period**.** A good compliance with the study protocols (always/most often compliant with the protocol) was claimed by 98% regarding hand washing, 89% with regard to the use of disinfectant, and 93% with regard to cleaning toys **Results of the hygiene intervention:** Crude incidence rates of all illnesses were similar at the intervention and non-intervention DCCs during both the baseline and the intervention periods. aIRRs of the illnesses at the intervention and non-intervention DCCs for the intervention period did not reach statistical significance**;** aIRRs of the illnesses were not statistically significant during the baseline period, indicating similar incidence rates of the illnesses before implementation of the intervention aIRRs of all illnesses were calculated separately for the individual seasons of the intervention period (seasons 3, 4, and 5). No significant aIRRs were seen for any of the illnesses, indicating that the effects of the intervention did not change with time. The results of the intervention were no different in children below 3 y of age compared with older children.	with the intervention protocols Overall participation of children who delivered questionnaires during the study period was around 51%. Selection bias based on the outcome variables cannot be excluded, but was unlikely Possible 'recall bias – as data was collected 6 months reterospectively **Limitations identified by review team:** **Evidence gaps and/or recommendations for future research identified by study authors: Not reported** **Source of funding: Not reported.** **Additional comments: None**

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
		(8) Furniture, floors, doorknobs, and toilets were cleaned and disinfected at least once a day. **Sample sizes at baseline:** children 930 (C) /734 (I)		(2.5 y). It was divided into 5 seasons, each covering 6 months. The 6-month seasons represented winters (October – March) and summers (April – September) of the 2.5 y of the study (winter 2000/2001, summer 2001, winter 2001/2002, summer 2002, and winter 2002/2003**)** **Method of analysis:** mixed effects hierarchical regression model was used to calculate the adjusted incidence rate ratios (aIRRs) with 95% confidence intervals (95% CI) assuming Poisson distribution for the outcome variables crude and aIRRs and incidence rate ratio's (IRR)of the number of illness episodes at the intervention and non-intervention DCCs at baseline and follow up Calculation of aIRRs of the number of illness episodes at the intervention and non-intervention DCCs for each of the 3 seasons of the intervention period (winter 2001/2002, summer 2002, and winter	Table a - Crude incidence rates of illness episodes at intervention and non-intervention day care centres for the baseline and intervention periods Fever: Intervention: baseline period 2.85 (2.69 – 3.01); intervention period 2.91 (2.78 – 3.03) Non-intervention: B - 2.94 (2.76 – 3.13); I - 2.75 (2.60 – 2.89) Cold: Intervention: B - 4.82 (4.58 – 5.06); I- 4.57 (4.37 – 4.76) Non-intervention : B - 4.88 (4.60 – 5.16); I -4.63 (4.41 – 4.85) Acute otitis media: Intervention: B - 0.63 (0.55 – 0.71) I - 0.68 (0.61 – 0.74) Non-intervention: B - 0.70 (0.59 – 0.80); I - 0.68 (0.60 – 0.75) Pneumonia: Intervention: B- 0.10 (0.07 – 0.13); I - 0.10 (0.08 – 0.12) Non-intervention: B -0.09 (0.06 – 0.12); I - 0.12 (0.09 – 0.15) Bronchial asthma: Intervention: B - 0.37 (0.30 – 0.44) ; I - 0.34 (0.29 – 0.40) Non-intervention: B -0.32 (0.24 – 0.39) I - 0.33 (0.26 – 0.40) Diarrhoea: Intervention: B - 0.94 (0.82 – 1.05); I -1.03 (0.94 – 1.12) Non-intervention: B - 0.91 (0.79 – 1.03); I -0.98 (0.87 – 1.09) Table b - Adjusted incidence rate ratios of the number of febrile,	

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
				2002/2003) in order to explore whether the effects of the intervention would change over time. To evaluate whether the effects of the hygiene intervention would differ across age groups we included an interaction parameter in the model between the hygiene intervention during the intervention period and age-groups of children, <3 y and ≥3 y of age. The characteristics of the children at the intervention and non-intervention DCCs were compared by Chi-squared test (categorical variables) and t –test (continuous variables).	respiratory, and gastrointestinal illness episodes at the intervention and non-intervention day care centers for the baseline and intervention periods: Fever: 0.99 (0.90 – 1.10) (Baseline) 0.99 (0.92 – 1.08) (intervention) Cold: 0.99 (0.92 – 1.09) (B) 0.95 (0.87 – 1.03) (I) Acute otitis media 0.90 (0.73 – 1.12) (B) 0.90 (0.80 – 1.02) (I) Pneumonia 0.98 (0.66 – 1.45) (B) 0.79 (0.59 – 1.06) (I) Bronchial asthma 1.08 (0.75 – 1.54) (B) 0.95 (0.75 – 1.21) (I) Diarrhoea 1.04 (0.85 – 1.27) (B) 0.97 (0.79 – 1.20) (I)	
Author(s): HEDIN et al. **Year:** 2006 **Citation:** Infection prevention at day-care centres: Feasibility and possible effects of intervention. Scandinavian Journal of Primary Health Care, 2006; 24: 44/49 **Country of study:** Va¨xjo¨ , Sweden **Aim of study:** a	**Source population(s):** six municipal day-care centres in Va¨xjo¨ all with one infant department with 12 to 15 children aged 1/3 years, and two departments with 17 to 21 children aged 3/ 5 years; parents and personnel **Overall sample size at start of study:** 154 children and 31 personnel in the intervention day-care	**Description:** all personnel were made aware of the recommendations of the Swedish National Board of Health and Welfare, the provisional version by three of the authors and each department was given a copy. In the course of the study, liquid soap and paper towels were used instead of terry towels and bars of	**Description:** control day-care centers the parents and personnel were informed at the start of the aim and arrangement of the study. No other activities were undertaken **Setting:** three municipal day-care centres in Va¨xjo¨ Sweden. **Sample sizes at baseline:** 157 children; 32 personnel;	**Outcomes evaluated:** 1) episode of sickness absence - parents completed a special form concerning the reason for the child's absence, the length of the sickness episode, whether a doctor had been consulted or if antibiotics had been prescribed – diagnosis had to be confirmed by a doctor	1) **Personnel's experience** - a greater proportion of the personnel at the intervention day-care centres thought they had enhanced their number of guidelines, and that more children were at home long enough after an infection episode compared with the start of the study 2) **Parents' experience of information** - more parents in the intervention group felt informed about infectious diseases and when to keep an infected child at home compared with the start of the study. In a	**Loss to follow-up?:** NR **Study sufficiently powered?:** Power calculation was not reported. **Limitations identified by author:** none reported **Limitations identified by review team:** Intervention involved numerous components difficult to attribute any effect to any one component **Evidence gaps and/or recommendations for future research identified by study authors:** Might have had significant results in the multilevel analyses if we

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
small intervention study at six day-care centres in Va¨xjo¨ to see how personnel and parents comprehended the Swedish National Board of Health and Welfare recommendations on how to handle infections in children and reduce contagion in day-care centres. Was there a reduction in sickness absence, care utilization, and consumption of antibiotics**.** **Study design: non randomized control trial** **Method of allocation:** Random (process of randomization not outlined) **Quality assessment:** Internal (-); External (+)	centres 157 children and 32 personnel in the control group. During the nine-month study (September to May), Parents 140 (91%) of the children in the intervention group and of 145 (92%) in the control group completed a questionnaire Concerning characteristics of the family. 127 (82%) (I) and 117 (74%) (C) of the parents, anonymously completed questionnaire about the receipt of information concerning infectious diseases in children. **Number analysed at end of study:** children 144 (I); 148 (C); personnel 32 (I)29 (C) Parents 111 (72%)(I) and 124 (79%) (C) **Inclusion/exclusion criteria:** NR **Participant characteristics: Mean age:** NR **Gender:** NR **Race/ethnicity:** NR **Other:** NR **Are groups similar at baseline?:** Children at day care centers age; numbers of day care personnel, no other information reported.	soap. Personnel were urged to take the children outside as much as possible, but no exact number of hours was specified. A study day on outdoor pedagogy was arranged for the personnel. Posters with information on respiratory tract infections and contagion were placed near the entrances. In connection with parents' meetings, one at the start of the study and one while the study was in progress, the authors informed the parents about infectious diseases and contagion. The use of antibiotics to cure infections in pre-school children was discussed, as was the risk of developing resistance through overuse. **Setting**: three municipal day-care centres in Va¨xjo¨ Sweden **Sample sizes at baseline:** 154 children; 31 personnel;	145 (92%)parents of children	Parents' reports regarding sickness absence were validated against the staff 's own absence lists regarding the number of sickness episodes and absent days 1) Sickness absence (total days and total episodes), 2)doctor's consultations, and antibiotic prescriptions **Independent variable** See intervention **Length of follow-up:** Nine month study – follow up not specified or frequency of data collection **Method of analysis:** multilevel Poisson regression analyses – per child 'department' (children were nested within departments, i.e. a clustering above the individual level. This level could have an effect on the behaviour of the children or the personnel)	separate question Two-thirds in both the intervention and the control group answered that they thought regular information about infectious diseases was desirable 3) **Children's infections** - Total absence for illness, as a percentage of the expected presence, was 6.6% (1537/22 610 days) in the intervention group and 6.8% (1678/23 955) in the control group. There were 583 sickness episodes in the intervention group and 698 in the control group reported by the personnel; Infectious diseases accounted for 96% of sickness absence, and roughly 60% of this was due to respiratory tract infections; Multilevel analysis was undertaken but a lack of detail and some confusion regarding conclusions and results reported were evidence – it outlined: significant intervention effect with the introduction of individual variables for sickness absence in days (Dept. variance [Day sickness absence] (SE) 0.04(0.02; $p<0.05$); Median mean ratio 1.21. A significant intervention effect for ''infection prone'' children for all outcomes. Sickness absence (days) - 1.48 (1.35/1.63) Sickness absence (episodes)1.36 (1.17/1.58) Doctor's consultation - 2.80 (2.13/3.67) Antibiotic prescriptions - 2.99 (2.06/4.34)	had included more day-care centres – larger study required **Source of funding:** Not reported. **Additional comments:** no statistically significant effect of the intervention was found, but there was a consistent pattern towards lower sickness absence, fewer doctor's consultations, and decreased antibiotic prescription in the intervention group. No details from authors concerning how 'infection prone' was determined.

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		127 (82%)of parents			For sickness absence in days, a significant effect was found for children with asthma 1.20 (1.09/1.31). There was no effect for the individual variables single parent, siblings, smoker, or own room. Increasing age had a small effect (data not shown in paper).	
Author(s): Lau et al. **Year: 2012** **Citation:** Hand hygiene instruction decreases illness-related absenteeism in elementary schools: a prospective cohort study. BMC Pediatrics 2012, 12:52 http://www.biomedcentral.com/1471-2431/12/52 **Country of study:** Chicago, USA **Aim of study:** compare absenteeism rates among elementary students given access to hand hygiene facilities versus students given both access and short repetitive instruction in use, particularly during influenza season when illness-related absences are at a peak.	**Source population(s):** two Chicago Public Elementary Schools among students grades pre-kindergarten to eighth grade (ages 4 14). **Overall sample size at start of study:** 981 students. **Number analysed at end of study:** 773 students. **Inclusion/exclusion criteria:** Data from grades pre-kindergarten and kindergarten were not used in analyses as a result of inconsistent attendance records, **Participant characteristics:** **Range:** 4-14 years old (6-14 considered in the study) **Mean age: NR** **Gender:** Male (n=461) female (n=520) **Race/ethnicity:** white (271), black (125), Hispanic/latino (545), others (40) **Other: NR** **Are groups similar at baseline?:** Yes all school	**Description: intervention** Hand sanitizer and hand washing facilities were made available to students in both the intervention and control group. Posters describing when to use the hand sanitizer were hung up throughout the schools (Figure 2). Intervention classrooms were given a protocol for hand sanitizer use and received regular instruction in hand hygiene from study personnel. Grade appropriate curriculum was used to instruct students in proper hand washing (included 30-minute interactive session, which used a black light experiment with glow-in-the-dark "germ" lotion, trivia games (grades 2	**Description: control** Hand sanitizer and hand washing facilities were made available to students in both the intervention and control group. Posters describing when to use the hand sanitizer were hung up throughout the schools (Figure 2). At the conclusion of the study, control classrooms also received the 30-minute lesson on hand hygiene. **Setting:** Chicago Public Elementary Schools **Sample sizes at baseline:** even grades to the control group (n = 16)	**Outcomes evaluated:** **1)** student absence as reported by parents 2) Percent total absent days 3)illness-related absent days 4)Teachers perceptions (23/30 teachers in participating schools) **Length of follow-up:** Intervention duration - October to May during the 2009/2010 academic year; data (rates) calculated at the end of academic year – 8 months **Method of analysis:** $\chi 2$ tests of independence were performed to determine whether the number of absent student-days (total and illness-related) differed significantly between intervention and control groups. Survey undertaken with teachers on perceptions of hand	1) Participant characteristics - Final sample of 773 students. A total 1,913 absences were recorded for students in grades 1 through 8 during the study period. Twenty seven recorded absences were not used in analyses due to missing data (i.e., reason and date of absence), for a total of 1,886 data points 2) Absenteeism rates - Percent total absent days 879/52734 (1.67%) control; 1007/56259 (1.79%)intervention [across both schools]; during influenza season [Oct-Dec] 365/18326 (1.99% P<0.01)- control; 309/19551 (1.58% - P<0.01)intervention - Both the collapsed total rate % total absent days (1.99% (C)-1.58% (I) P<0.01) and collapsed illness-related rate % illness-related absent days (1.57% (C)- 1.15% (I) P<0.01) of absenteeism were significantly lower in the intervention groups during influenza season. This difference peaked during the influenza season (when intervention began) and declined in the following months. The peak in percent absent days matched the peak in number of influenza-like illnesses in 2009 (both regular and pandemic i.e. H1N1) reported by the City of Chicago	**Loss to follow-up?:** Twenty seven recorded absences were not used in analyses due to missing data (i.e., reason and date of absence) **Study sufficiently powered?:** Power calculation was not reported. **Limitations identified by author:** The sample was small and convenience-based, resulting in low statistical power. Small sample size may be the reason for correct directionality without statistical significance until results from both schools were analyzed as a whole. Significant differences detected in outcomes were likely conservative due to limitations in the study design: Per request of school administration, alcohol-free hand sanitizer used rather than alcohol-based hand sanitizer. No data on influenza vaccination rates of children in the participating schools, and did not attempt to stop children in the intervention group from passing on hand hygiene instruction to children in the control group. Moreover, the intervention was conducted at a time of heightened

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Study design: non-RCT **Method of allocation:** Classrooms were systematically assigned to an intervention or control group by grade (cluster design) **Quality assessment: Internal (-); External (+)**	children in the Chicago area – slight difference in terms of race/ethnicity across the schools (Alcott 54% white; Walsh 92.7% Hispanic/Latino)	through 8), and a demonstration with finger puppets (pre-kindergarten and kindergarten), as well as three 10-minute review sessions every two months, **Sample sizes at baseline:** odd grades to the intervention group (n = 15 clusters)		hygiene	3) Teachers' perceptions -majority of respondents agreed that students wash their hands during the school day, but did not believe that students do so properly – Narrative data suggest that students most often wash their hands after restroom breaks and before lunch – Hand sanitizer use was reported to be commonplace in both schools, although half of teachers believed their students used hand sanitizer incorrectly - Walsh teachers observed that students only used hand sanitizer before meals and after recess while teachers at Alcott reported that most students used hand sanitizer as needed. Barriers to hand hygiene were consistent with those reported in other studies and included time constraints and limited access to materials/facilities	hand hygiene awareness following the H1N1 outbreak, which likely resulted in more vigilance in hand hygiene among both control and intervention groups. Analysis did not correct for clustering at the class level and a simple t-test of absenteeism rates in the two groups at the cluster level (n = 31) did not show any significant associations due to lack of statistical power - Results need to be interpreted cautiously. **Limitations identified by review team:** clusters within the schools is not clear – randomization by grades but the number of clusters is not clearly outlined (how many classes per grade – as the allocated number for control and intervention clusters doesn't appear to tally) – information provided across the 2 schools has been highlighted as different – this could have implications to the findings **Evidence gaps and/or recommendations for future research identified by study authors:** Not reported **Source of funding:** Not reported. **Additional comments: None**
Author(s): Little et al. **Year: 2015** **Citation**: An internet-delivered handwashing intervention to	**Source population(s):** Adult patients (aged 18 years and over) identified from GPs list living with at least one other person (the index person) **Overall sample size at**	**Description:** Access to a bespoke automated web-based intervention. 4-weekly sessions, each with new content. Session 1: included information about: the medical	**Description:** No intervention and control group who did not answer question on hand-washing in baseline questionnaire **Setting:** Home based	**Outcomes evaluated:** 1) Episodes of respiratory tract infections reported after 16 weeks, as documented by the index person; 2) Duration of symptoms	1) Episodes of RTIs during 16 weeks post randomisation, intervention vs. control: Respiratory infections: 51% vs. 59%, , aIRR 0.86 (95%CI: 0.83 to 0.89), p<0.0001 Household members: 44% vs. 49%, aIRR 0.82 (95%CI: 0.76 to 0.88),	**Loss to follow-up?:** 84% followed up to 16 weeks, 95% medical notes were reviewed. **Study sufficiently powered?:** 80% power calculation, estimated sample size 15,908

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modify influenza-like illness and respiratory infection transmission (PRIMIT): a primary care randomised trial. The Lancet, Published Online: 06 August 2015 DOI: http://dx.doi.org/10.1016/S0140-6736(15)60127-1 **Country of study:** UK **Aim of study:** to demonstrate whether an intervention to modify hand washing reduces RTIs among adults Study design: Method of allocation: Online by an automated computer-generated random number programme **Quality assessment: Internal (++); External (++)**	**start of study:** 344 GP offices, 20,066 patients **Number analysed at end of study:** 16,908 completed questionnaires, 19,117 medical notes reviewed **Inclusion/exclusion criteria:** Patients with severe mental illness, or terminally ill, those reporting a skin complaint that would limit hand washing. **Participant characteristics control vs. intervention:** **Mean age:** 56.50 (13.64) vs. 56.66 (13.62) **Gender (female):** 55.95% vs. 56.02% **Race/ethnicity:** nr **SES (years in education):** 8.68 (3.20) vs. 8.71 (3.19) **Other:** size of household: 2.56 (0.95) vs. 2.55 (0.92) Children under 16: 17.60% vs. 17.31% No ongoing health problems: 70.58% vs. 69.69% Influenza vaccination: 36.22% vs. 32.48% **Are groups similar at baseline?: p=nr**	team; the importance of preventing seasonal and pandemic flu; the role of hand-washing in interrupting transmission; and instructions for picking up a supply of hand-gel from their GP. Participants entered details of their current hand-washing habits and completed a plan to maximise intention formation for hand-washing. Automated tailored feedback helped users improve their plan (by highlighting situations in which users could increase the frequency of hand-washing), and participants were encouraged to sign the plan and post it up in a prominent place in the household to help involve household members Session 2-4: reinforced helpful attitudes and norms and addressed negative beliefs. They included expert recommendations for hand-washing (technique and frequency). Feedback to reinforce hand-washing was tailored to self-reported intended frequency of hand-washing, and the perceived difficulty and	**Sample sizes at baseline:** 9,981	measured as duration of symptoms rated moderately bad, the number of days where work/normal activities were impaired; 3) transmission of respiratory infections, linked to whether other family members had had a similar infection in the week before or after; 4) Gastrointestinal infections; and 5) attendance at GP practice and use of health services resources in the 12 months post randomisation based on review of patients notes **Length of follow-up:** Incidences of infection over 16 weeks post randomisation. Attendance over 12 months post randomization . **Method of analysis:** Intention to treat analysis. Logistic regression, no evidence of clustering by GP practice so not accounted for in model. Sub-group analysis; age, influenza vaccination status, family size, children aged under 16 years, prior attendance with	p<0.0001 Moderately bad symptom days: 2.1 days vs. 2.6 days, aIRR 0.79 (95%CI: 0.74 to 0.83), p<0.0001 Total days of infection: 5.2 days vs. 6.5 days aIRR 0.91 (95%CI: 0.87 to 0.95) p<0.0001 Shorter duration of illness: 9.8 days vs. 10.6 days, IRR 0.91 (95%CI 0.87 to 0.95), p<0.001 2) Transmission of infection intervention vs. control: To index person: 7.8% vs. 9%, p<0.0001 From index person: 6.8% vs. 8.8%, p<0.0001 3) Consultation rates during 16 weeks, intervention vs. control: Over 16 weeks: 10.0% vs. 10.7%, p=0.014 Over 12 months: 16.0% vs. 17.3%, p=0.001 4) Antibiotic prescription intervention vs. control: Over 16 weeks: 5.6% vs. 6.4%, p=0.002 Over 12 months: 9.3% vs. 10.5%, p<0.0001	**Limitations identified by author:** Free-standing web-site would be expected to attract those more interested in preventing infections **Limitations identified by review team:** Episodes of infection self-reported. No data is reported to suggest how many in the intervention read the education content of the website. Evidence gaps and/or recommendations for future research identified by study authors: none identified Source of funding: Medical Research Council **Additional comments:** Two additional groups were included (a control with baseline questionnaire and an intervention without baseline questionnaire). Results suggest that fewer infections in the control group when they were asked baseline questions about hand washing.

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		Intervention	Comparator(s)			
		efficacy of carrying out the behaviour; those reporting low perceived efficacy were shown information to promote more positive efficacy beliefs, those reporting high perceived difficulty were given advice about overcoming barriers, and those reporting high intended hand-washing adherence were shown pages with additional advice (e.g. on other preventative measures, and involving other family members) Prompt emails sent once a month to encourage use of the sessions, to complete the questionnaires and to maintain hand washing. **Setting:** Home based **Sample sizes at baseline:** 9,967		respiratory infections, and skin complaints.		
Author(s): **Sandora et al** **Year:** 2005 **Citation:** A Randomized, Controlled Trial of a Multifaceted Intervention Including Alcohol-Based Hand Sanitizer and Hand-Hygiene Education to Reduce	**Source population(s):** Families based on attendance of their children in specific child care centers – selected from Twenty-six potential study centers in 3 Massachusetts neighborhoods (Boston, Brookline, and Cambridge) **Overall sample size at start of study:** 292 families (out of 647	**Description: intervention** Intervention group: received a supply of alcohol-based hand sanitizer (Purell Instant Hand Sanitizer; GOJO Industries, Inc, Akron OH; active ingredient: 62% ethyl alcohol) to use in the home during a 5-month study period.	**Description control:** Families whose centers were assigned to the control group did not receive hand sanitizer or materials related to hand hygiene; instead, they received biweekly educational materials about a healthy diet including fruits and vegetables. Control families were	**Outcomes evaluated:** 1) Overall rates of secondary respiratory and GI illness (defined as the number of secondary illnesses per susceptible person-month). **Additional outcomes included** 1)primary respiratory and GI-illness rates**.**	1) **Participant characteristics** -. Of the eligible families, 292 (82%) agreed to enroll and provided written consent; 155 families (14 child care centers) were assigned randomly to the intervention group, and 137 families (12 child care centers) were assigned randomly to the control group. In the intervention group, 12 families withdrew before completion of the 5-month study period, and 3 were lost to follow-up; in the control group, 11 families withdrew, and 8 were lost to follow-up. The proportion	**Loss to follow-up?:** Twenty seven recorded absences were not used in analyses due to missing data (i.e., reason and date of absence) **Study sufficiently powered?:** Under the assumption of 2.14 secondary cases per family in the control group during the study period (based on data from previous study), 348 families would be required to detect a 20% decrease in secondary infections with 80% power. This calculation

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Illness Transmission in the Home PEDIATRICS Vol. 116 No. 3 September 2005 **Country of study:** Massachusetts, USA **Aim of study:** to assess the effectiveness of a multifactorial hand-hygiene intervention in reducing respiratory and GI-illness transmission in the homes of families with children enrolled in out-of-home child care - increasing use of alcohol-based hand sanitizer by supplying families with the product in the context of a vigorous hand-hygiene educational and behavior change campaign **Study design:** cluster randomized, controlled trial **Method of allocation:** Randomization was clustered (with the child care center as the unit of randomization)- Random assignments were generated by	invited); (155 intervention group; 137 control group) **Number analyzed at end of study:** ITT undertaken – (intervention – n=3 lost to follow up – n = 12 discontinued intervention; control n=8 lost to follow up, n=11 discontinued intervention) **Inclusion criteria:** A family was eligible for inclusion in the study when (1) the family had at least 1 child between 6 months and 5 years of age enrolled in out-of-home child care (*the oldest child who met these criteria was defined as the index child), (2) the index child was enrolled in out-of-home child care with at least 5 other children for 10 hours per week, (3) the family planned to reside in the area and keep the index child enrolled in the center for the duration of the study, (4) the family had access to a telephone, and (5) the primary home caregiver could speak English or Spanish. A household member was defined as an individual who spent 3 nights per week in the home **Exclusion criteria**: excluded families whose	In addition, intervention families received biweekly hand-hygiene educational materials at home for 5 months. These materials consisted of engaging fact sheets and tips to educate families about hand hygiene, as well as games and toys designed to serve as triggers for awareness of hand-hygiene practices. **Sample sizes at baseline:** 155 families	asked not to use hand sanitizer during the study period. No placebo for the sanitizer was provided because we believed that it would be unethical if families used an inactive hand-hygiene product as a substitute for routine handwashing**.** **Setting: family homes - Massachusetts neighborhoods (Boston, Brookline, and Cambridge)** **Sample sizes at baseline:** 137 families	2) amount of hand sanitizer used (as reported by the primary caregiver) on a biweekly basis 3) any adverse events related to the hand sanitizer on a biweekly basis **Length of follow-up: Intervention duration -** survey that asked about family demographics as well as knowledge and practices regarding hand hygiene and illness transmission repeated at the conclusion of the ***5-month study period*** Families also received a symptom diary to record the timing and duration of illnesses among family members. Caregivers were contacted by telephone ***biweekly*** to elicit reports of symptoms of respiratory and GI illnesses in the family during the preceding 2 weeks. **Method of analysis:** Analysis undertaken on an ITT basis – Baseline demographic characteristics in the	of families who completed the study did not differ between intervention and control groups (P = .28, Fisher's exact test) 2) **Respiratory illness rates** - A total of 1802 respiratory illnesses occurred in 258 families; 1359 (75%) of these were primary illnesses. The overall respiratory illness incidence rate was 0.42 illnesses per person-month. A total of 443 secondary respiratory illnesses occurred over 18173 susceptible person-days at risk, producing a transmission rate of 0.74 secondary illnesses per susceptible person-month. The unadjusted incidence rate ratio (IRR) for secondary respiratory illness in intervention families compared with control families was 1.05 (95% confidence interval [CI]: 0.78 –1.42; P=.75). **3) GI Illness** - A total of 252 GI illnesses occurred in 138 families; 224 (89%) of these were primary illnesses. The overall GI-illness incidence rate was 0.06 illnesses per person-month. Twenty-eight secondary GI illnesses occurred during 3359 susceptible person-days at risk, producing a transmission rate of 0.25 secondary illnesses per susceptible person-month. The unadjusted IRR for secondary GI illness in intervention families compared with control families was 0.48 (95% CI: 0.21–1.10; P=.08). 3) **Predictors of GI and respiratory**	assumes that the correlation of illness burden among families in the same child care center is 0.01. Final enrollment was below our preplanned sample size of 348 families; however, our observed sample size of 292 families (137 control and 155 intervention) still provides 75% power to detect a 20% reduction in respiratory illness transmission. **Limitations identified by author:** Documentation of illness was based on symptom reporting by caregivers rather than microbiologic confirmation of infection**;** Neither the participants nor the investigators were blinded; did not directly observe hand sanitizer use in this study, and it is possible that families over-reported the amount of sanitizer used to conform to social expectations. Study design does not allow us to separate the impact of hand sanitizer use from the effect of the educational intervention; the low initial rate of participation may limit generalizability to families who are willing to take part in such a study; Families were largely white and many had high income and education levels, the results may be difficult to generalize to families of different cultural backgrounds or lower socioeconomic status. **Evidence gaps and/or recommendations for future research identified by study authors:** none **Source of funding:** Glaser Pediatric Research Network. Study funds and hand sanitizer were provided by GOJO Industries, Inc (Akron, OH). The sponsor did not participate in

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computer using a permuted-blocks design with random block sizes - Assignments were concealed in opaque envelopes, and centers were assigned to control or intervention groups by a study investigator as they were enrolled. **Quality assessment: Internal (++); External (++)**	homes also functioned as family child care centers and families with a household member whose occupation included working with children under the age of 6 for 10 hours per week. We also excluded families who reported using alcohol-based hand sanitizer in the home at least once a day. **Participant characteristics:** Age of index child*: control 3.0 intervention 2.7 Age of primary care giver: control 37.1 intervention 36.3 Race: white – 104 control, 123 intervention; black - 18 control, 15 intervention; Other 11 control, 17 intervention Ethnicity – Hispanic 9 control, 9 intervention; Non-Hispanic 124 control, 144 intervention Other: Educational level of primary care giver – control </= high school 15, college 40, advanced degree 80; Intervention 11, 60, 83 respectively) Are groups similar at baseline?: Yes – Baseline Demographic characteristics in the control and intervention groups were compared using Fisher's exact test			control and intervention groups were compared using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables. The number of secondary illnesses in each family was modeled by a Poisson distribution. Generalized estimating equations were used to compare transmission rates between the control and intervention groups, accounting for correlations between families within a child care center Preplanned stratified analysis to assess whether the rate of respiratory illness transmission in intervention families was associated with amount of sanitizer use.	**illness transmission** - After adjustment for race, household income, education level, and occupation of the primary caregiver; number of children aged 0 to 5 in the household; previous experience using hand sanitizers; and baseline hand-hygiene practices in the home, the rate of secondary GI illness was significantly lower in intervention families compared with control families (IRR: 0.41; 95% CI: 0.19–0.90; P=.03). The overall rate of secondary respiratory illness was not significantly different between groups; the IRR in the intervention group was 0.97 compared with the control group (95% CI: 0.72–1.30; P= .83). **Association between rate of respiratory illness transmission in intervention families and amount of sanitizer use** - the IRR of secondary respiratory illness for those who used the larger amount of hand sanitizer was 0.81 compared with those who used the smaller amount (95% CI: 0.65–1.09; P=.06). In addition, comparing each stratum within the intervention group with control families, those who used the larger amount of hand sanitizer had an IRR of 0.83 (95% CI: 0.60 –1.17) for secondary respiratory illness, whereas those who used the smaller amount had an IRR of 1.02 (95% CI: 0.74 –1.41). This dose-response relationship was not observed for GI illness; the adjusted IRR for secondary GI illness was similar in those who used 2oz of hand sanitizer per 2-week period compared with those who used </= to 2oz (IRR: 0.93; 95% CI: 0.21– 4.16).	data analysis or manuscript preparation and did not have approval rights over the publication. **Additional comments:** none

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	for categorical variables and Wilcoxon rank sum test for continuous variables – adjustments made for the analysis				**Adverse effects -** Forty-five families reported 112 adverse events related to hand sanitizer use in 97 (7%) of the 1387 telephone calls; 21 of these families reported an adverse event only once, and 24 of them reported an adverse event on 2 or more occasions. Seventy-one (63%) of the 112 reported reactions were "dry skin," and 20 (18%) were "irritation." Other reported adverse events such as "stinging" (n=11), "smells bad" (n=7), "dislike it" (n=2), "allergic reaction" (n=2), and "too slippery" (n=1).	
Author(s): Taylor et al **Year:** 2004 **Citation:** Effectiveness of a Parental Educational Intervention in Reducing Antibiotic Use in Children A Randomized Controlled Trial - The Pediatric Infectious Disease Journal • Volume 24, Number 6, June 2005 **Country of study:**	**Source population(s):** children 24 months or older and their parents **Overall sample size at start of study:** 499 eligible children were enrolled **Number analysed at end of study:** Data on 4924 visits were reviewed – 94.6% completed the 2 month observation period (n=472) **Inclusion/exclusion criteria:** eligible patients were healthy children	**Description:** Intervention - Parents of study children receive a pamphlet and videotape (featuring one of their child's pediatricians) promoting the judicious use of antibiotics **Sample sizes at baseline:** 252 parent/child dyads	**Description: control** Parents of study children brochures about injury prevention. **Setting:** Offices of primary care pediatricians who are members of a regional practice-based research network **Sample sizes at baseline:** 247 parent/child dyads	**Outcomes evaluated:** **Primary outcomes**: number of visits for upper respiratory tract infections (URIs), number of diagnoses and antibiotic prescriptions for otitis media and/or sinusitis and total number of antibiotics per patient among children in the intervention and control groups **Secondary outcomes**: were total number	An educational intervention aimed at parents did not result in a decrease in the number of antibiotic prescriptions in their children - Of 4924 visits - 28.8% of these visits were because of URI symptoms. The mean number of visits per study patient for URI symptoms was 2.8. including all visits, the mean number of diagnoses of otitis media in study children was 2.1, mean number of diagnoses of otitis media and/or sinusitis was 2.3 and mean number of antibiotic prescriptions was 2.4; there were no significant differences between children in the intervention and	**Loss to follow-up?:** 94.6% of study patients completed the entire 12-month observation period in the practice in which they had been enrolled**.** **Study sufficiently powered?:** **Limitations identified by author:** **Bias:** discussion with parents, specific practice patients may have been identified as study participants **Under-powered:** It is also possible that there was a small positive effect from the intervention that we were unable to detect because of our sample size. We had a power of 80% to detect a difference of 0.5 antibiotic prescriptions during the

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Seattle, USA **Aim of study:** To determine whether an educational intervention aimed at parents leads to fewer antibiotic prescriptions for their children **Study design:** Placebo-controlled, randomized controlled trial **Method of allocation:** Randomization was based on a computer-generated list of study numbers that were consecutively assigned to enrolled patients. In addition, randomization was stratified by practice and in blocks of 10. **Quality assessment: Internal (++); External (++)**	younger than 24 months old seen in the offices of participating pediatricians and their parents. **Participant characteristics:** Mean age: 8.8+/-6.3 (I); 8.8 +/- 5.9(C) Gender: NR Other – antibiotics in previous year: 1.1+/- 1.9 (I); 1.1+/- 2.1 (C) **Are groups similar at baseline?:** Yes - To account for potential confounding despite randomization, parental education level, number of siblings, day-care attendance, cigarette smokers in the household, previous antibiotic use and age, among children in the intervention and control groups were compared according to *Chi 2* tests for categorical data and t tests for continuous variables (P<0.05)			of visits per study patient and number of visits for URI symptoms per child. **Length of follow-up:** data on outpatient visits during a 12-month observation period were collected **Method of analysis**: compared each outcome for children in the intervention group with those in the control group using Poisson regression analysis, adjusted for clustering into different practices Poisson regression analysis comparing the number of antibiotic prescriptions in intervention and control patients including intervention-season of enrollment interaction term. Because of the possibility that the effect of the intervention might be different among parents of children of differing ages, subgroup analyses were done including patients who were younger than 12 months old or 12 months of age or older at enrollment	control groups for any of these outcomes. Overall physicians prescribed 1 or more antibiotics during 45.9% of visits for a chief complaint of URI symptoms; 92% of antibiotic usage in children presenting with URI symptoms was for a diagnosis of otitis media and/or sinusitis. Overall the “average” study patient had 9.9 visits, 2.8 visits for URI symptoms, 2.1 diagnoses of otitis media, and received 2.4 prescriptions for antibiotics during the 12-month observation period; a total 1176 antibiotic prescriptions were written for enrolled children. The effect of the intervention on total number of antibiotic prescriptions was similar among patients enrolled during the autumn or winter months and those enrolled during spring and summer (P=0.72).	12-month observation period between children in the 2 groups; the clinical importance of a smaller effect is questionable **Confounding** - We measured the number of prescriptions given to patients rather than the number of antibiotics actually administered to study children - The practice of shared decision-making between practitioner and parent has been found to significantly reduce the number of antibiotics administered to children with otitis media **Limitations identified by review team: None** **Evidence gaps and/or recommendations for future research identified by study authors: Not reported** **Source of funding: Not reported.** **Additional comments: None**

Study Details	Population	Comparisons		Outcomes	Results (largely as presented by study authors)	Notes
		Intervention	Comparator(s)			
				To account for potential confounding parental education level, number of siblings, day-care attendance, cigarette smokers in the household, previous antibiotic use and age, among children in the intervention and control groups were compared according to Chi 2 tests for categorical data and t tests for continuous variables. Any variable that was not equally distributed between the 2 groups (P< 0.05) was included in the regression models		

Appendix A - Papers excluded at full paper stage from the RAND evidence review

Prescription only studies excluded from RAND evidence review

Title reference	Initial reason for exclude	Decision
Ashe D, Patrick PA, Stempel MM, Shi Q, Brand DA. Educational posters to reduce antibiotic use. J Pediatr Health Care 2006;20(3):192-7	Outcome prescription rates	include
Bell N. Antibiotic resistance: the Iowa experience. American Journal of Managed Care 2002;8(11):988-94	Outcome prescription rates	exclude: not patient-only
Bernier A, Delarocque-Astagneau E, Ligier C, Vibet MA, Guillemot D, Watier L. Outpatient Antibiotic Use in France between 2000 and 2010: after the Nationwide Campaign, It Is Time To Focus on the Elderly. Antimicrobial Agents and Chemotherapy 2014;58(1):71-77	Outcome prescription rates	exclude: not public-only (mass-media: public and professionals exposed to campaign)
Flottorp S, Oxman AD, Havelsrud K, Treweek S, Herrin J. Cluster randomised controlled trial of tailored interventions to improve the management of urinary tract infections in women and sore throat. BMJ. 2002 Aug 17;325(7360):367.	Evaluated rates of antibiotic use/antibiotic prescribing	exclude: not public-only (mass-media: public and professionals exposed to campaign)
Gonzales R, Corbett KK, Leeman-Castillo BA, et al. The "minimizing antibiotic resistance in Colorado" project: impact of patient education in improving antibiotic use in private office practices. Health Serv Res 2005;40(1):101-16	Outcome prescription rates	include
Gonzales R, Corbett KK, Wong S, et al. "Get smart Colorado": impact of a mass media campaign to improve community antibiotic use. Medical Care 2008;46(6):597-605	Outcomes prescription rates	exclude: not public-only (mass-media: public and professionals exposed to campaign)
Gonzales R, Sauaia A, Corbett KK, et al. Antibiotic treatment of acute respiratory tract infections in the elderly: effect of a multidimensional educational intervention. Journal of the American Geriatrics Society 2004;52(1):39-45	Outcome prescription rates	include
Hemo B, Shamir-Shtein NH, Silverman BG, et al. Can a nationwide media campaign affect antibiotic use? American Journal of Managed Care 2009;15(8):529-34	Outcome prescription rates	questioned why not in main review as has asures of patient knowledge. Reason: Israel not in included country list.
Molstad S, Erntell M, Hanberger H, et al. Sustained reduction of antibiotic use and low bacterial resistance. A ten-year follow-up of the Swedish Strama programme. International Journal of Antimicrobial Agents 2007;29:S33-S33	Outcome prescription rates	exclude: surveillance
Patient education may reduce unnecessary use of antibiotics by adults. AHRQ Research Activities 2005(299):8-8	Outcome not measuring change in participants' understanding/knowledge/awareness - prescription rates	exclude: commentary on another (included) study
Sabuncu E, David J, Bernede-Bauduin C, et al. Significant reduction of antibiotic use in the community after a nationwide campaign in France, 2002-2007. PLoS Med 2009;6(6):e1000084	Outcome prescription rates	exclude: not public-only (mass-media: public and professionals exposed to campaign)
Sung L, Arroll J, Arroll B, Goodyear-Smith F, Kerse N, Norris P. Antibiotic use for upper respiratory tract infections before and after a education campaign as reported by general practitioners in New Zealand. New Zealand Medical Journal 2006;119(1233):U1956	Outcome prescription rates	Exclude: about GPs' views
Taylor JA, Kwan-Gett TSC, McMahon EM, Jr. Effectiveness of a parental educational intervention in reducing antibiotic use in children: a randomized controlled trial. Pediatric Infectious Disease Journal 2005;24(6):489-93	Outcome prescription rates	include

Incidence of infection outcome studies excluded from RAND evidence review

Title reference	Initial reason for exclude	Decision
Golding GR, Quinn B, Bergstrom K, et al. Community-based educational intervention to limit the dissemination of community-associated methicillin-resistant Staphylococcus aureus in Northern Saskatchewan, Canada. BMC Public Health 2012;12:15	Targets both prescribers and patients. Outcome incidence of infection.	Exclude: targets prescribers and public/patients
Gudnason T, Hrafnkelsson B, Laxdal B, Kristinsson KG. Does hygiene intervention at day care centres reduce infectious illnesses in children? An intervention cohort study. Scandinavian Journal of Infectious Diseases 2013;45(5):397-403	Outcome incidence of infection	include
Hedin K, Petersson C, Cars H, Beckman A, Hakansson A. Infection prevention at day-care centres: feasibility and possible effects of intervention. Scand J Prim Health Care 2006;24(1):44-9	Targets both prescribers and patients. Outcome incidence of infection.	include
Lau CH, Springston EE, Sohn M-W, et al. Hand hygiene instruction decreases illness-related absenteeism in elementary schools: a prospective cohort study. BMC Pediatr 2012;12:52	Outcome incidence of infection	include
Sandora TJ, Taveras EM, Shih M-C, et al. A randomized, controlled trial of a multifaceted intervention including alcohol-based hand sanitizer and hand-hygiene education to reduce illness transmission in the home. Pediatrics 2005;116(3):587-94	Outcome incidence of infection	include