NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Public Health & Social Care Centre

A review of reviews of educational interventions designed to change the public's knowledge and behaviour in relation to antimicrobial use and antimicrobial resistance that target healthcare professionals and patients

Final Report: June 2015

Charlotte Haynes & Claire McLeod

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Acknowledgements

We would like to thank Paul Levay and Thomas Hudson at NICE for developing and testing the search strategy and Ruaraidh Hill at NICE for his help in sifting the identified papers.

Executive Summary

Introduction

The National Institute for Health and Care Excellence (NICE) has been asked by the Department of Health to develop a public health guideline aimed at delaying antimicrobial resistance: 'Antimicrobial stewardship: changing risk-related behaviours in the general population'. This guideline will focus on public education about:

- the importance of using antimicrobials correctly
- the dangers associated with their overuse and misuse
- changes in behaviour that can avert the problems associated with the misuse of antimicrobials, such as infection prevention and control measures.

The aim of this review is to identify systematic reviews which evaluate the effectiveness of antimicrobial use/resistance educational interventions that target both prescribers and the general public[1] in changing the knowledge and/or behaviour of the public in relation to antimicrobial use and antimicrobial resistance. The secondary objective is to determine the relative effectiveness of these combined interventions versus interventions that focus only on the public or focus only on prescribers.

Methods

A systematic review of reviews was conducted for reviews of educational interventions that target both the general public and prescribers[2] and aim to change the public's behaviour and knowledge of antimicrobial use and resistance. The reviews had to be published in English between 2001 and May 2015.

Results

Nine reviews were included in this review of reviews. The evidence statements based on the findings from these reviews are presented below.

[1] This includes patients. For ease of reading 'the general public' or 'public' will be used to include patients. 'Patients' will be specified when the target population of an intervention is patients.
[2] The terms 'prescribers', 'clinicians', and 'healthcare professionals' have been used inter-changeably within this report.

Evidence statement 1 – Knowledge and attitudes

Two reviews [1,2] found that multi-component interventions improve the public's knowledge of appropriate antimicrobial use (specifically in relation to antibiotics). One provided a narrative review[1] of public health campaigns and the other, a meta-analysis[2] of patient-only and combined patient and clinician targeted interventions, indicated that there was a statistically significant increase in knowledge and attitudes across these studies. It is not possible to conclude which components of an intervention are more effective than others.

1 Huttner 2010
2 Thoolen 2012

Evidence statement 2 – Antibiotic prescribing

There is strong evidence from eight reviews[1-8] that multi-component educational interventions that target both clinicians and patients/the public are effective at reducing antibiotic prescribing for self-limiting conditions. However the evidence concerning whether patient education, clinician education or a combination of both is superior in reducing antibiotic prescribing for self-limiting conditions is inconsistent.

One review[1] showed modest effects of public health campaigns on reducing antibiotic prescribing.

Three reviews[2-4] indicated that multi-component interventions including both clinician education and patient/public education are more effective at reducing inappropriate antibiotic prescribing than single-component interventions.

Two reviews[5,6] found that there were no significant differences in the effectiveness of single-component patient or clinician education only interventions compared to combined patient and clinician education interventions .

One review[7] concluded that while multi-component interventions were most effective, this was most likely due to the inclusion of physician education rather than patient education. And another review[8] concluded that inappropriate antibiotic use is most likely to be achieved through targeting healthcare professionals to delay or refuse antibiotics for self-limiting conditions rather than by educating patients or the public.

1 Huttner 2010
2 Arnold 2005,
3 Edeghere 2010,
4 Vodicka 2013
5 Ranji 2006
6 Ranji 2008
7 Van der Velden 2012
8 Thoolen 2012

Evidence statement 3 – Antibiotic resistance

Four reviews[1-4] reported on antibiotic resistance following educational interventions that reduced antibiotic prescribing/use. One review[1] found mixed effects on antibiotic resistance. One review[2] found no evidence of a change in antibiotic resistance, although few studies reported on this and follow-up periods were short; but an update of this work[3] found evidence of a reduction in the incidence of penicillin-resistant *S.pneumoniae* in one of three clinician and patient education intervention studies that assessed antimicrobial resistance. One review[4] indicated that public health campaigns may be associated with reductions in antimicrobial resistance, although some of the campaigns reported increases in antibiotic resistance over time (causality in either direction was not proven).

1 Arnold 2005,
2 Ranji 2006
3 Ranji 2008
4 Huttner 2010

Evidence statement 4 – Adverse effects

Three reviews[1-3] reported on adverse effects with educational interventions. Two reviews[1,2] found no evidence of adverse effects, however few studies reported on this and none were powered for rarer events such as hospitalisations. One review[3] found that, overall, reductions in antibiotic prescribing were not correlated with any adverse events but highlighted that an English study had found an increase in hospitalisations and mortality associated with community acquired pneumonia due to a decrease in antibiotic use over the time period.

1 Ranji 2008
2 Vodicka 2013
3 Huttner 2010

Background

The National Institute for Health and Care Excellence (NICE) has been asked by the Department of Health to develop a public health guideline aimed at delaying antimicrobial resistance: 'Antimicrobial stewardship: changing risk-related behaviours in the general population'. This guideline will focus on public education about:

- the importance of using antimicrobials correctly
- the dangers associated with their overuse and misuse
- changes in behaviour that can avert the problems associated with the misuse of antimicrobials, such as infection prevention and control measures.

NICE was also asked to develop a separate guideline on antimicrobial stewardship which focussed on healthcare systems and prescriber behaviour: 'Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use'. The latter guideline reviewed evidence on the effectiveness of prescriber-targeted interventions to reduce inappropriate antimicrobial prescribing; it did not include interventions that targeted both prescribers and patients. The former guideline has focussed on patient/general public-targeted interventions that evaluate the effectiveness of educational interventions in changing the public's behaviour to ensure they only ask for antimicrobials when appropriate and use them correctly; and as such the commissioned evidence review for the guideline focussed on interventions targeting predominantly only patients or the general public.

The committee responsible for developing the 'Antimicrobial stewardship: changing risk-related behaviours in the general population' guideline wanted to ensure that interventions that target both the public[1] and prescribers would be included in this guideline if they were not covered in 'Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use'. Hence, the NICE team agreed to undertake a rapid review of systematic reviews that evaluated the effectiveness of educational interventions on antimicrobial use or resistance targeting both the public and healthcare professionals in changing the public's behaviour to ensure they only ask for antimicrobials when appropriate and use them correctly. This review will assist the committee in answering the following key question:

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?

Review objectives

To review systematic reviews which evaluate the effectiveness of antimicrobial use/resistance educational interventions that target both healthcare professionals and the public in changing the knowledge and/or behaviour of the public in relation to antimicrobial use and antimicrobial resistance. The secondary objective is to determine the relative effectiveness of these combined interventions versus interventions that focus only on the public or focus only on prescribers.

Methods

A systematic review of reviews was conducted for reviews of educational interventions that target both the public and healthcare professionals and aim to change the public's behaviour and knowledge of antimicrobial use and resistance. The reviews had to be published in English between 2001 and May 2015. For full details of the searches and inclusion/exclusion criteria see Appendix 1: Review protocol.

Study selection at title and abstract stage was undertaken by two reviewers, with the first 100 papers dual screened independently and discussed between the reviewers to ensure consistency of approach. The remaining papers were divided equally between the reviewers. Any papers flagged as 'unsure' for inclusion were discussed between the two reviewers. One reviewer independently assessed studies for inclusion at full paper. These were then assessed for inclusion by a second reviewer and any disagreements were discussed with the first reviewer. Reviews were extracted into structured tables and a narrative synthesis was undertaken.

Results

Appendix 2: PRISMA flow chart shows the process for identifying the relevant reviews and

Appendix 3: List of studies excluded at full paper shows the reasons for exclusions. A total of 1022 records were screened at title and abstract stage, of which 29 were assessed at full paper stage. From this 9 reviews were included in the review of reviews. Please note that these 9 reviews overlap in terms of included studies, so there will be some double counting of evidence.

An overview of the reviews is presented in Table 1, and narratively described below, grouped by outcome. See Appendix 4: Extraction sheets for the full details of each review.

Knowledge and attitudes

Only two reviews reported on knowledge and attitudes of the public/patients following interventions which aimed to change their antibiotic use (Huttner 2010 and Thoolen 2012). Both reviews concluded that multi-component educational interventions improve the public's knowledge of appropriate antibiotic use.

Brief, narrative summary of reviews

Huttner 2010 undertook a narrative synthesis of 22 national campaigns and 6 regional campaigns which all highlighted that antibiotic resistance is an important problem and that misuse of antibiotics promotes bacterial resistance. Most highlighted to the public that the majority of respiratory illnesses are caused by viruses and cannot be treated with antibiotics and gave advice to follow the prescription and not to skip doses. All except one campaign targeted both the public and healthcare professionals. Huttner 2010 concluded that, where available, post-campaign surveys indicated that those exposed to the campaigns were more likely to agree with 'standards of appropriate use of antibiotics' and were less likely to expect antibiotics; but that changing knowledge about which infections are caused by viruses or bacteria was not very effective.

Thoolen 2012 undertook a meta-analysis of patient-oriented interventions designed to improve appropriate antibiotic use. Included studies were a mix of patient-oriented only approaches (n=16) and combined patient and clinical education (n=12), with 11 studies assessing the effect on patients' knowledge and attitudes about antibiotics. There was an overall small but significant effect of these interventions on improving knowledge about appropriate antibiotic use (Cohen's d=0.23, p<0.001). Studies that

were found to be effective were a mix of intervention types including delayed prescription or no prescription with or without advice, group education, educational materials including brochures and video. It was not possible to assess whether there was a difference in effectiveness between patient-targeted vs patient and healthcare professional targeted interventions.

Antibiotic prescribing

All 9 reviews assessed the effectiveness of interventions on prescribing rates. However only 8 provided information directly relevant to this review (Lee 2015 is not included). The 8 reviews present a mixed picture of whether patient education, clinician education or a combination of both is superior in reducing inappropriate antibiotic prescribing for self-limiting conditions. One review (Huttner 2010) found that campaigns targeting both the public and healthcare professionals are effective at reducing antibiotic use, but was not able to compare their effectiveness with interventions targeting only the public/patients or healthcare professionals. Three reviews (Arnold 2005, Edeghere 2010 and Vodicka 2013) indicated that multi-component interventions including both clinician education and patient/public education are more effective at reducing inappropriate antibiotic prescribing than single-component interventions. Two reviews (Ranji 2006 and Ranji 2008) found that there were no significant differences in the effectiveness of single-component patient or clinician education only interventions compared to combined patient and clinician education interventions. One review (Van der Velden) concluded that while multi-component interventions were most effective, this was most likely due to the inclusion of physician education rather than patient education. And another review (Thoolen 2012) concluded that inappropriate antibiotic use is most likely to be achieved through targeting healthcare professionals to delay or refuse antibiotics for self-limiting conditions rather than by educating patients or the public.

Review authors also concluded that the effectiveness of interventions is influenced by context, population and type of infection. Many also noted the effect of education style, advocating for ‘active’ rather than ‘passive’ education of both patients and clinicians; and highlighted the importance of physician communication with patients in order to reduce prescription rates and to ensure that patient satisfaction is not damaged.

Brief, narrative summary of reviews

Huttner 2010 found that public health campaigns targeting both healthcare professionals and the public have modest effects on reducing inappropriate antibiotic prescribing.

Arnold 2005 assessed the effectiveness of clinician interventions, alone or in combination with other interventions (including patient education interventions), in improving the selection, dose and treatment duration of antibiotics prescribed by clinicians in ambulatory healthcare settings (includes primary care, and healthcare settings where patients are not admitted to hospital at the time of assessment, e.g. A&E). They concluded that simple, single-intervention studies (printed educational materials, audit and feedback) generally resulted in small changes in prescribing behaviour. Studies examining the effect of active education of healthcare professionals produced modest but statistically significant results and were more effective than studies using passive education. Patient educational materials, along with limited clinician education, produced only small changes in prescribing rates. Multi-faceted interventions involving physicians, patient and community education consistently produced moderate changes in prescribing behaviours and were found to be effective in reducing antibiotic prescribing, after addressing local barriers to change.

Edeghere 2010 undertook a narrative synthesis which compared the effectiveness of interventions categorised by the authors as multi-faceted, delayed antibiotic, use of ancillary testing[3], or single interventions on reducing antibiotic prescribing for self-limiting conditions in ambulatory healthcare settings. The multi-faceted interventions consisted of patient and clinician education plus at least one other type of intervention component such as reminders, academic detailing and audit and feedback. Single interventions were a mix of different types of interventions that included patient education only, clinician only, but also combined patient and clinician education interventions. Delayed antibiotic interventions were a mix of studies in which delayed prescriptions were given to patients with or without 'passive' patient education. As such, the information provided does not allow for conclusions

[3] As this is not relevant to this review, is out of scope for the 'Antimicrobial stewardship: changing risk-related behaviours in the general population' guideline and covered in other NICE guidelines, details concerning these findings are not reported.

to be drawn concerning the relative effectiveness of patient-only vs clinician-only vs combined patient and clinician education interventions. Edeghere 2010 concluded that the multi-faceted interventions produced moderate to small changes in prescribing behaviour, and that the largest changes were reported by studies of varying quality (low to medium), while the smallest change was found in one high quality study. They noted that "*multifaceted interventions appear to be effective in changing prescribing behaviour but as with previous reviews, we are unable to disentangle the contribution of the individual components to the observed benefit nor recommend the best combinations of interventions to employ as any observed benefit in practice is likely to depend on the clinical setting and target population*." (Edeghere 2010)

Vodicka 2013 undertook a systematic review of interventions which aimed to reduce primary care antibiotic prescribing for respiratory illnesses in children. As with other reviews, due to clinical and statistical heterogeneity of included studies a meta-analysis was not appropriate and so narrative analysis was undertaken. Interventions were grouped into those targeting clinicians and parents, targeting clinicians only, or targeting parents only. They concluded that the most effective interventions "*target both parents and clinicians during consultations, provide automatic prescribing prompts, and promote clinician leadership in the intervention design*". They noted the limited effectiveness of passive education of parents in parent education only interventions (such as the use of waiting room posters or leaflets); and that the content of printed information may have an impact on effectiveness, with those containing 'actionable' information such as self-care advice being more effective than those describing generic information on the appropriate use of antibiotics.

Ranji 2006 and **Ranji 2008** undertook a quantitative and narrative synthesis to determine the relative effectiveness of different types of interventions aiming to reduce antimicrobial prescribing in outpatient/primary care settings. They found that interventions were significant at reducing prescribing, but found no significant difference in effectiveness between single-component (patient education or clinical education only) versus multi-component interventions (including combined clinician and patient education interventions). They highlighted the importance of active

versus passive education of clinicians on reducing inappropriate prescribing of antibiotics (although there was only a trend towards a significant difference in effectiveness on antibiotic prescribing between these strategies).

Van der Velden 2012 found that multi-component interventions were most often effective at reducing antibiotic prescribing for respiratory illnesses, and it was the inclusion of physician educational material that was associated with the “most often effective” studies - the addition of educational materials for patients gave no significant added value. Studies were included in the review on the basis that they were “an intervention primarily targeted at physicians in a primary care setting aiming to improve antibiotic prescription for” respiratory tract infections. Details of the content of interventions were limited to a basic categorisation. No indication of content of educational materials or how these were delivered to physicians or patients was provided.

Lee 2015 undertook a narrative synthesis of RCTs that evaluated clinician focussed educational interventions that aimed to reduce antibiotic prescribing. Only 2 of 28 RCTs were combined clinician and patient education interventions and there were no patient/public only RCTs. In addition, the poor reporting of the methods used in the review to determine effectiveness of the different educational components of clinician education interventions or the contribution of patient education components to the reduction in prescribing rates, indicates that this review cannot be used to determine whether or not clinician education alone is more effective than either patient education alone or a combination of clinician and patient education. The main focus of the Lee 2015 paper is on the content of education for healthcare professionals, along with some discussion of education for patients, the general public and school children which is based on evidence from sources beyond the systematic review element of their paper.

Thoolen 2012 undertook a meta-analysis of patient-oriented interventions designed to improve appropriate antibiotic use that were a mix of patient-only approaches and combined patient and clinical education. There was an overall small but significant effect size of interventions on antibiotic use, with interventions involving delayed or no prescriptions having the largest effect sizes. The authors concluded that “*the promotion of more prudent use of antibiotics in patients is better achieved by*

encouraging health professionals to delay or refuse the prescription of antibiotics rather than by educating patients about the negative aspects of antibiotics".

Delayed prescribing studies[4]

Apart from Thoolen 2012, several other systematic reviews reported here also evaluated the effectiveness of delayed prescriptions, and all found that these are highly effective at reducing prescribing rates (Arnold 2005, Edeghere 2010, Thoolen 2012, Ranji 2006 and 2008). However, several of the review authors noted that while these interventions may appear to be very successful, in most delayed prescription studies the control groups are given prescriptions to fill immediately (even when they might not be indicated, as in acute cough illness), making the antibiotic use rate in these groups close to 100%, which is very different from the antibiotic-use rates in control groups from other types of studies (Arnold 2005, Ranji 2006 and 2008).

Antibiotic resistance

Four reviews reported on efforts to determine the effectiveness of educational interventions on rates of antibiotic resistance. Huttner 2010 indicated that public health campaigns may be associated with reductions in antimicrobial resistance, although some of the campaigns reported increases in antibiotic resistance over time (causality in either direction was not proven). Arnold 2005 found mixed effects concerning antibiotic resistance. Ranji 2006 found no evidence of a change in antibiotic resistance (although few studies reported on this and follow-up periods were short); while an update of this work by Ranji 2008 found evidence of a reduction in the incidence of penicillin-resistant *S.pneumoniae* in one of three clinician and patient education intervention studies that assessed antimicrobial resistance (again all studies had short - 6 month – follow up periods).

Adverse effects

Three reviews reported on interventions that assessed potential adverse effects such as increases in the incidence of invasive infections due to bacteria, increases in hospital admissions or deaths following educational interventions that reduced

[4] Please note that delayed prescribing studies are out of scope for the 'Antimicrobial stewardship: changing risk-related behaviours in the general population' and have been covered in other NICE guidelines, including 'Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use'.

prescribing rates/use of antibiotics (Ranji 2008, Huttner 2010 and Vodicka 2013). Ranji 2008 found that no studies assessing potential adverse effects (11 trials from 9 studies) identified any adverse consequences to patients. Vodicka 2013 found no evidence of adverse effects, however they noted that few studies reported on this and none were powered for rarer events such as hospitalisations. Huttner 2010 found that, overall, reductions in antibiotic prescribing were not correlated with any adverse events but did highlight that an English study had found an increase in hospitalisations and mortality associated with community acquired pneumonia due to a decrease in antibiotic use over the time period.

Table 1 Overview of included reviews

Review	Key inclusion criteria	Interventions	Comparators	Key results	Author conclusions
Arnold 2005	Interventions to improve antibiotic prescribing in health professionals and consumers in an ambulatory care setting, and limited to RCTs, quasi-RCTs, interrupted time series, and controlled before and after studies published between 1966 and 2000.	Multi-faceted interventions, printed educational materials for physicians, audit and feedback, educational meetings, educational outreach visits, financial and healthcare system changes, physician reminders, and patient-based interventions.	Comparators included no intervention, usual care or another intervention. Some studies included 3 arms.	A narrative synthesis was presented grouping 39 studies by 8 broad intervention type headings. Results were not reported in a consistent manner which makes reporting problematic. Many intervention types showed mixed effects. Multi-faceted interventions (7 studies) generally showed some reduction in antibiotic usage. 4 studies showed mixed effects on antibiotic resistance.	The selection of the most effective intervention to improve antibiotic prescribing appears to depend on the local barriers to change. Multifaceted interventions where educational interventions occur on many levels are effective in reducing antibiotic prescribing, after addressing local barriers to change.
Edeghere 2010	Interventions to improve antibiotic prescribing in health professionals and consumers in an ambulatory care setting, and limited to RCTs, quasi-RCTs, interrupted time series, and controlled before and after studies published between 2000 and 2008.	A range of interventions were studies including multi-faceted interventions that included an educational component directed at providers, service users or both; delayed antibiotic prescribing; ancillary testing; and single interventions such as education alone.	Where reported, comparators included no intervention, passive education provided, and education only.	A narrative synthesis was presented grouping 49 studies by 4 broad intervention type headings. The absolute change in antibiotic prescribing was: -1.3% to -28.1% in RCTs with multi-faceted interventions (15 studies);-15% to -79% with delayed prescriptions (9 studies); mixed effects with single interventions (14 studies).	The effectiveness of interventions to improve antibiotic prescribing in ambulatory settings varies depending on the type and setting for the intervention, and the targeted behaviour and disease condition. Delayed antibiotic prescribing strategies show some benefit in reducing the use of antibiotics used in self-limiting infections in the community. Multifaceted interventions appear to be effective at changing prescribing behaviour in a variety of settings and

Review	Key inclusion criteria	Interventions	Comparators	Key results	Author conclusions
					healthcare systems.
Huttner 2010	No clear criteria were provided beyond large scale public health campaigns undertaken between 1990 and 2007 in high income countries. NB this review does not appear to be fully systematic.	All campaigns used a multi-component approach. Public targeted components focussed on mass distribution of lay information, including pamphlets, posters, and mass media in television, radio and public transport. Clinician targeted components focussed on mass distribution of more technical information, including mailing of educational material, guidelines and intensive academic detailing.	None/before the campaign	A narrative synthesis of 22 national campaigns and 6 regional campaigns was presented. Campaign awareness was reported for 6 campaigns and ranged from 9.2% to 71%. Knowledge and awareness of appropriate use of antibiotics and expectation of antibiotics improved, but not knowledge about which infections are caused by viruses or bacteria. Antibiotic prescribing was reported for 14 campaigns and ranged from no difference (Greece – unclear time period) to 36% reduction in prescribing (Belgium – over 7 years). Antibiotic resistance was measured in 12 campaigns and showed mixed effects. Adverse effects were rarely reported. Retrospective analyses of an English campaign reportedly indicated an increase in hospitalisation and mortality associated with community acquired pneumonia due to a decrease in antibiotic use.	Although causality is not proven, the results of several campaigns suggest they reduced antibiotic prescribing, at least in high prescribing countries. Multifaceted campaigns repeated over several years appear to be the most effective. The effect of campaigns on resistance and adverse events is less clear.
Lee 2015	No clear criteria were provided beyond educational interventions for	Interventions varied but involved literature seminars, mailing campaigns, small-group education, educational	Not reported	A narrative synthesis of 28 RCTs was presented, along with a broader discursive overview of the literature.	Continuous efforts to educate people about appropriate antibiotic use are important to manage antibiotic resistance.

Review	Key inclusion criteria	Interventions	Comparators	Key results	Author conclusions
	teaching prudent antibiotic usage published between 1983 and 2014 in English. NB this review does not appear to be fully systematic.	outreach visits, guidelines and leaflets, alone or in combination.		Antibiotic prescription was reduced by 34.1% in the clinician only education intervention groups compared with control. Looking at individual strategies, the effectiveness of interventions compared with control for antibiotic prescribing was largest for small-group education (-52%), guidelines and leaflets (-42%) and educational outreach visit (30%). Only 2 RCTs were identified that also included a patient education component, the review authors reported that these reduced antibiotic prescribing by 14%. NB: it was not clear how these results were calculated – caution is advised when interpreting results.	Medical and nonmedical undergraduate students' curriculum should include training on appropriate antibiotic usage.
Ranji 2006	Interventions to reduce inappropriate antibiotic prescribing in an outpatient setting, and limited to RCTs, interrupted time series, and controlled before and after studies published between 1966 and 2005.	Interventions varied and often involved more than one component. Key components included: clinician education, patient education, both clinician and patient education, delayed prescribing, clinical reminders, patient self-management, financial and regulatory incentives, and organisational change.	The control group varied from no intervention to another active intervention (some trials also had three arms).	54 studies were included in a quantitative and narrative synthesis. Interventions targeting inappropriate use were effective at reducing prescribing, with a median effect of -8.9% reduced antibiotic prescribing (IQR -12.4% to -6.7%), in intervention groups compared with comparison groups. The absolute reduction in antibiotic prescribing rates was 8.9%. Interventions targeting antibiotic	Quality improvement efforts are generally effective at reducing both inappropriate use of antibiotics and inappropriate choice of antibiotics. There is no single effective strategy, although strategies that include active clinician education may be more effective than passive education, particularly for addressing the antibiotic choice. Greater reductions in overall prescribing may be achieved through efforts targeting prescribing for all

Review	Key inclusion criteria	Interventions	Comparators	Key results	Author conclusions
				choice were effective, with a median absolute improvement of 10.6% (IQR 3.4% to 18.2%) in prescribing of recommended antibiotics in the intervention groups compared with the comparison groups. There was no difference in antibiotic resistance in two studies, although both had short follow-up periods.	acute respiratory infections, rather than targeting single conditions.
Ranji 2008	Interventions to reduce unnecessary antibiotic prescribing in an outpatient setting, and limited to RCTs, interrupted time series, and controlled before and after studies published between 1966 and 2005.	Interventions varied but involved the following interventions alone or in various combinations: Mailed educational newsletter; educational seminars; educational outreach for clinicians; written material for patients (or parents); audit and feedback; mass media campaigns; computer-based or paper-based decision-support; financial disincentives for patients; educational outreach; self-management guides; financial incentives for patients; educational video; delayed prescriptions.	Not reported	43 studies were included. Among 30 studies the median reduction in proportion of subjects receiving antibiotics was 9.7% (IQR 6.6-13.7%) over 6 months median follow-up, equivalent to a relative reduction of 25%. No single strategy was most effective although there was trend towards active clinician education strategies (median effect 7%, IQR 7-10.1%) being more effective than passive strategies (median effect 12.9%, IQR 8.1-19.2%) although this was not statistically significant (p=0.096).	Quality improvement strategies are effective at reducing antibiotic prescribing in an ambulatory setting, although there is still room for improvement. Active rather than passive clinician education and strategies targeting all ARIs rather than single conditions or age groups are most effective. Delayed prescriptions were an effective strategy but against a backdrop of near universal antibiotic prescribing; thus this approach may not be a useful strategy for controlling antibiotic prescribing costs and resistance.
Thoolen 2012	Interventions to reduce antibiotic prescribing in the public or patients and limited to RCTs, quasi-RCTs, and	Over half of studies focussed on patient orientated approaches, whilst the remaining studies focussed on patient and physician	Most studies had usual care as a comparator, whilst the	28 studies were included in a quantitative (meta-analysis) and narrative synthesis. 21 studies reported on antimicrobial use, with effect sizes	The promotion of interventions that delay or refuse prescriptions are likely to achieve better control of antibiotic usage than

Review	Key inclusion criteria	Interventions	Comparators	Key results	Author conclusions
	controlled before and after studies published between 1993 and 2008.	education. Intervention components (alone or in combination) included: video and brochure, information leaflet, multiple materials, physician intervention, delaying prescription, or no prescription.	remaining studies had an active comparator	ranging from 0.19 to -0.86 with interventions compared with controls. The overall effect size was statistically significant (d -0.21, p<0.001). The studies reporting the greatest effect sizes involved delaying or refusing prescriptions. 11 studies reported on knowledge and attitudes with effect sizes ranging from d 0.0 to 0.42 with interventions compared with controls. The overall effect size was statistically significant (d=0.23, p<0.001). 11 studies reported no significant difference in satisfaction (d= -0.019, p<0.44).	interventions that educate patients about the negative use of antibiotics. There are no negative effects in terms of patient satisfaction.
Van der Velden 2012	Interventions targeted at physicians to reduce antibiotic prescribing and published between 1990 and 2009.	Interventions had various components, including: educational information for the physician, educational meetings, audit and feedback, educational outreach, educational material for respiratory tract patients, educational information for practice patients, educational material for the public, and financial incentives.	Not reported	58 studies were included in a quantitative and narrative synthesis. 73% reported decreased antibiotic usage. Overall antibiotic prescription rate was reduced by 11.6%. Near patient testing alone (-72%), and communication skills training plus near-patient tested were reported to reduce antibiotic prescribing (-44%) by the largest amounts. The features of interventions that seemed to increase effectiveness were: multiple intervention	Physician education is a crucial for optimising antibiotic prescribing. Multiple interventions which included physician education were the most effective. Communication skills training of physicians is effective. Near-patient testing is also effective. Physician education with patient education was not significantly more effective than physician education alone.

Review	Key inclusion criteria	Interventions	Comparators	Key results	Author conclusions
				components (OR 6.5, 95% CI 1.9-22) and physician education (OR 5.5, 95% CI 1.7-18).	
Vodicka 2013	Educational or behavioural interventions targeted at physicians, parents or both to reduce antibiotic prescribing in primary care, reported in controlled studies and published upto 2012.	The interventions varied greatly but almost all were complex interventions. Intervention components for clinicians included: written material, clinician focus groups, lectures, newsletters, group education, feedback. Intervention components for parents included: education on what to expect at consultation, antibiotic resistance, self-care advice, telephone contact, posters, and handouts.	Not reported	17 studies were included in a quantitative and narrative synthesis. 8/10 studies of interventions in clinicians and parents reported significantly decreased prescribing rates ranging from 6-21%. One study reported no difference and one reported increased antibiotic usage. 1/6 studies of interventions in clinicians only reported significantly decreased prescribing rates of approximately 9% (depending on condition), 2/6 reported significant reductions in inappropriate prescribing (29-34%), and 3/6 found no difference or an increase in prescribing. None of the 3 studies in parents only found significant reductions in antibiotic prescribing. Only three studies reported complications or re-consultations which did not indicate an increased risk of adverse events due to decreased prescribing. However, studies were not powered to detect for rarer outcomes, such as hospitalisations.	Conflicting evidence from the included studies indicated that the most effective interventions target both parents and clinicians during consultations, provide automatic prescribing prompts, and promote clinician leadership in the intervention design.

Evidence statements

Evidence statement 1 – Knowledge and attitudes

Two reviews [1,2] found that multi-component interventions improve the public's knowledge of appropriate antimicrobial use (specifically in relation to antibiotics). One provided a narrative review[1] of public health campaigns and the other, a meta-analysis[2] of patient-only and combined patient and clinician targeted interventions, indicated that there was a statistically significant increase in knowledge and attitudes across these studies. It is not possible to conclude which components of an intervention are more effective than others.

1 Huttner 2010
2 Thoolen 2012

Evidence statement 2 – Antibiotic prescribing

There is strong evidence from eight reviews[1-8] that multi-component educational interventions that target both clinicians and patients/the public are effective at reducing antibiotic prescribing for self-limiting conditions. However the evidence concerning whether patient education, clinician education or a combination of both is superior in reducing antibiotic prescribing for self-limiting conditions is inconsistent.

One review[1] showed modest effects of public health campaigns on reducing antibiotic prescribing.

Three reviews[2-4] indicated that multi-component interventions including both clinician education and patient/public education are more effective at reducing inappropriate antibiotic prescribing than single-component interventions.

Two reviews[5,6] found that there were no significant differences in the effectiveness of single-component patient or clinician education only interventions compared to combined patient and clinician education interventions .

One review[7] concluded that while multi-component interventions were most effective, this was most likely due to the inclusion of physician education rather than patient education. And another review[8] concluded that inappropriate antibiotic use is most likely to be achieved through targeting healthcare professionals to delay or refuse antibiotics for self-limiting conditions rather than by educating patients or the public.

1 Huttner 2010
2 Arnold 2005,
3 Edeghere 2010,
4 Vodicka 2013
5 Ranji 2006
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Evidencestatement 3 – Antibiotic resistance

Four reviews[1-4] reported on antibiotic resistance following educational interventions that reduced antibiotic prescribing/use. One review[1] found mixed effects on antibiotic resistance. One review[2] found no evidence of a change in antibiotic resistance, although few studies reported on this and follow-up periods were short but an update of this work[3] found evidence of a reduction in the incidence of penicillin-resistant

S.pneumoniae in one of three clinician and patient education intervention studies that assessed antimicrobial resistance. One review[4] indicated that public health campaigns may be associated with reductions in antimicrobial resistance, although some of the campaigns reported increases in antibiotic resistance over time (causality in either direction was not proven).

1 Arnold 2005,
2 Ranji 2006
3 Ranji 2008
4 Huttner 2010

Evidence statement 4 – Adverse effects

Three reviews[1-3] reported on adverse effects with educational interventions. Two reviews[1,2] found no evidence of adverse effects, however few studies reported on this and none were powered for rarer events such as hospitalisations. One review[3] found that, overall, reductions in antibiotic prescribing were not correlated with any adverse events but highlighted that an English study had found an increase in hospitalisations and mortality associated with community acquired pneumonia due to a decrease in antibiotic use over the time period.

1 Ranji 2008
2 Vodicka 2013
3 Huttner 2010

Conclusions

The reviews present a diverse picture of which educational interventions are effective for controlling antibiotic prescribing. Multi-component interventions that include both physician and public education appear to be effective in reducing antibiotic usage. However, delayed prescriptions alone, or physician education alone are also effective in certain contexts. The effect of educational interventions on antibiotic resistance, and knowledge and attitudes is limited as few studies report on this. There is little evidence of the adverse effects of educational interventions due to few studies reporting on this and short follow-up periods.

Limitations

This was a review of reviews and as such it was limited by the reporting of the reviews and the reviews' inclusion/exclusion criteria. Some reviews were badly reported and/or synthesised which limited interpretation. Some reviews also included studies that may not have been strictly within scope of the NICE 'Antimicrobial stewardship: changing risk-related behaviours in the general population' guideline.

Our searches were limited to reviews published since 2001 in English, which may have resulted in some relevant reviews being omitted. However, the included reviews do include a large number of studies from pre-2001 and some have included non-English studies.

Our inclusion of semi-systematic reviews does make interpretation of results at times more difficult, but does provide a much broader picture of the literature and intervention types. In particular, evidence of public health campaigns (Huttner 2010) was not from a fully systematic review but the methods were appropriate for identifying public health campaigns and do provide useful information of their effectiveness that would not have been likely to be found had the authors used a standard systematic review of the literature.

References

Arnold S and Straus S. Interventions to improve antibiotic prescribing practices in ambulatory care. The Cochrane Library 2005, Issue 4.

Edeghere O, Wilson J, and Hyde C. Interventions to improve prescribing of antibiotics by healthcare professionals in ambulatory care settings. DPHE 2010, Report No 73.

Huttner B, Gossens H, Verheij T, Harbath S on behalf of the CHAMP consortium. Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. Lancet Infect Dis 2010; 10: 17-31.

Lee C-R, Lee J, Kang L-W, Jeong B, Lee S. Educational Effectiveness, Target, and Content for Prudent Antibiotic Use. BioMed Res Int 2015: http://dx.doi.org/10.1155/2015/214021

Ranji S, Steinman M, Shojania K, Lewis R, Arnold S, and Gonzales R. Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies. 2006. AHRQ Publication No. 04(06)-0051-4.

Ranji S, Steinman M, Shjania K, and Gonzales R. Interventions to reduce unnecessary antibiotic prescribing. Med Care 2008; 46: 847-62

Thoolen B, de Ridder D, and van Lensvelt-Mulders G. Patient-orientated interventions to improve antibiotic prescribing practices in respiratory tract infections: a meta-analysis. Health Psych Rev 2012; 6 (1): 92-112.

Van der Velden A, Pijpers E, Kuyvenhoven M, Tonkin-Crine S, Little P and Verheij T. Effectiveness of physician targeted interventions to improve antibiotic use for respiratory tract infections. Br J Gen Pract 2012; e802.

Vodicka T, Thompson M, Lucas P, Heneghan C, Blair P et al on behalf of the Target Programme team. Reducing antibiotic prescribing for children with respiratory tract infections. Br J Gen Pract 2013; DOI: 10.3399/bjgp13X669167.

Appendix 1: Review protocol

	Details
Guideline details	
Guideline	Antimicrobial stewardship - changing risk-related behaviours in the general population
Objective of review	To review systematic reviews which compare patient/public education interventions with interventions that target healthcare professionals (with or without a patient education component).
Review details	
Review title	A review of reviews of educational interventions designed to change the public's knowledge and behaviour in relation to antimicrobial use and antimicrobial resistance that target healthcare professionals and patients.
Review methods	
Review question(s)	Are educational interventions that target both patients and healthcare professionals effective at changing the public's knowledge and behaviour in relation to antimicrobial use and antimicrobial resistance?
Sub-question(s)	What is the relative effectiveness of combined interventions that target both patients and healthcare professionals versus interventions that focus only on the public or focus only on healthcare professionals?
Searches	**Search approach:** **Search concepts:** **Limits:** Publication limit 2001-current English-language studies **Databases (RQ 1.1 and RQ 1.2):** • Medline and Medline in Process via Ovid • The Cochrane Library: CDSR, HTA and DARE via Wiley • Embase via Ovid Search strategy: see below. **Websites** The following websites will be browsed: • DOPHER via http://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=9 • Google Scholar http://scholar.google.co.uk/ • Healthevidence via http://healthevidence.org/search-login.aspx • NICE Evidence http://www.evidence.nhs.uk/ • TRIP https://www.tripdatabase.com/ • Web of Science via http://apps.webofknowledge.com

Condition or domain being studied	Antimicrobial use and misuse, antimicrobial resistance
Participants/ population	Included: • General public or patients AND healthcare professionals/prescribers Excluded: • Healthcare professionals/prescribers only OR patient/public only (no combined) • Low income countries only
Intervention(s), exposure(s)	Educational interventions for the general public/patients and/or for healthcare professionals
Comparator(s)/ control	Included: • no intervention • educational interventions for the general public/patients and/or for healthcare professionals
Types of study to be included initially	Systematic reviews
Primary/Critical outcomes	Changes in: • knowledge and awareness of when, why and how antimicrobials should be used • knowledge and awareness of antimicrobial resistance • knowledge of the type of support people can expect from health professionals in relation to the use of antimicrobials • demand for antimicrobials (particularly antibiotics) (e.g. changes in consultation rates, requesting antibiotics for a cold or flu) • adherence to prescribed antimicrobials • inappropriate antimicrobial use (e.g. self-medicating with antimicrobials without advice from a healthcare professional) • antimicrobial prescribing
Risk of bias (quality) assessment	The quality of systematic reviews is not being assessed for the purposes of the draft review. Quality assessment may be undertaken at a later date using the relevant checklist recommended in the NICE guidelines manual
Strategy for data synthesis	Data will be synthesised in tabular form and using narrative synthesis methods.
General information	
Type of review	Review of reviews

Search strategy

All searches were run on 15 May 2015. The following search strategy was also run in Cochrane Library databases and adapted as appropriate before running in Embase.

Database(s): **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present

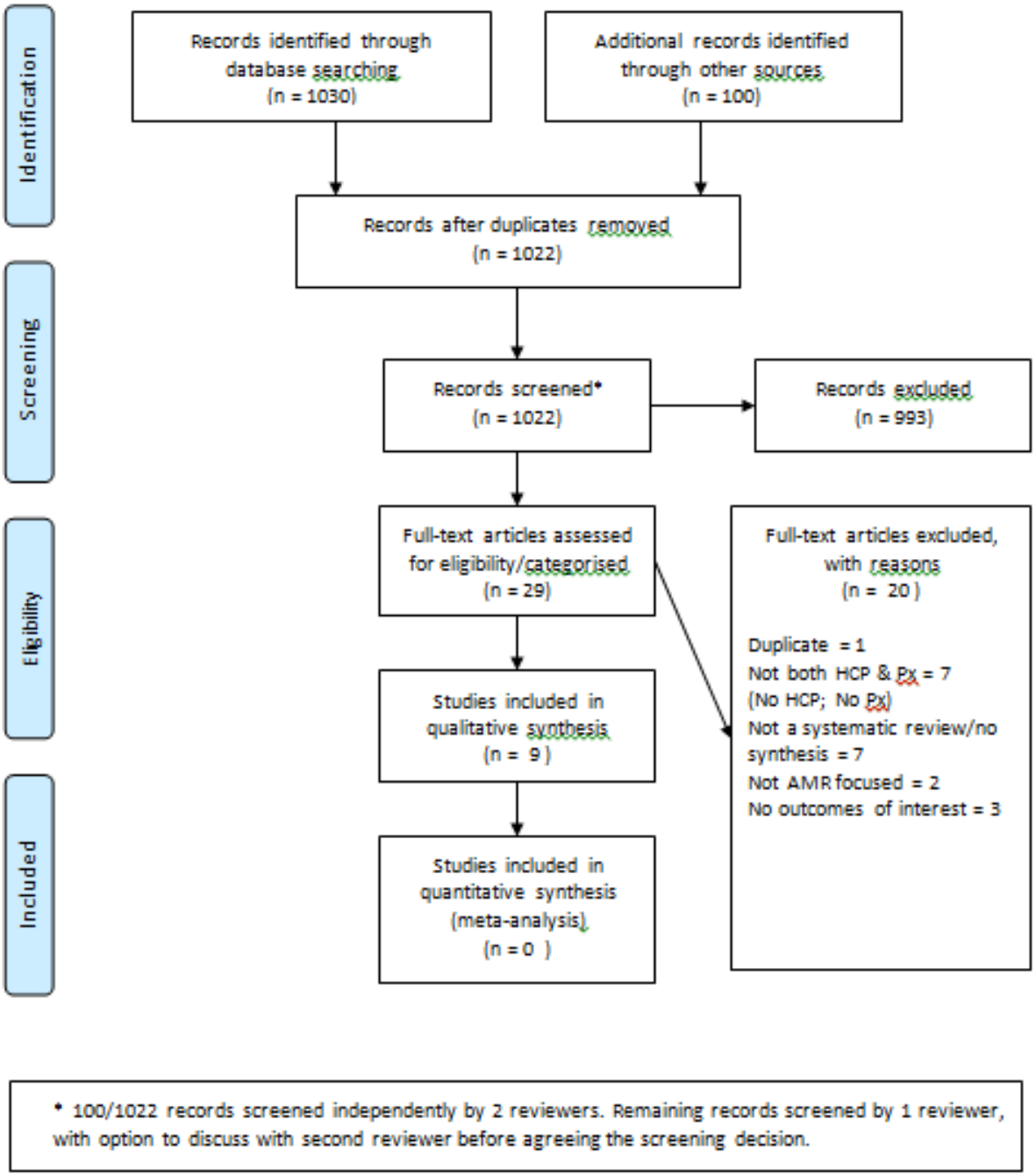
Search Strategy:

#	Searches	Results
1	exp Drug Resistance, Bacterial/ or exp Drug Resistance, Multiple/	77059
2	anti-infective agents/ad, tu or anti-bacterial agents/ad, tu or antibiotics, antitubercular/ad, tu or antitubercular agents/ad, tu or antifungal agents/ad, tu or anti-infective agents, local/ad, tu or antiparasitic agents/ad, tu or anthelmintics/ad, tu or antiprotozoal agents/ad, tu or antiviral agents/ad, tu or anti-retroviral agents/ad, tu	240811
3	(antibiotic* or anti-biot* or "anti biot*" or antimicrob* or "anti microb*" or antibacter* or anti-bacter* or "anti bacter*" or antiviral* or anti-viral* or "anti viral*" or antiparasitic* or anti-parasitic* or "anti parasitic*" or antifungal* or anti-fungal* or "anti fungal*").ti,ab.	437123
4	or/1-3	620443
5	((multifacet* or multicomponent* or multitarget* or multisector* or multipartner* or multidisciplin* or multi facet* or multi component* or multi target* or multi sector* or multi partner* or multi disciplin*) adj3 (intervention* or program* or initiative* or collaborat* or coordinat* or counsel* or educat* or learning or informat* or communicat* or advice* or advis* or literacy or publication* or curriculum* or curricula* or teach* or trainer* or training or resource* or session* or workshop* or material* or outreach)).ti,ab.	10346
6	physician-patient relations/ or professional-family relations/ or professional-patient relations/	94235
7	Decision Support Techniques/	13389
8	((shared or informed or collaborat*) adj3 (decision* or choice*)).ti,ab.	11106
9	or/5-8	126794
10	4 and 9	1393
11	exp education, professional/ or exp inservice training/ or vocational education/	264388
12	exp Schools, Health Occupations/ or exp Students, Health Occupations/	79447
13	11 or 12	303084
14	4 and 13	1035
15	behavior therapy/ or Education/ or Models, Educational/ or Education, Distance/ or Education, Continuing/ or Curriculum/ or Teaching materials/ or Teaching/ or computer-assisted instruction/ or exp Programmed Instruction as Topic/	159553
16	Pamphlets/ or exp Audiovisual aids/ or communications media/ or exp marketing/ or Advertising as Topic/ or Persuasive Communication/ or Social Networking/ or internet/	173158
17	Libraries/ or Library materials/ or Library Services/ or Information services/ or Information	32425

	Dissemination/ or access to information/ or Information Literacy/ or Information Seeking Behavior/	
18	((outreach or written or printed or oral or campaign* or resource* or disseminat*) adj1 information).ti,ab.	5910
19	(marketing or advertis* or publicis* or publiciz* or publicity or mass media or media campaign* or communication* media).ti,ab.	37661
20	(internet* or social media or social network* or facebook or twitter or blog* or SMS or short messaging service* or smartphone* or mobile app or mobile apps or mobile application* or tweet or text messag* or texting or emailing or podcast* or ((mobile or cell* or smart) adj (phone* or telephone*))).ti,ab.	52927
21	or/15-20	404652
22	Physician's Practice Patterns/ or Nurse's Practice Patterns/ or Dentist's Practice Patterns/ or Inappropriate Prescribing/pc	46604
23	((practice* or practise* or prescri* or dispens*) adj2 pattern*).ti,ab.	8941
24	exp health personnel/ or "Attitude of Health Personnel"/ or exp professional role/	478405
25	or/22-24	518799
26	4 and 21 and 25	330
27	((counsel* or educat* or learning or informat* or communicat* or pamphlet* or handout* or hand-out* or hand out* or booklet* or leaflet* or advice* or advis* or literacy or literature or video* or audio* or web* or website* or poster or posters or publication* or curriculum* or curricula* or teach* or trainer* or training or program* or intervention* or resource* or meeting*1 or session*1 or workshop*1 or visit*1 or material*1 or initiative*1 or outreach) adj3 (clinician* or doctor* or physician* or nurse* or pharmacist* or general practitioner* or prescriber* or dispenser* or dentist*)).ti,ab.	88221
28	((behavior* or behaviour*) adj3 (change* or changing or alter* or modification* or modify or modifying or modifies or modified or therapy or therapies) adj3 (clinician* or doctor* or physician* or nurse* or pharmacist* or general practitioner* or prescriber* or dispenser* or dentist*)).ti,ab.	830
29	27 or 28	88792
30	4 and 29	1971
31	14 or 26 or 30	3065
32	Patient Education as Topic/ or Consumer Health Information/ or Patient Education Handout/	77851
33	4 and 32	1360
34	exp patients/ or exp parents/ or exp Family/ or Caregivers/	323039
35	Patient Acceptance of Health Care/ or Patient Satisfaction/ or exp patient compliance/	145934
36	attitude to health/	74234

37	or/34-36	509377
38	health education/ or health promotion/ or Health Communication/ or health literacy/ or Public Health/ed or self efficacy/	120574
39	21 or 38	501926
40	37 and 39	47514
41	4 and 40	321
42	((counsel* or educat* or learning or informat* or communicat* or pamphlet* or handout* or hand-out* or hand out* or booklet* or leaflet* or advice* or advis* or literacy or literature or video* or audio* or web* or website* or poster or posters or publication* or curriculum* or curricula* or teach* or trainer* or training or program* or intervention* or resource* or meeting*1 or session*1 or workshop*1 or visit*1 or material*1 or initiative*1 or outreach) adj3 (public* or patient* or family or families or mother* or father* or parent* or carer* or caregiver* or care-giver* or inpatient* or in-patient* or outpatient* or out patient* or population* or community or communities)).ti,ab.	405867
43	((behavior* or behaviour*) adj3 (change* or changing or alter* or modification* or modify or modifying or modifies or modified or therapy or therapies) adj3 (public* or patient* or family or families or mother* or father* or parent* or carer* or caregiver* or care-giver* or inpatient* or in-patient* or outpatient* or out patient* or population* or community or communities)).ti,ab.	3727
44	42 or 43	408368
45	4 and 44	10094
46	33 or 41 or 45	11269
47	31 and 46	730
48	10 or 47	2039
49	limit 48 to yr="2001 -Current"	1566
50	limit 49 to english language	1494
51	Meta-Analysis as Topic/ or exp Review Literature as Topic/ or (Meta-Analysis or review).pt.	2019835
52	(metaanaly* or metanaly* or (meta adj2 analy*)).ti,ab.	77345
53	(systematic* adj3 (review* or overview* or synthesis)).ti,ab.	73142
54	((quantitative* or qualitative*) adj3 (review* or overview*)).ti,ab.	3974
55	(pool* adj1 (analy* or data)).ti,ab.	11427
56	or/51-55	2059186
57	50 and 56	274
58	remove duplicates from 57	268

Appendix 2: PRISMA flow chart



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Appendix 3: List of studies excluded at full paper

In total 20 studies were excluded from the review.

Study reference	Reason for exclusion
Anonymous. Avoiding antibacterial overuse in primary care. [Review] [31 refs]. *Drug & Therapeutics Bulletin* 45 (4):25-28, 2007.	Not a systematic review/no synthesis
Andrews T *et al*. Interventions to Influence Consulting and Antibiotic Use for Acute Respiratory Tract Infections in Children: A Systematic Review and Meta-Analysis. *Plos One* 7 (1), 2012.	No HCP (healthcare professional component)
Bennett JW and Glasziou PP. Computerised reminders and feedback in medication management: a systematic review of randomised controlled trials. *Med.J.Aust.* 178 (5):217-+, 2003.	Not combination of HCP & Px intervention
Christiansen K, Carbon C, and Cars O. Moving from recommendation to implementation and audit: Part 2. Review of interventions and audit. *Clin.Microbiol.Infect.* 8 (SUPPL. 2):107-128, 2002.	Not a systematic review/no synthesis
Dixon J and Duncan CJ. Importance of antimicrobial stewardship to the English National Health Service. [Review]. *Infection & Drug Resistance* 7:145-152, 2014.	Not a systematic review/no synthesis.
Dixon J and Duncan CJ. Importance of antimicrobial stewardship to the English National Health Service. [Review]. *Infection & Drug Resistance* 7:145-152, 2014.	Duplicate (see above)
Drug and Therapeutics Bulletin. An introduction to patient decision aids. [Review]. *BMJ* 347:f4147, 2013.	Not AMR focussed
Edgar T, Boyd SD, and Palame MJ. Sustainability for behaviour change in the fight against antibiotic resistance: a social marketing framework. [Review] [62 refs]. *J.Antimicrob.Chemother.* 63 (2):230-237, 2009.	Not a systematic review/no synthesis
Fendrick AM, *et al*. Diagnosis and treatment of upper respiratory tract infections in the primary care setting. [Review] [73 refs]. *Clinical Therapeutics* 23 (10):1683-1706, 2001.	Not combination of HCP & Px intervention
Foucault C and Brouqui P. How to fight antimicrobial resistance. [Review] [114 refs]. *FEMS Immunology & Medical Microbiology* 49 (2):173-183, 2007.	Not a systematic review/no synthesis
Goff DA. Iphones, ipads, and medical applications for antimicrobial stewardship. *Pharmacotherapy* 32 (7):657-661, 2012.	Not a systematic review/no synthesis
Hansen MP, *et al.* Antibiotic Resistance: What are the Opportunities for Primary Care in Alleviating the Crisis?. [Review]. *Frontiers in Public Health* 3:35, 2015.	No outcomes of interest
Llor C and Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. [Review]. *Therapeutic Advances in Drug Safety* 5 (6):229-241, 2014.	Not a systematic review/no synthesis
Lu CY, *et al*. Interventions designed to improve the quality and efficiency of medication use in managed care: A critical review of the literature - 2001-2007. *BMC Health Serv.Res.* 8, 2008.	Not combination of HCP & Px intervention
Platt FW and Keating KN. Differences in physician and patient perceptions of uncomplicated UTI symptom severity: understanding the communication gap. [Review] [33 refs]. *Int.J.Clin.Pract.* 61 (2):303-308, 2007.	Not combination of HCP & Px intervention

Ryan R, *et al.* Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. [Review][Update of Cochrane Database Syst Rev. 2011;(5):CD007768; PMID: 21563160]. *Cochrane Database Syst.Rev.* 4:CD007768, 2014.	Not AMR focussed
Ryan R, *et al*. Consumer-oriented interventions for evidence-based prescribing and medicines use: an overview of systematic reviews. *Cochrane Database Syst.Rev.* (5), 2011.	No outcomes of interest
Turnidge j. Responsible prescribing for upper respiratory tract infections. [Review] [49 refs]. *Drugs* 61 (14):2065-2077, 2001.	No outcomes of interest
von G, Reymond JP, Beney J. Clinical and economic outcomes of pharmaceutical services related to antibiotic use: a literature review. [Review] [62 refs]. *Pharmacy World & Science* 29 (3):146-163, 2007.	No Px (patient intervention component)
Wertheimer AI and Santella TM. Medication noncompliance: What we know, what we need to learn. *Fabad J.Pharm.Sci.* 28 (4):207-214, 2003.	Not combination of HCP & Px intervention

Appendix 4: Extraction sheets

<table>
<tr><td colspan="2">Authors: Arnold S and Straus S.
Year: 2005
Citation: Interventions to improve antibiotic prescribing practices in ambulatory care. The Cochrane Library 2005, Issue 4.
Aim of study: To assess the effectiveness of professional interventions, alone or in combination, in improving the selection, dose and treatment duration of antibiotics prescribed by healthcare providers in the outpatient setting; and to evaluate the impact of these interventions on reducing the incidence of antimicrobial resistance.
Review design: Systematic review.</td></tr>
<tr><td colspan="2">Review search parameters</td></tr>
<tr><td>Databases and websites searched:
MEDLINE, EMBASE, and EPOC.

Other methods undertaken (e.g., reference checking):
The bibliographies of included studies were also searched.

Years searched:
1966/1980 to May 2000/2002.</td><td>Inclusion criteria, including study type, country:
Type of infection: NR.
Population: healthcare professionals and healthcare consumers.
Intervention: interventions to improve antibiotic prescribing.
Comparator: NR.
Outcomes: rate of appropriate antibiotic prescribing. Secondary outcomes were adverse effects and resistance.
Setting: ambulatory care.
Study design: RCTs, quasi-RCTs, interrupted time series, and controlled before and after studies.
Other: No language restrictions.

Exclusion criteria:
Studies of medical trainees only were excluded.

Number of studies included:
39 studies.</td></tr>
<tr><td colspan="2">Review population, type of study and setting</td></tr>
<tr><td>Characteristics of population/s:
Some studies were conducted in adults or children only, whereas others were in people of all ages.</td><td>Setting and type of included studies:
The studies were conducted in a variety of countries including: the USA, the UK, Canada, the Netherlands, Australia, Sudan, Iran and Japan.
All studies were conducted in an ambulatory care setting.</td></tr>
<tr><td colspan="2">Interventions</td></tr>
<tr><td>Intervention/s description:
Multi-faceted interventions, printed educational materials for physicians, audit and feedback, educational meetings, educational outreach visits, financial and healthcare system changes, physician reminders, and patient-based interventions.</td><td>Control/comparison/s description:
Comparators included no intervention, usual care or another intervention. Some studies included 3 arms.</td></tr>
<tr><td colspan="2">Outcomes and method of analysis</td></tr>
<tr><td>Outcomes:
The decision to prescribe an antibiotic; or the rate of</td><td>Methods of analysis:
A narrative synthesis was presented. Meta-analysis</td></tr>
</table>

prescribing a recommended choice, dose or duration of use of antibiotics. Secondary outcome measures were antibiotic resistance measures and adverse event measures. **Follow-up periods:** NR	was deemed inappropriate due to heterogeneity. **Quality assessment:** Quality criteria for the EPOC study group.
Results	
Antimicrobial use and prescribing *Comparison 1: printed educational materials compared to another intervention or controls (four studies – all healthcare professional (HCP) only).* 1 study found a statistically significant reduction in antibiotic use and 3 studies found no difference. *Comparison 2: audit and feedback (with or without printed educational materials) compared to another intervention or controls (four studies – all HCP only except 1: HCP and patient (PT)).* The studies found no effect or a small effect. (NB Results were not presented in a consistent manner which makes reporting problematic.) *Comparison 3: group educational meetings (with or without audit and feedback and printed educational materials) compared to another intervention or controls (ten studies – all HCP only).* The majority of studies showed modest reductions in antibiotic usage. (NB Results were not presented in a consistent manner which makes reporting problematic.) *Comparison 4: educational outreach visits (academic detailing) compared to another intervention or controls (eight studies – all HCP only).* The studies showed mixed effects. (NB Results were not presented in a consistent manner which makes reporting problematic.) *Comparison 5: financial or healthcare delivery changes compared to another intervention or controls (two studies – neither HCP nor PT focussed; i.e. not relevant).* *Comparison 6: physician reminders compared to another intervention or controls (three studies – all HCP only).* The studies showed mixed effects. (NB Results were not presented in a consistent manner which makes reporting here problematic.) *Comparison 7: patient-based interventions compared to another intervention or controls (five studies – all PT only except 1: HCP and PT - same study as in comparison 1).* Two studies of patient education showed reductions in antibiotic usage of -7.2 to -15.2%. Three studies of delayed prescriptions showed significant reductions in patients obtaining prescriptions of -45% to -74.5%.	**Quality assessment** Most of the studies had methodological limitations. **Sample sizes** NR.

Comparison 8:multi-faceted interventions (combinations of multiple interventions to physicians, patients and the general public) (7 studies – HCP and PT targeted interventions) The majority of studies showed some reductions in antibiotic usage or prescribing. (NB Results were not presented in a consistent manner which makes reporting here problematic.) **Antibiotic resistance** 4 studies (3 of which were HCP and PT targeted) showed mixed effects on antibiotic resistance. (NB Results were not presented in a consistent manner which makes reporting problematic.) **Patient/public knowledge and attitudes** NR	
Conclusions. limitations and other information	
Author conclusions The selection of the most effective intervention to improve antibiotic prescribing appears to be condition and situation specific. Local barriers to change need to be identified and addressed. Simple, single-intervention studies (printed educational materials, audit and feedback) generally resulted in small changes in prescribing behaviour. Studies examining the effect of 'interactive' [aka active] education of healthcare professionals produced modest but statistically significant results and are more effective than didactic lectures [i.e. passive education]. The effects of physician reminders were mixed and number of studies too small to draw any definite conclusions. A delayed prescription may be the most effective intervention to reduce the use of antibiotics for certain conditions. Patient educational materials, along with limited physician education, produced small changes in prescribing rates. Multi-faceted interventions involving physicians, patient and community education consistently produced moderate changes in prescribing behaviours. These are effective in reducing antibiotic prescribing, after addressing local barriers to change. **Evidence gaps and/or recommendations for future research and policy** Future research should focus on which elements of interventions are the most effective. In addition, patient-based interventions and physician reminders show promise and warrant further study. The cost-effectiveness of interventions has not been established. **Source of funding** NR.	**Author limitations** NR. **Limitation identified by review team** The grouping of studies into 8 intervention types may not have been the most informative grouping. The reporting of results varied greatly across studies which hindered both reporting and interpretation. Lack of direct comparison of effectiveness in changing prescribing between HCP and PT targeted interventions versus HCP-only or PT-only interventions.

NA = not applicable; NR = not reported

Authors: Edeghere O, Wilson J, and Hyde C.

Year: 2010

Citation: Interventions to improve prescribing of antibiotics by healthcare professionals in ambulatory care settings. DPHE 2010, Report No 73.

Aim of study: To assess the effectiveness of interventions to improve prescribing of antibiotics by healthcare professionals in ambulatory care settings

Review design: Systematic review.

Review search parameters

Databases and websites searched:

MEDLINE, EMBASE, CINAHL, CENTRAL, and DARE**.**

Other methods undertaken (e.g., reference checking):

The bibliographies of included studies were also searched.

Years searched:

January 2000 to June 2008.

Inclusion criteria, including study type, country:

Type of infection: NR.

Population: healthcare professionals and healthcare consumers.

Intervention: interventions to improve antibiotic prescribing.

Comparator: any intervention, usual care, no intervention.

Outcomes: the decision to prescribe an antibiotic; or the rate of prescribing a recommended choice, dose or duration of use of antibiotics. A range of secondary outcomes were also reported in the review.

Setting: ambulatory care.

Study design: RCTs, quasi-RCTs, interrupted time series, and controlled before and after with at least 3 data points before and after intervention.

Other: Any language. Any country.

Exclusion criteria:

Specialist and non-ambulatory care settings. Hospital controls.

Number of studies included:

49 studies.

Review population, type of study and setting

Characteristics of population/s:

Some studies were conducted in adults or children only, whereas others were in people of all ages.

Setting and type of included studies:

The studies were conducted in a variety of countries including: the USA, the UK, Canada, the Netherlands, Australia, Sudan, Iran and Japan.

38 RCTs, 9 controlled before and after, 2 interrupted time series.

All studies were conducted in an ambulatory care setting.

Interventions

Intervention/s description:

A range of interventions were apparent in studies:

Multi-faceted interventions (21 studies) consisted of at least two different types of interventions: combined patient and provide education plus one or more of the following: audit and prescribing feedback, academic

Control/comparison/s description:

Where reported, comparators included no intervention, passive education provided, and education only.

detailing, computerised decision support tools or reminders, prescribing restrictions and financial penalties, communication training. Delayed antibiotic prescribing (9 studies) Ancillary testing (5 studies) Single interventions (14 studies): these included education to only patients or providers but also included education aimed at both, computerised decision support tools/reminders.	
Outcomes and method of analysis	
Outcomes: The decision to prescribe an antibiotic; or the rate of prescribing a recommended choice, dose or duration of use of antibiotics. Secondary outcome measures were antibiotic resistance measures and adverse event measures. **Follow-up periods:** NR	**Methods of analysis:** A narrative synthesis was presented. Meta-analysis was deemed inappropriate due to significant clinical heterogeneity. **Quality assessment:** The Cochrane guideline for assessing risk of bias.
Results	
Antimicrobial use and prescribing *Multifaceted interventions* 15 RCTs/C-RCTs reported on overall antibiotic (AB) prescription/use; 13 found a significant reduction in use from baseline, and 2 found no difference. The absolute change (post) ranged from -1.3% to -28.1%. 5 CBAs reported on overall AB prescription of recommended antibiotics, with inconsistent results. 3 CBAs reported on inappropriate AB prescribing, all found a significant reduction in use from baseline. 1 ITS reported a significant overall reduction in AB prescribing. *Delayed antibiotic prescriptions* 9 studies (6 of which included passive patient education) reported on overall antibiotic usage; 8 found a significant reduction in use from baseline, and 1 (which did not included passive patient education) found no difference. The absolute change (post) ranged from -15% to -79%. *Ancillary testing – not reported as out of scope and all interventions healthcare professional only* *Single interventions* The single interventions studies showed mixed effects. **Patient/public knowledge and attitudes** NR	**Quality assessment** The quality of studies was reportedly variable. **Sample sizes** NR.
Conclusions. limitations and other information	

Author conclusions The effectiveness of interventions to improve antibiotic prescribing in ambulatory settings varies depending on the type and setting for the intervention, and the targeted behaviour and disease condition. Delayed antibiotic prescribing strategies show some benefit in reducing the use of antibiotics used in self-limiting infections in the community. Multifaceted interventions appear to be effective at changing prescribing behaviour in a variety of settings and healthcare systems. The ideal combination of interventions is uncertain as is the key component of these multifaceted interventions. **Evidence gaps and/or recommendations for future research and policy** There is a need for good quality cost-effectiveness studies, particularly of complex multifaceted interventions. **Source of funding** Health Protection Agency.	**Author limitations** NR. **Limitation identified by review team** The review was narratively dense and lacking in summary tables of included studies which made it difficult to get an overview of all of the included studies, such as the populations, settings interventions and comparators. Likewise quality assessment was not presented in a clear summary table which hindered interpretation. Interventions were categorised into heterogeneous groupings so conclusions about effectiveness of different types of interventions should be interpreted with caution.

NA = not applicable; NR = not reported

Authors: Huttner B, Gossens H, Verheij T, Harbath S on behalf of the CHAMP consortium.

Year: 2010

Citation: Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. Lancet Infect Dis 2010; 10: 17-31.

Aim of study: To give more comprehensive and updated information about the characteristics and effectiveness of large-scale public campaigns in high-income countries with the aim of improving the use of antibiotics.

Review design: Comprehensive search and structured interviews

Review search parameters

Databases and websites searched:

PubMed, Google

Other methods undertaken (e.g., reference checking):

The bibliographies of included studies were searched;

Interviews

Years searched:

NR although the authors reported identifying campaigns undertaken between 1990 and 2007.

Inclusion criteria, including study type, country:

Infection: NR.

Population: NR.

Intervention: large scale public campaigns

Comparisons: NR

Outcomes: NR

Setting: NR

Study design: NR

Country: high income countries.

Exclusion criteria:

Campaigns in regions of less than 100 000 inhabitants, campaigns focusing only on vaccination uptake or on proper use of medications in general, and campaigns targeting hand washing only.

RCTs and clinical research 'recently reviewed by other groups' [reference to Arnold & Strauss 2005 and Ranji et al. 2008]

Number of studies included:

22 national campaigns and 6 regional campaigns were included. (NB campaigns done in England and Northern island were classed as regional and 30 US regional campaigns were grouped as 1 national campaign for analysis).

Review population, type of study and setting

Characteristics of population/s:

All campaigns focussed on respiratory tract infections.

The general public was targeted by most campaigns. All but five campaigns specifically targeted parents of young children. Some campaigns specifically targeted other groups, such as the elderly.

Health care professionals were targeted in all but one campaign, particular focus on primary care. Fifteen campaigns targeted paediatricians, sixteen also targeted pharmacists.

Setting and type of included studies:

Study designs were not reported.

16 campaigns were located in Europe (3 in parts of the UK), 3 were in North America, 2 in Oceania, and 1 in Israel.

Interventions

Intervention/s description:

All campaigns used a multi-component approach. Public targeted components focussed on mass distribution of lay information, including pamphlets, posters, and mass

Control/comparison/s description:

NA

media in television, radio and public transport. Clinician targeted components focussed on mass distribution of more technical information, including mailing of educational material, guidelines and intensive academic detailing. Key messages: all highlighted that antibiotic resistance is an important problem and misuse of antibiotics promotes bacterial resistance. Most highlighted that most respiratory illnesses are caused by viruses and cannot be treated with antibiotics; and gave advice to follow the prescription and not to skip doses. All but 3 campaigns were over 1 years duration (from 2 years to >10 years)	
Outcomes and method of analysis	
Outcomes: Awareness of campaigns, knowledge and attitudes of the public, professional knowledge and perceived patient demand, use of antibiotics, resistance to antimicrobials, adverse events, costs. **Follow-up periods:** Not reported consistently although some studies provided follow-up between 1 and 10 years.	**Methods of analysis:** A narrative synthesis was presented. **Quality assessment:** NR (presumably not undertaken).
Results	
Campaign awareness Campaign awareness was reported for 6 campaigns (3 in UK) and ranged from 9.2% to 71%. **Antimicrobial use and prescribing** Antibiotic prescribing was reported for 14 campaigns and ranged from no difference (Greece – unclear time period) to 36% reduction in prescribing (Belgium – over 7 years). **Antimicrobial resistance** Changes in antimicrobial resistance rate were reported for 12 campaigns. For penicillin non-susceptible *Streptococcus pneumonia* (PNSP) rates ranged from a significant increase (New Zealand over 1 year) to a 7.7% decrease in PNSP (Belgium – over 7 years). NB: resistance rates could not be causally linked with campaigns. **Patient/public knowledge and attitudes** Post-campaign surveys indicated that those exposed to the campaigns were more likely to agree with 'standards of appropriate use of antibiotics' and were less likely to expect antibiotics (UK). Changing knowledge about which infections are caused by viruses or bacteria was not very effective (no effect in NZ, Canada; France: 54% public unaware most respiratory illnesses not caused by bacteria and that antibiotics won't work for them). Some evidence of a paradoxical effect, leading to an increase in likelihood of self-medication (in those aware of the	**Quality assessment** NA **Sample sizes** NA

'Andybiotic' campaign, UK). **Adverse effects** The campaigns did not measure under-prescribing indicators. There were indications for several countries that reductions in antibiotic prescribing were not correlated with any adverse events (e.g. Increase in incidence of invasive infections due to bacteria, increase in hospital admissions or deaths). An English study reportedly indicated an increase in hospitalisation and mortality associated with community acquired pneumonia due to a decrease in antibiotic use. Another UK study showed a reduction in hospitalisation and death when administered antibiotics on day of diagnosis for lower respiratory infections. **Costs** The costs of campaigns ranged from 10,000 euros to 22,500,000 euros. NB costs were not comparable due to different costing methods. Three campaigns (New Zealand, Belgium, France) reported cost savings due to reduced antibiotic expenditure ranging from 70 million euros to 850 million euros. **Adherence** NR	
Conclusions. limitations and other information	
Author conclusions Although causality is not proven, the results of several campaigns suggest they reduced antibiotic prescribing, at least in high prescribing countries. Multifaceted campaigns repeated over several years appear to be the most effective. The effect of campaigns on resistance and adverse events is less clear. It is also unclear whether changes in the use of antibiotics are because of a change in the behaviour of healthcare professionals, patients, or both, or how important the effect is beyond secular trends. **Evidence gaps and/or recommendations for future research and policy** The authors suggested that further research is needed to determine which strategy is most effective. There is also a need for more research into potential adverse effects. **Source of funding** Sixth Framework Programme of the European Commission in the context of the CHAMP study (SP5A-CT-2007-044317).	**Author limitations** There was a lack of detail about the campaigns from published literature; therefore there was a heavy reliance on personal communication and the recollection of personnel. There may have been a risk of publication bias, although this is reduced by personal communication. Several campaigns not evaluated. Scope and quality of evaluation of the remaining campaigns varied greatly. **Limitation identified by review team** This was not a standard literature review, although given the focus on mass media campaigns the approach was likely more informative than a strict systematic review. However, because of the lack of a transparent and systematic process it is difficult to judge the reliability of the results and author conclusions. The fidelity of campaigns and applicability to UK practice is also uncertain. The reliance on personal communication may also have introduced bias.

NA = not applicable; NR = not reported

Authors: Lee C-R, Lee J, Kang L-W, Jeong B, Lee S.

Year: 2015

Citation: Educational Effectiveness, Target, and Content for Prudent Antibiotic Use. BioMed Res Int 2015: http://dx.doi.org/10.1155/2015/214021

Aim of study: To assess the importance of educating prescribers and the public (adults and children) and discuss some relevant aspects, including the content of teaching programs, training the trainer, and evaluation of program effectiveness.

Review design: A review with some systematic elements.

Review search parameters

Databases and websites searched:

The Cochrane library, MEDLINE/PubMed, http://www.nice.org.uk, http://www.cadth.ca, http://www.controlled-trials.com, http://www.biomedcentral.com.

Other methods undertaken (e.g., reference checking):

Studies of educational programs for teaching prudent antibiotic use were also examined. (NB it was not reported how these studies were identified but it does not appear to be systematic)

Years searched:

1983 to 2014.

Inclusion criteria, including study type, country:

Type of infection: NR.

Population: NR.

Intervention: educational interventions for teaching prudent antibiotic usage.

Outcomes: NR.

Setting: NR.

Study type: NR.

Exclusion criteria:

Non-English language.

Number of studies included:

28 RCTs.

It was not reported how many studies of prudent antibiotic usage were also included.

Review population, setting and type of study

Characteristics of population/s:

NR

Setting and type of included studies:

NR

Interventions

Intervention/s description:

Interventions varied but involved literature seminars, mailing campaigns, small-group education, educational outreach visits, guidelines and leaflets, alone or in combination.

Control/comparison/s description:

NR

Outcomes and method of analysis

Outcomes:

Antibiotic prescribing, inappropriate antibiotic use

Follow-up periods:

NR

Methods of analysis:

NR. A narrative description of studies was reported with no details of how or if studies had been combined.

Quality assessment:

NR

Results	
Antimicrobial use and prescribing Antibiotic prescription was reduced by 34.1% in the clinician only education intervention groups compared with control. Looking at individual strategies, the effectiveness of interventions compared with control for antibiotic prescribing was: small-group education = 52%; guidelines and leaflets = 42% educational outreach visit = 30% interactive seminars = 25% combination = 23% mailing campaigns = 9%. The number of inappropriate antibiotic prescriptions was reportedly reduced by 41% in the intervention groups compared with control. [NB it was not possible to determine how these results were estimated and how many studies contributed data as the authors provided no details about this.] Only 2 RCTs were identified that also included a patient education component, the review authors reported that these reduced antibiotic prescribing by 14%. No RCTs were identified that only targeted patient/public education. **Patient/public knowledge and attitudes** NA **Other** A discussion of educational strategies for teaching prudent antibiotic use was also presented in the paper. However, this does not appear to be systematic and appears to be based on opinion. As such, it has not been presented here.	**Quality assessment** NR **Sample sizes** NR
Conclusions. limitations and other information	
Author conclusions Continuous efforts to educate people about appropriate antibiotic use are important to manage antibiotic resistance. Medical and nonmedical undergraduate students' curriculum should include training on appropriate antibiotic usage. **Evidence gaps and/or recommendations for future research and policy** NR **Source of funding** The National Research Foundation of Korea funded by the Ministry of Science, ICT & Future Planning (2011-0027928).	**Author limitations** NR **Limitation identified by review team** The study was badly structured and reported. Only part of the study appears to be systematic, but even in this section the reporting of methods and results made it impossible to determine how the results were estimated and how many studies contributed data. Caution is advised when interpreting the results.

NA = not applicable; NR = not reported

Authors: Ranji S, Steinman M, Shojania K, Lewis R, Arnold S, and Gonzales R.*

Year: 2006

Citation: Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies. AHRQ Publication No. 04(06)-0051-4.

Aim of study: To assess the effectiveness of quality improvement strategies to reduce inappropriate antibiotic prescribing, both inappropriate antibiotic selection and inappropriate use.

Review design: Systematic review

Review search parameters

Databases and websites searched:

Cochrane Collaboration Effective Practice and Organisation of Care (EPOC) database and MEDLINE.

Other methods undertaken (e.g., reference checking):

The bibliographies of included studies were also searched.

Years searched:

January 1966 to August 2005.

Inclusion criteria, including study type, country:

Type of infection: acute illness.

Population: NR.

Intervention: interventions to reduce inappropriate antibiotic prescribing. QI strategies were classified as clinician education, patient education, provision of delayed prescriptions, audit and feedback, clinician reminders, and financial or regulatory incentives.

Outcomes: The primary outcomes were antibiotic prescribing or the percentage of patients prescribed a recommended antibiotic or guideline-concordant antibiotic therapy.

Setting: Outpatient setting (clinic, urgent care, or emergency care).

Study type: randomised controlled trials, controlled before and after studies and interrupted time series.

Exclusion criteria:

Non-English language.

Number of studies included:

54 studies (74 comparisons).

Review population, setting and type of study

Characteristics of population/s:

Most studies focussed on acute respiratory infection, others focussed on specific diseases such as diarrhoea, urinary tract infection, and tonsillitis. Some studies did not specify the disease.

Some studies were specifically in adults or children, whilst others were in all patients.

Setting and type of included studies:

Most studies were in an out-patient primary care setting.

24 studies were conducted in the USA, 11 in Europe 3 from Australia, two from Canada, and the remaining studies from a range of countries including, Africa, Sri Lanka, Zambia, and Israel.

Interventions

Intervention/s description:

Interventions varied and often involved more than one component. Key components included: clinician education (N=27 comparisons), patient education (N=18), both clinician and patient education (N=12), delayed prescribing (N=5), clinical reminders (N=2), patient self-management (N=1), financial and regulatory incentives (N=1), and organisational change (N=1).

Control/comparison/s description:

The control group varied from no intervention to another active intervention (some trials also had three arms).

Outcomes and method of analysis

Outcomes: The primary outcomes were antibiotic prescribing or the percentage of patients prescribed a recommended antibiotic or guideline-concordant antibiotic therapy. Secondary outcomes included effects on antimicrobial resistance, intervention safety (disease outcomes and adverse events), prescribing costs, and patient satisfaction. **Follow-up periods:** Median follow-up = 6 months.	**Methods of analysis:** Quantitative analysis was undertaken by calculating median effect sizes and interquartile ranges (IQR) were reported. Nonparametric tests (Wilcoxon or Kruskal-Wallis) were used to compare medians. Potential confounders (such as study location and population) were explored. Stratified analysis was undertaken to assess differences in median effect sizes based on pre-specified criteria. Population effect sizes were also calculated to assess which interventions would have greatest effect at the population level. Studies not suitable for quantitative analysis were narratively described. **Quality assessment:** Internal validity was assessed according to method of treatment assignment, blinding, and analyses, using Cochrane Collaboration methodology Generalisability was assessed according to 4 study design criteria.
Results	
Antimicrobial use and prescribing *Inappropriate use* Interventions targeting inappropriate use were effective at reducing prescribing, with a median effect of -8.9% reduced antibiotic prescribing (IQR -12.4% to -6.7%), in intervention groups compared with comparison groups. The absolute reduction in antibiotic prescribing rates was 8.9%. Median effect sizes by intervention type: two patient education only studies: -4.9% (IQR -9.9% to -0.2%), nine clinician education only studies:-8.1% (IQR -13.7% to -7.0%); no difference in effectiveness (p=0.848 by Kruskal-Wallis test). Comparison of six combined clinician and patient education studies (median effect size not reported) with clinician education only was non-significant (p=0.478). Of the twelve studies with multiple components (six clinician and patient education, two clinician education and audit and feedback, one patient education and audit and feedback, three with patient education, clinician education, and audit and feedback) none were more effective than those using single strategies (p=0.82 by Wilcoxon rank-sum test). *Antibiotic selection choice – use of narrow-spectrum agents when indicated rather than broad spectrum antibiotics* Interventions targeting the antibiotic choice were effective, with a median absolute improvement of 10.6% (IQR 3.4% to 18.2%) in prescribing of recommended antibiotics in the intervention groups compared with the comparison groups. Clinician education combined with audit and feedback	**Quality assessment** Most studies failed to meet all quality assessment criteria and were rated as 'fair quality'. **Sample sizes** Quantitative analysis: 100 to 16,572 (one study NR) Studies not meeting criteria for quantitative analysis: 81 to 154,742 (several studies NR)

had the smallest median effect (3.4%) but this was based on only one study, combination of clinician and patient education had the largest effect (22.8%) but was based on only two studies; differences not statistically significant (P=0.18).

Antimicrobial resistance

There was no difference in antimicrobial resistance in 2 studies. However, the authors noted that both of these studies had short follow-up (less than 6 months).

Patient/public knowledge and attitudes

NA

Costs

Two studies of inappropriate use reported cost savings.

Three studies of inappropriate choice reported 20-30% relative reductions in prescribing costs.

Features of successful interventions

The authors noted that there was no single effective strategy, but that strategies involving active clinician education with or without patient education appeared effective.

The authors also noted that interventions targeting all respiratory tract infections may be more effective than those targeting specific infections.

Conclusions. limitations and other information

Author conclusions

Quality improvement efforts are generally effective at reducing both inappropriate use of antibiotics and inappropriate choice of antibiotics. There is no single effective strategy, although strategies that include active clinician education may be more effective than passive education, particularly for addressing the antibiotic choice. Greater reductions in overall prescribing may be achieved through efforts targeting prescribing for all acute respiratory infections, rather than targeting single conditions.

Evidence gaps and/or recommendations for future research and policy

There is a need for better quality studies. Studies are also needed that report on potential harms of the intervention, and costs and cost-effectiveness.

Source of funding

The AHRQ.

Author limitations

The authors were unable to perform formal meta-analysis. Many studies lacked details which may have resulted in unmeasured confounders. Most follow-up periods were less than a year.

Limitation identified by review team

The review included some studies which did not include an education component (clinician reminder, delayed prescriptions).

Many of the studies were conducted in countries that may have very different antibiotic prescribing polices, which may make the generalisability to the UK setting difficult.

NA = not applicable; NR = not reported

* This study is linked to Ranji 2008 and overlaps substantially in terms of studies included. It does appear to present a different analysis to Ranji 2008 but the conclusions are very similar.

Authors: Ranji S, Steinman M, Shjania K, and Gonzales R.*

Year: 2008

Citation: Interventions to reduce unnecessary antibiotic prescribing. Med Care 2008; 46: 847-62

Aim of study: To assess the effectiveness of quality improvement strategies to reduce antibiotic prescribing for acute outpatient illnesses for which antibiotics are often prescribed.

Review design: Systematic review

Review search parameters

Databases and websites searched:

Cochrane Collaboration Effective Practice and Organisation of Care (EPOC) database and MEDLINE.

Other methods undertaken (e.g., reference checking):

The bibliographies of included studies were also searched.

Years searched:

January 1966 to August 2005 (EPOC)

June 2005 to March 2007 (MEDLINE)

Inclusion criteria, including study type, country:

Type of infection: acute non-bacterial illness.

Population: NR.

Intervention: interventions to reduce unnecessary prescribing. Studies had to report on 1 of 6 distinct antibiotic-prescribing strategies.

Outcomes: antibiotic prescribing or antibiotic use before and after intervention.

Setting: outpatient setting.

Study type: randomised controlled trials, controlled before and after studies and interrupted time series.

Exclusion criteria:

Non-English language.

Number of studies included:

43 (55 trials).

Review population, setting and type of study

Characteristics of population/s:

Acute non-bacterial illness. Most studies (38 studies) focussed on acute respiratory infection (ARIs). Other diseases included: sore throat, acute bronchitis, otis media, and common cold

Some studies were specifically in adults or children, whilst others were in all patients.

Setting and type of included studies:

40 studies were in an out-patient primary care setting. It was not reported which other settings were included but presumably all were out-patient.

Most studies were conducted in the USA (17 studies) or Europe (12 studies). Other countries included: New Zealand, Canada, Mexico, Australia, Cuba, Indonesia, South Africa, Sri Lanka, Zambia, and Israel.

Interventions

Intervention/s description:

Interventions varied but involved the following interventions alone or in various combinations: Mailed educational newsletter; educational seminars; educational outreach for clinicians; written material for patients (or parents); audit and feedback; mass media campaigns; computer-based or paper-based decision-support; financial disincentives for patients; educational outreach; self-management guides; financial incentives for patients; educational video; delayed prescriptions.

Control/comparison/s description:

NR

Outcomes and method of analysis	
Outcomes: Antibiotic prescribing or antibiotic use before and after intervention **Follow-up periods:** NR	**Methods of analysis:** Quantitative analysis was undertaken by calculating median effect sizes and interquartile ranges (IQR) were reported. Nonparametric tests (Mann -Whitney or Kruskal-Wallis) were used to compare medians. Potential confounders (such as study location and population) were explored. Planned subgroup analysis of passive versus active education was undertaken. Studies not suitable for quantitative analysis were narratively described. **Quality assessment:** Internal validity was assessed according to method of treatment assignment, blinding, and analyses. Generalisability was assessed according to 4 study design criteria.
Results	
Antimicrobial use and prescribing Among 30 trials eligible for quantitative analysis the median reduction in proportion of subjects receiving antibiotics was 9.7% (IQR 6.6-13.7%) over 6 months median follow-up, equivalent to a relative reduction of 25%. No single strategy was more effective than another (comparisons of clinician education alone, patient education alone, clinician education combined with patient education, and clinician education combined with patient education, audit, and feedback) *P*=0.85 for comparison across all strategies by Kruskal-Wallis test. There was trend towards active clinician education strategies (median effect 7%, IQR 7-10.1%) being more effective than passive strategies (median effect 12.9%, IQR 8.1-19.2%) but this was not statistically significant (p=0.096). Studies that aimed to improve prescribing in all ARIs rather than specific ARIs seemed to exert a larger effect on community prescribing rates. Confounding factor: higher baseline prescribing rates were associated with larger effect sizes. Other factors such as population size and disease were not independent confounders. **Patient/public knowledge and attitudes** NA **Antimicrobial resistance** Three studies assessed AMR. All reduced prescribing (clinician and patient education interventions) but only one study reduced incidence of penicillin-resistant *S.pneumoniae* (6 moth follow-ups in studies).	**Quality assessment** Most studies failed to meet all quality assessment criteria. Overall quality described as fair. **Sample sizes** Quantitative analysis: 100 to 16,572 (one study NR) Studies not meeting criteria for quantitative analysis: 81 to 154,742 (several studies NR)

Adverse effects

Eleven trials (9 studies) addressed intervention safety by measuring post intervention use of health services (e.g. return office visits or telephone consultations) and found no increases. Seven trials (6 studies) measured the time to symptom resolution through patient interviews or diaries; 6 trials found no difference between intervention and control groups. 1 study measured clinical adverse effects and found significantly less diarrhoea in patients not receiving antibiotics.

Costs

See Ranji et al 2006

Other

A narrative synthesis is also reported in the paper. Of note are 7 delayed prescription studies (4 in the UK) which reported reducing antibiotic usage by between 15% and 74.5%, but were reportedly undertaken in countries and time periods of near universal antibiotic usage.

Conclusions. limitations and other information

Author conclusions

Quality improvement strategies are effective at reducing antibiotic prescribing in an ambulatory setting, although there is still room for improvement. Active rather than passive clinician education and strategies targeting all ARIs rather than single conditions or age groups are most effective. Delayed prescriptions were an effective strategy but against a backdrop of near universal antibiotic prescribing; thus this approach may not be a useful strategy for controlling antibiotic prescribing costs and resistance.

Evidence gaps and/or recommendations for future research and policy

There is a need for longer-term of prescribing patterns and antimicrobial resistance patterns, cost benefit analysis, and potential harms of the intervention.

The authors suggested that future studies should report on patient numbers and clusters and the ICC.

Source of funding

A Department of Veterans Affairs HSR&D Research career Development award. The work is based on work undertaken for the AHRQ (contract No 290-02-0017).

Author limitations

The authors were unable to perform formal meta-analysis. The median effect size analysis may have lacked power to detect small differences due to the small number of trials in each group. It was also an indirect analysis as few studies compared different strategies head to head. The categorisation of QI strategies was also broad. There was a lack of detail in individual studies on intervention components.

Limitation identified by review team

There were limited details of the included studies and quality assessment (possibly due to space constraints) which makes it difficult to interpret the review confidently.

The review included some studies which did not include an education component (clinician reminder, delayed prescriptions).

Many of the studies were conducted in countries that may have very different antibiotic prescribing polices, which may make the generalisability to the UK setting difficult.

NA = not applicable; NR = not reported

* This study is linked to Ranji 2006 and overlaps substantially in terms of studies included. It appears to present a different analysis to Ranji 2006 but the conclusions are very similar.

Authors: Thoolen B, de Ridder D, and van Lensvelt-Mulders G.

Year: 2012

Citation: Patient-orientated interventions to improve antibiotic prescribing practices in respiratory tract infections: a meta-analysis. Health Psych Rev 2012; 6 (1): 92-112.

Aim of study: To assess the effectiveness of interventions aimed at patients to reduce their use of antibiotics and provide insight on the effective components.

Review design: Systematic review with meta-analysis.

Review search parameters

Databases and websites searched:

PSYCHINFO, EMBASE and MEDLINE.

Other methods undertaken (e.g., reference checking):

The bibliographies of included studies were also searched.

Years searched:

1993 to 2008.

Inclusion criteria, including study type, country:

Type of infection: respiratory tract or urinary tract or sore throat or cough or otitis or bronchitis or pneumonia or tonsillitis

Population: general population or patients of a general practice or clinic.

Intervention: interventions to reduce antibiotic prescribing.

Outcomes: knowledge and attitudes, antibiotic use, satisfaction with treatment

Setting: primary care or general population.

Study design: RCTs, quasi-RCTs, and controlled before and after.

Other: Outcomes had to be reported in terms of percentage or means. Studies had to have a minimum post test results.

Exclusion criteria:

NR.

Number of studies included:

28 studies.

Review population, type of study and setting

Characteristics of population/s:

15 studies focussed on upper respiratory tract infections (RTI), six on lower RTI, 5 on general RTIs and 2 on infections in general.

15 studies targeted parents and 13 targeted adults or did not focus on a specific age.

Setting and type of included studies:

20 studies focussed on patients in a primary care setting and 8 studies focussed on specific groups in the community.

16 studies were conducted in the USA, 6 in the UK (other countries not reported).

Interventions

Intervention/s description:

16 studies reported on patient-orientated approaches alone. 12 studies focussed on patient and physician education.

Intervention components (alone or in combination) included: video and brochure, information leaflet, multiple materials, physician intervention, delaying prescription, or no prescription.

Control/comparison/s description:

Most studies had usual care as a comparator (18 studies), whilst10 studies had an active comparator.

Outcomes and method of analysis	
Outcomes: knowledge and attitudes, antibiotic use, satisfaction with treatment. **Follow-up periods:** NR	**Methods of analysis:** Meta-analysis was conducted to calculate Cohen's d effect sizes. Statistical heterogeneity was estimated using the Q score. A mixed random-effect meta-analysis was used to explore predictors of variance. Regression analysis and a series of ANOVAs were used to assess the relative effects of predictors. **Quality assessment:** Not reported.
Results	
Antimicrobial use and prescribing 21 studies reported effect sizes on antibiotic use ranging from 0.19 to -0.86 with interventions compared with controls. The overall effect size was statistically significant (*d* -0.21, p<0.001). The studies reporting the greatest effect sizes involved delaying or refusing prescriptions. There was significant statistical heterogeneity indicating that studies may not be suitable for pooling. Predictors analysis indicated that the heterogeneity could be completely explained by the study country, with US studies (all of which used prescription rates from provider or pharmacies as outcome measure, while other countries mainly relied on patient self-report) significantly less effective. Effect of moderating factors was assessed for all non-US studies (n=16) using a series of mixed model ANOVAs (NB analysis 'must be considered explorative at best'). Interventions involving the delayed or no prescriptions had an effective size of -0.62 compared to -0.14 for interventions which did not. The predictive value of other variables: no information (*d*=-0.64) vs information (*d*=-0.41) vs information guided by theoretical considerations (*d*=-0.14); clinician focus (*d*=-0.10) or no clinician focus (*d*=-0.50), were most likely confounded by the variation in prescription styles. **Patient/public knowledge and attitudes** 11 studies reported effect sizes ranging from d 0.0 to 0.42 with interventions compared with controls. The overall effect size was statistically significant (d=0.23, p<0.001). There were 5 studies with moderate effect sizes (*d*=0.30-0.50) which involved a mixture of different intervention types, and 2 with small effect sizes (*d*=0.20-0.29). None of the potential predictors analysed had a significant impact on results. **Other: Satisfaction** 11 studies reported no significant difference in satisfaction (d= -0.019, p<0.44). There was little	**Quality assessment** NA **Sample sizes** Less than 100 to whole communities.

variation between studies.	
Conclusions. limitations and other information	
Author conclusions The promotion of interventions that delay or refuse prescriptions are likely to achieve better control of antibiotic usage than interventions that educate patients about the negative use of antibiotics. There are no negative effects in terms of patient satisfaction. **Evidence gaps and/or recommendations for future research and policy** Further research on the reasons patients have for wanting antibiotics. Future interventions should include behaviour change theory. **Source of funding** The European Community FP6 Research Programme of the CHAMP consortium (SP5A-CT-2007-044317).	**Author limitations** There was a lack of consistency in reporting outcomes. There was a lack of content and theoretical background to interventions. **Limitation identified by review team** There was a clear effect of country on the effectiveness of interventions which indicates results from some countries may be less generalisable to the UK setting, and pooling of studies from several countries may not be reliable. Not all studies included an educational component. Studies did not appear to have undergone formal quality assessment.

NA = not applicable; NR = not reported

Authors: Van der Velden A, Pijpers E, Kuyvenhoven M, Tonkin-Crine S, Little P and Verheij T.

Year: 2012

Citation: Effectiveness of physician targeted interventions to improve antibiotic use for respiratory tract infections. Br J Gen Pract 2012; e802

Aim of study: To assess the overall effectiveness of physician targeted interventions to improve antibiotic use for respiratory tract infections and to identify intervention features mostly contributing to a positive intervention outcome.

Review design: Literature review (appears to be systematic)

Review search parameters

Databases and websites searched:

Cochrane library, EMBASE and MEDLINE.

Other methods undertaken (e.g., reference checking):

The bibliographies of included studies were also searched.

Years searched:

January 1990 to July 2009.

Inclusion criteria, including study type, country:

Type of infection: respiratory tract infections.

Population: physicians.

Intervention: interventions targeted at physicians aiming to reduce antibiotic prescribing.

Outcomes: prescriptions measured in defined daily doses, prescriptions or rates.

Setting: primary care.

Study design: NR.

Country: high income countries.

Exclusion criteria:

Non-English language.

Number of studies included:

58 studies (87 interventions).

Review population, type of study and setting

Characteristics of population/s:

Respiratory tract infections.

Setting and type of included studies:

41% of studies were controlled before and after studies and 29% were RCTs. The remaining study deigns were RCTs without baseline, or interrupted time series.

Interventions

Intervention/s description:

Of the 87 interventions, 59 aimed to decrease total prescriptions, and 28 aimed to increase use of first-choice antibiotic.

71% were targeted at more than one type of respiratory infection.

40% targeted other groups as well as physicians.

77% were multi-component interventions. Interventions had various components: 70% of interventions included educational information for the physician, 56% had educational meetings, 37% had audit and feedback, 28% had educational outreach, 24% had educational material for patients presenting with respiratory tract illnesses, 20% had educational information for practice patients, 17% had educational material for the public, and 7% included financial incentives.

Control/comparison/s description:

NR

Outcomes and method of analysis	
Outcomes: Prescriptions measured in defined daily doses, prescriptions or rates. **Follow-up periods:** NR	**Methods of analysis:** A narrative synthesis was conducted grouping studies into several intervention categories. Associations of intervention features with effectiveness was estimated by logistic regression and expressed as odds ratios (OR) and 95% confidence intervals (95% CI). **Quality assessment:** Not reported but there is a mention that this was undertaken (discussion).
Results	
Antimicrobial use and prescribing Decreasing antibiotic usage (59 comparisons) 73% reported decreased antibiotic usage. Overall antibiotic prescription rate was reduced by 11.6%. Near patient testing alone (-72%), and communication skills training plus near-patient tested (-44%) were reported to reduce antibiotic prescribing by the largest amounts. Multi-component interventions were more frequently effective than single component interventions (OR 6.5, 95% CI 1.9-22), with the most often effective intervention element being educational material for the physician, which showed an independent association with a positive intervention outcome (OR 5.5, 95% CI 1.7-18). Physician education combined with an educational meeting was significant (OR 3.5, 95% CI 1.2-10), physician education with patient education showed a non-significant trend towards increased effectiveness s (OR 5.8, 95% CI 1-35). Increasing first-choice antibiotic use (28 comparisons) 32% of reported increased use of first-choice antibiotic. Overall first choice antibiotic rate increased by 9.6%. **Patient/public knowledge and attitudes** NA	**Quality assessment** NA **Sample sizes** NR
Conclusions. limitations and other information	
Author conclusions Physician education is crucial for optimising antibiotic prescribing. Multiple interventions which included physician education were the most effective. Communication skills training of physicians is effective. Near-patient testing is also effective. Physician education with patient education was not significantly more effective than physician education alone. **Evidence gaps and/or recommendations for future**	**Author limitations** There was heterogeneity of outcomes, baseline prescribing, intensity of interventions, and geographic location. The authors also acknowledged the risks of publication bias, language bias and selection bias of participants. **Limitation identified by review team**

research and policy Further research to focus on how to provide physicians with the relevant knowledge and tools, and when to add in additional intervention elements. **Source of funding** Sixth Framework Programme of the European Commission in the context of the CHAMP study (SP5A-CT-2007-044317).	There were limited details of the included studies and no details of the quality assessment (possibly due to space constraints) which makes it difficult to interpret the review confidently. It was unclear which countries were included, thus it's difficult to judge how applicable the results are to the UK. Details of interventions were not reported. In particular, it was unclear what the content of the patient education component of interventions were.

NA = not applicable; NR = not reported

Authors: Vodicka T, Thompson M, Lucas P, Heneghan C, Blair P et al on behalf of the Target Programme team.

Year: 2013

Citation: Reducing antibiotic prescribing for children with respiratory tract infections. Br J Gen Pract 2013; DOI: 10.3399/bjgp13X669167

Aim of study: To assess the effectiveness of primary care behavioural or educational interventions to reduce antibiotic prescribing for children with respiratory tract infections.

Review design: Systematic review

Review search parameters

Databases and websites searched:

Cochrane library, EMBASE, CINAHL, PsychINFO and MEDLINE/pubMed.

Other methods undertaken (e.g., reference checking):

The bibliographies and citations of included studies were also searched.

Years searched:

Inception to June 2012.

Inclusion criteria, including study type, country:

Type of infection: respiratory tract infections.

Population: children.

Intervention: educational or behavioural interventions targeted at physicians, parents or both that aimed to reduce antibiotic prescribing.

Comparisons: no treatment, or alternative treatment controls.

Outcomes: change in proportion of antibiotic prescriptions, or change in 'appropriate' antibiotic prescribing.

Setting: primary care.

Study design: Controlled studies that used a randomised, cluster randomised, non-randomised or one-group pre- and post- test design.

Country: high income OECD countries.

No language restrictions.

Exclusion criteria:

In-patient setting, studies of children with chronic illnesses or serious comorbidities, evaluations of treatment guidelines, public health interventions, diagnostic test.

Number of studies included:

17 studies (19 interventions).

Review population, type of study and setting

Characteristics of population/s:

Respiratory tract infections. Where described, the age range varied from less than 2 years old to less than 18 years old.

Setting and type of included studies:

12 studies used a randomised design, 3 used pre – and post designs, and 2 were non-randomised.

10 studies were conducted in the USA, 3 in Israel, 3 in Europe, and 1 in Australia.

The interventions were delivered in family practices or paediatric care settings, apart from one study in an after-hours clinic.

Interventions

Intervention/s description:

The interventions varied greatly but almost all were complex interventions.

Clinicians and parents (10 studies)

Control/comparison/s description:

NR

Intervention components for clinicians included: written material, clinician focus groups, lectures, newsletters, group education, feedback. Intervention components for parents included: education on what to expect at consultation, antibiotic resistance, self-care advice, telephone contact, posters, and handouts. Clinicians only (6 studies) Intervention components included: 1-day session, computerised algorithm of care, links to studies that provide information, watchful waiting guidelines. Parents only (3 studies) Intervention components included: educational posters, personalised videotape message, clinician feedback and education, pamphlets.	
Outcomes and method of analysis	
Outcomes: Change in proportion of antibiotic prescriptions, or change in 'appropriate' antibiotic prescribing. **Follow-up periods:** 1 week to 2 years reported for studies conducted in clinicians and parents	**Methods of analysis:** Mean differences (MD) or odds ratios (ORs) were calculated with 95% confidence intervals (95% CIs), using yate's correction and Fisher's exact test. Statistical and clinical heterogeneity prevented pooling of data; a narrative synthesis was presented. **Quality assessment:** Quality was assessed using a framework from the Cochrane handbook and studies were classified as low, moderate or high risk of bias.
Results	
Antimicrobial use and prescribing Clinicians and parents (10 studies) 8/10 studies reported significantly decreased prescribing rates ranging from 6-21%. One study reported no difference and one reported increased antibiotic usage. Clinicians only (6 studies) 1/6 studies reported significantly decreased prescribing rates of approximately 9% (depending on condition), 2/6 reported significant reductions in inappropriate prescribing (29-34%), and 3/6 found no difference or an increase in prescribing. Parents only (3 studies) None of the interventions found significant reductions in antibiotic prescribing. **Features of successful interventions** Providing automatic computer prompts for evidence-based prescribing, promoting clinician leadership or participation in the design of treatment guidelines,	**Quality assessment** 14 studies had a moderate risk of bias, 2 had a low risk of bias and 1 had a high risk of bias. **Sample sizes** Where reported, the number of clinicians ranged from 6 to 1116. NB: sample sizes were reported in different ways (practice level, clinician level, parent level) making interpretation difficult.

and/or peer education were effective components. Passive strategies targeting only parents, such as waiting room posters or pamphlets, did not appear to be effective. **Patient/public knowledge and attitudes** NA **Adverse effects** Only three studies reported complications or re-consultations which did not indicate an increased risk of adverse events due to decreased prescribing. However, studies were not powered to detect for rarer outcomes, such as hospitalisations.	
Conclusions. limitations and other information	
Author conclusions Conflicting evidence from the included studies indicated that the most effective interventions target both parents and clinicians during consultations, provide automatic prescribing prompts, and promote clinician leadership in the intervention design. **Evidence gaps and/or recommendations for future research and policy** The cost-effectiveness of interventions is unknown. Qualitative evidence of why some interventions are more effective than others may increase understanding. The authors also identified on-going studies of interest (such as HAPPY AUDIT). **Source of funding** NIHR grant for applied research programme (RP-PG-0608-10018).	**Author limitations** Most studies did not report how many parents or clinicians completed the intervention activities. There may have been a risk of publication bias. Studies reporting appropriate prescribing may be subject to changes in labelling which may bias the results. The diagnostic criteria for respiratory tract infections were not clearly described. **Limitation identified by review team** This review was generally well reported. The vast range of intervention components and lack of detail on these components does make interpretation difficult, although this is not a failure of the review, rather a feature of the evidence base. The fidelity of interventions and applicability to UK practice is also uncertain.

NA = not applicable; NR = not reported