An Roinn Sláinte
Department of Health

Supplementary Material

Changing Behaviour: Reducing Unnecessary Antibiotic Prescribing. A Systematic Review and Meta-analysis.

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A. Additional Information on the Methods for Estimating Effect Size

This Appendix provides additional information on the statistical methods for estimating effect size. It supplements Section 2.4 of the Main Report. This meta-analysis was conducted to examine the efficacy of behaviour change initiatives to reduce antimicrobial consumption, prescribing, and dispensing, respectively, relative to control. Studies were pooled in Review Manager v.5.4.1 to calculate a mean risk ratio estimate using random-effects modelling with inverse-variance weighting. Risk ratios were calculated as (RI / NI) / (RC / NC), where RI / NI = the number of 'risk' events (antimicrobial consumption, prescribing, dispensing per patient) divided by the total at-risk patient events in the intervention group and RC / NC = the number of 'risk' events divided by the total at-risk patient events in the control group. When only percentage rates were reported in a given study, the absolute risk was calculated using the relevant subsample size of the intervention or control group, respectively (e.g., Legare et al., 2011, 2012). Studies that did not report the respective subsample sizes were not synthesised as the appropriate study inverse-variance weighting could not be determined (e.g., per 1000 patients; Butler et al., 2012; D'Hulster et al., 2022; Gold et al., 2021; McNulty et al., 2018).

As several studies incorporated a cluster randomised controlled trial (cRCT) design, the clustering in the data had to be accounted for in order to avoid the unit-of-analysis error whereby the unit of analysis (patients) is different from the unit of allocation (cluster, e.g., GP practice). The samples within clusters tend to be more similar in terms of confounders and treatment response than otherwise would be observed between individually randomised participants (Donner et al., 2001; Killip et al., 2004), and unless corrected, will contribute to inappropriately high levels of precision and over-weighting in the meta-analysis (Higgins et al., 2023). The clustering in the data was accounted for by reducing the size of the trial to its "effective sample size". This was achieved by dividing the cRCT sample size by the design effect: $1 = (M - 1) \times ICC$, where M is the average cluster size and ICC is the intracluster correlation coefficient (Higgins et al., 2023).

Where reported in a study, the study-specific intraclass correlation coefficient (ICC) was used in calculations of the effect size. Elsewhere, an estimate of 0.06 was inputted based on Adams et al. (2004). Once cRCTs were reduced to their effective sample size, the corrected data for events (antimicrobial prescription; consumption) and total were entered into RevMan for calculation of the risk ratio effect estimates.

In order to explore how this estimate may have impacted the findings, sensitivity analyses were conducted whereby the effect sizes generated from cluster randomised controlled trials were recalculated assuming an ICC = 0.16 unless otherwise reported in the study. This is informed by the high-quality cluster RCT conducted by Little et al., (2013), where an ICC=0.16 was used for sample size calculations, determined by the mean ICC for prescribing at practice level across three trials (Cals et al., 2009; Coenen et al., 2004; Welschen et al., 2004; ICC at practice level = 0.12, 0.17, and 0.18 respectively).

A mean, weighted risk ratio effect estimate and 95% confidence intervals were generated for each meta-analysed outcome and presented visually on Forest plots to illustrate the study-level and summary-level effect estimate(s). The meta-analysis was interpreted in accordance with the Z statistic at .05 alpha level. Heterogeneity was assessed using the Chi2 index at an alpha level of $p < .10$ due to the low power of this test (Deeks et al., 2021). I2 quantified the extent of total heterogeneity that was due to true differences and not sampling error, interpreted in accordance with 25-49% = low, 50-74% = moderate, 75%+ = high (Borenstein et al., 2021).

B. Description of Interventions by Study

Studies	Interventions
Altiner et al, 2007 Germany N = 61 practitioners and 1,707 patients	Participants: GPs and their patients in North-Rhine/Westphalia-Lippe, Germany. Intervention Category: Communication training + Educational. Control: Usual care. Intervention: One hundred and four GPs in North-Rhine/Westphalia-Lippe, Germany were cluster randomized into intervention and control. GPs randomized to receive the intervention were visited by peers. Peers motivated the GPs to explore patients' expectations and demands thoroughly and open-mindedly, to elicit anxieties and expectations and to make antibiotic prescribing a subject in the consultation. The intervention strategy was focused on the communication within the encounter, not on sharing knowledge about antibiotic prescribing. The researchers also developed a patient leaflet and a poster for the waiting room. These materials contained brief evidence-based information about acute cough and antibiotics, but mainly focused on the patients' role within the antibiotic misunderstanding. By explaining the reasons why GPs often feel a pressure to prescribe antibiotics, patients were expected to be enabled to raise and clarify the issue themselves within the consultation. Primary Outcome Measured: Antibiotic prescription.
Arroll et al, 2002 New Zealand N = 129 patients	Participants: Patients presenting with the common cold. Intervention Category: Delayed script filling. Control: Usual care: Patients received a prescription with instructions to start taking the antibiotic medication immediately. Intervention: The intervention group was given a prescription for antibiotics with instructions to fill it after 3 days if symptoms failed to improve. General practitioners prescribed any antibiotic that they considered most appropriate.

	In both groups, patients were advised to return to see their doctor if symptoms worsened. Primary Outcome Measured: Antibiotic use. Secondary Outcome Measured: Symptom scores.
Bourgeois et al, 2010 USA N = 12 practitioners	Participants: 12 General paediatric practices in the Boston area. Intervention Category: Decision support tool. Control: Usual care. Intervention: The study randomized 12 practices either to receive the acute respiratory illness interactive template or to the control group. Antibiotic rates among all eligible ARI (acute respiratory illness) diagnoses were compared among control and intervention ARI visits, controlling for clustering by clinician. Primary Outcome Measured: Antibiotic prescribing.
Breil et al, 2006 Switzerland N = 45 general practices	Participants: General practices. Intervention Category: (1) Educational, (2) Communication training + Educational. Control: Usual care. Intervention: (1) Thirty physicians received evidence-based guidelines for the management of acute respiratory tract infections; (2) 15 physicians randomised to the full intervention additionally received training in patient-centred communication. Primary Outcome Measured: Antibiotic prescription.

	Secondary Outcome Measured: Patient satisfaction and enablement, re-consultation rates, days with restrictions, and days off work.
Butler et al, 2012 UK N = 262 practitioners	Participants: General medical practitioners. Intervention Category: Educational. Control: Usual care. Intervention: A multifaceted educational programme following the Stemming the Tide of Antibiotic Resistance (STAR) educational programme, which included a practice-based seminar reflecting on the practices' own dispensing and resistance data, online educational elements, and practising consulting skills in routine care. The intervention was a blended learning experience as it used a combination of various learning methods and topics. Primary Outcome Measured: Total numbers of oral antibiotic items dispensed for all causes per 1000 practice patients in the year after the intervention, adjusted for the previous year's dispensing.
Cals et al, 2009 Netherlands N = 40 practitioners	Participants: General practitioners. Intervention Category: (1) Point of care testing, (2) Communication training, (3) Point of care testing + communication training. Control: Usual care. Intervention: (1) General practitioners' use of C reactive protein point of care testing and (2) training in enhanced communication skills separately and (3) combined, and usual care. Primary Outcome Measured: Antibiotic prescribing at the index consultation.

	Secondary Outcome Measured: antibiotic prescribing during 28 days' follow-up, re-consultation, clinical recovery, and patients' satisfaction and enablement.
Chappell et al, 2021 New Zealand N = 1,214 practitioners	Participants: General practitioners. Intervention Category: Audit and feedback. Control: No letter Intervention: The trial tested the effects of a letter mailed to high-prescribing GP's that presented their prescribing data in comparison to their peers. Primary Outcome Measured: Antibiotic prescribing.
Christakis et al, 2001 USA N = 38	Participants: Primary care paediatric clinic. Intervention Category: Audit and feedback Control: Usual Care. Intervention: Providers in the treatment arm were immediately greeted with pop-up screens based on their selection of antibiotic, indication, and duration. The screens were designed to convey the evidence in stages. Each first screen was a 5-line summary of the evidence. At the bottom of the first screen were options to: 1) see more information; 2) see the abstract of the articles from which the summaries were derived; 3) see the articles themselves that had been scanned and could be viewed in a portable document format using Acrobat reader; or 4) have the references e-mailed to the provider automatically. Main Outcome Measured: Proportion of prescriptions for otitis media that were for otitis media that were for <10 days and frequency with which antibiotics were prescribed.

Curtis et al, 2021 UK N = 1,401 practitioners	Participants: General Practices. Intervention Category: (1) Audit and feedback (behavioural), (2) Audit and feedback. Control: Usual care (no letter). Intervention: The highest prescribing practices in England for broad-spectrum antibiotics were allocated to: (1) feedback intended to create behavioural impact optimization; (2) plain feedback; or no intervention. Feedback was sent monthly for 3 months by letter, fax, and email. Each included a link to a prescribing dashboard. Main Outcome Measured: Dashboard usage and change in prescribing.
De la Poza Abad et al, 2016 Spain N = 600 patients	Participants: Patients over 18 years old with uncomplicated acute respiratory tract infections. Intervention Category: (1) Delayed script filling, (2) Delayed script collection. Control: Usual care of immediate antibiotic treatment. Intervention: The intervention arms included immediate antibiotic treatment as well as two delayed antibiotic prescribing strategies with structured advice to use a course of antibiotics in case of worsening of symptoms or not improving. The two prescribing strategies include (1) prescription given to patient during consultation or (2) a prescription was left at the reception of the primary care centre 3 days after the first medical visit. Main Outcome Measured: Antibiotic use.
D'Hulster et al, 2022 Belgium N = 10,375 practitioners	Participants: General Practitioners and Patients. Intervention Category: Communication + Educational. Control: Usual care. Intervention: In a closed cohort stepped-wedge cluster randomized trial all Belgian GPs were invited to participate in online communication skills training

	courses (TRACE and INTRO) and provided with linked patient information booklets. Main Outcome Measured: Antibiotic prescribing rate per 1000 patient contacts.
Dowell et al, 2001 UK N = 191 patients	Participants: Adult patients with uncomplicated cough. Intervention Category: Delayed script collection. Control: Usual care, subjects were given a prescription for an antibiotic of the GP's choice immediately. Intervention: A prescription for an antibiotic of the GP's choice was lodged at reception and patients were invited to collect it after one week if required. Primary Outcome measured: Antibiotic use measured as the rate of collected/filled prescriptions. Secondary Outcome Measured: Duration of symptoms.
Ferrat et al, 2016 France N = 203 practitioners	Participants: General practitioners. Intervention Category: Educational. Control: Usual care. Intervention: Among 203 randomized GPs, 168 completed the study, 70 in the intervention group and 98 in the control group. Intervention GPs were randomized to attending only a 2-day interactive educational seminar on evidence-based guidelines about managing respiratory tract infections or also 1 day of problem-solving training. Primary Outcome measured: Percentage of change in the proportion of prescriptions containing an antibiotic for any diagnosis.
Figueiras et al, 2020 Spain	Participants: All primary care physicians working for the Spanish National Health Service (NHS) in Galicia. Intervention Category: Educational + Decision support tool.

N = 2,610 practitioner	Control: Usual care. Intervention: The researchers designed one multifaceted low-cost intervention. This intervention consisted of a one-hour educational outreach visits tailored to training needs identified in a previous study; an online course integrated in practice accreditation; and a clinical decision support system. To tackle the perception that antibiotic resistance is not a problem at a community level, the outreach visit highlighted: (i) data on the impact of resistance (mortality, morbidity); (ii) data on antibiotic use in Spain and Galicia; and (iii) the relationship between antibiotic use and resistance. Secondly, to address complacency (attitude that motivates the prescribing of antibiotics to fulfill professionals' perceptions of their patients' expectations), the outreach visit stressed: (i) the importance of communication skills and, (ii) the effectiveness of delayed prescribing (prescription with the physician advising the patient to collect it in a few days' time if the symptoms show no improvement). In addition, patient-support materials were distributed in the waiting rooms. Thirdly, to address fear (attitude relating to fear of possible future complications in the patient) and insufficient knowledge, the researchers encouraged delayed prescribing, held a training course (online integrated practice-accreditation course and offered access to an internet-based clinical decision support system. Primary Outcome Measured: Changes in the ESAC (European Surveillance of Antimicrobial Consumption) quality indicators for outpatient antibiotic use.
Finkelstein et al, 2001 USA N = 8,815 patients	Participants: Practitioner (General Practice) and Patients (Children > 3months and <6 years) Intervention Category: Educational. Control: Not exposed to the educational programme. Intervention: The 1-year targeted educational intervention was designed to change both physician and parental behaviour to decrease unnecessary antimicrobial use. The intervention included 2 meetings of the practice with a

	physician peer leader, using CDC-endorsed summaries of judicious prescribing recommendations; feedback on previous prescribing rates were also provided. Parents were mailed a CDC brochure on antibiotic use, and supporting materials were displayed in waiting rooms. Primary Outcome measured: The rate of antibiotic courses dispensed per person-year in experimental and control practices.
Francis et al, 2009 UK N = 558 patients and 108 practitioners	Participants: Children aged from 6 months to 14 years, presenting to primary care with an acute respiratory tract infection and general practitioners. Intervention Category: Communication + Educational. Control: Usual care. Intervention: Clinicians in the intervention group were trained in the use of an 8-page interactive booklet on respiratory tract infections in children and asked to use the booklet during consultations with recruited patients. The training was provided online and described the content and aims of the booklet and encouraged its use within the consultation to facilitate the use of certain communication skills, mainly exploring the parent's main concerns, asking about their expectations, and discussing prognosis, treatment options, and any reasons that should prompt re-consultation. The booklet was then provided to the parents as a take home resource. Primary Outcome Measured: 1. Antibiotics taken within first two weeks. 2. Rate of antibiotic prescribed at index consultation. Secondary Outcome Measured: Re-consultation rates - The proportion of children who attended a face-to-face consultation about the same illness during the two-week follow-up period.
Gerber et al, 2013 USA N = 162 practitioners	Participants: Paediatric clinicians. Intervention Category: Audit and feedback + Educational Control: Usual care. Intervention: A 1-hour on-site clinician education session (June 2010) followed by 1 year of personalized, quarterly audit and feedback of prescribing for bacterial and viral ARTIs or usual practice.

	Primary Outcome Measured: Rates of broad-spectrum (off-guideline) antibiotic prescribing for bacterial ARTIs and antibiotics for viral ARTIs for 1 year after the intervention.
Gjelstad et al, 2013 Norway N = 382 practitioners	Participants: General Practitioners. Intervention Category: Audit and feedback + Education. Control: Intervention targeting prescribing practice for older patients. Intervention: The intervention was delivered by specially trained general practitioners acting as peer academic detailers. The intervention group had two visits from these specially trained general practitioners. The first presenting the national clinical guidelines for antibiotic use and recent research evidence on acute respiratory tract infections, the second based on feedback reports of each general practitioner's antibiotic prescribing profile from the preceding year. Regional one day seminars were arranged as a supplement. Primary Outcome Measured: Prescription rates and proportion of non-penicillin V antibiotics prescribed at the group level before and after the intervention, compared with corresponding data from the controls.
Gold et al, 2021 UK N = 920	Participants: Practices whose STAR-PU-adjusted prescribing was in the 20th–95th percentiles and had increased by > 4% year-on-year in the 2 previous financial years. Intervention Category: Audit and feedback. Control: Usual care. Intervention: Intervention practices received a letter on 1st March 2018 stating 'The great majority (80%) of practices in England reduced or stabilised their antibiotic prescribing rates in 2016/17. However, your practice is in the minority that have increased their prescribing by more than 4%.'.

	Primary Outcome Measured: STAR-PU-adjusted rate of antibiotic prescribing in the months from March to September 2018.
Gold et al, 2022 UK N = 1,851 practitioners	Participants: General practitioners who are high prescribers of antibiotics. Intervention Category: Audit and feedback. Control: The control for the main trial (C) was no letter. For the two other trials included in the study (A and B), the control was the standard overall practice letter. Intervention: The main trial compared a broad-spectrum message and a chart to a no-letter control. The study also included other trials, one compared a broad-spectrum message and chart to the standard-practice overall prescribing letter. Another trial compared an overall-prescribing message with a chart to the standard practice overall letter. Primary Outcome Measured: The primary outcomes were practices' percentage of broad-spectrum prescribing (trials C and A) and overall antibiotic prescribing (trial B) each month from November 2018 to April 2019 (all weighted by the number and characteristics of patients registered in the practice).
Gonzales et al, 2013 USA N = 33 practitioners	Participants: Primary care clinicians in rural central and northeast Pennsylvania. Intervention Category: (1) Decision support tools (Print), (2) Decision support tools (Computerised). Control: Received no intervention tools. Intervention: A 3-arm cluster randomized trial of different implementation strategies to reduce antibiotic use for uncomplicated acute bronchitis, including (1) a traditional printed decision support (PDS) strategy arm, (2) a computer-assisted decision support (CDS) strategy integrated into the workflow of an electronic health record (EHR) arm, and a control arm. The

	PDS and CDS arms both received intervention components guided by the PRECEDE-PROCEED model, which included tools addressing predisposing factors, reinforcing factors, and enabling factors. Clinician education was delivered for each clinic by a clinical champion who participated in a half-day training session. Clinical champions were provided with data about their specific clinic's performance on the acute bronchitis Health-care Effectiveness Data and Information Set measure and with a teaching slide set to use when reviewing this information with the clinicians in their respective clinics. Patient education was provided through brochures. Primary Outcome Measured: Percentage change in number of antibiotic prescriptions for uncomplicated acute bronchitis. Secondary Outcome Measured: Re-consultation rates: defined a return visit as a subsequent visit occurring within 30 days of an incident visit.
Hallsworth et al, 2016 UK N = 1,581 practices	Participants: GP practices whose prescribing rate for antibiotics was in the top 20% for their National Health Service (NHS) Local Area Team. Intervention Category: (1) Audit and feedback + Educational, (2) Educational. Control: Received no communication or intervention materials Intervention: The study design incorporated two interventions. GP practices were first randomised to the intervention or control group for the first intervention. (1) Every GP in a practice in the feedback intervention group was sent a clinician-focused letter and leaflet from England's Chief Medical Officer. The letter stated that the practice was prescribing antibiotics at a higher rate than 80% of practices in its NHS Local Area Team. The leaflet was patient focused on "Treating your infection" developed for the TARGET programme that also enables back-up prescribing. The control group received no communication. (2) Practices were then re-randomised to the intervention or control group for the second intervention. In the second intervention, practices either received patient-focused posters and leaflets or no communication. Primary Outcome Measured: The rate of antibiotic items dispensed per 1000 population.
Hoffman et al, 2022	Participants: General practitioners. Intervention Category: Decision support tools + Educational.

Australia N = 122 practitioners	Control: Usual care. Intervention: Intervention group GPs were given brief decision aids for 3 ARIs (acute otitis media, acute sore throat, acute bronchitis) and video-delivered training. Training videos: One video (7 1/2 mins) explained shared decision making, its role in ARI consultations, and the purpose of patient decision aids. Another video (7 1/2 mins) was of a consultation between a GP and a standardised patient demonstrating how the decision aid could be incorporated into a consultation. The videos are available: https://iebh.bond.edu.au/education-services/research-tools. Primary Outcome Measured: Dispensing rate of target antibiotic classes (routinely used for ARIs), extracted for 12 months before, and following, randomization. Secondary Outcome Measured: GPs' knowledge of antibiotic benefit-harm evidence; prescribing influences; acceptability, usefulness, and self-reported resource use; and dispensing rate of all antibiotics.
Hoye et al, 2013 Norway N = 156 practitioners	Participants: General practitioners. Intervention Category: (1) Educational, (2) Decision support tools + Educational. Control: Usual care. Intervention: There were two interventions used in this trial. The first is an educational intervention and the second was a pop-up feedback intervention. (1) In the educational intervention delayed prescribing, described as giving the patient a prescription and advising to delay for a certain amount of time before deciding whether to fill it, was presented and recommended at specially trained GP peer outreach visits and a 1-day seminar.

	(2) In the second pop-up intervention, one group of the respiratory tract infection (RTI)-arm GPs, chosen based on the electronic patient-record (EPR) system they used, had a compatible pop-up software application installed on their computers. Printing a prescription for antibiotics from the computer would trigger a screen pop-up requesting confirmation that the prescription was a delayed prescription. Primary Outcome Measured: Antibiotic-dispensing rates.
Hurlimann et al, 2014 Switzerland N = 140 practices	Participants: General practices. Intervention Category: (1) Audit and feedback + Educational (penicillin for RTIs), (2) Audit and feedback + Educational (SXT for lower UTIs), (3)) Audit and feedback + Educational (quinolones for COPD exacerbation). Control: Usual care. Intervention: The intervention consisted of providing guidelines on treatment of respiratory tract infections (RTIs) and uncomplicated lower urinary tract infections (UTIs), coupled with sustained, regular feedback on individual antibiotic prescription behaviour for 2 years. Primary Outcome Measured: Percentage of antibiotics prescribed.
Ilett et al, 1999 Australia N = 112 practitioners	Participants: General practitioners. Intervention Category: Educational. Control: Doctors in the control group were not visited nor given the chart. Intervention: A panel of experts prepared a best practice chart of recommended drugs for upper and lower respiratory tract infections, otitis media and urinary tract infections. The adviser made a 10–15 min visit to each prescriber in the active group (June–July), gave them the chart and discussed its recommendations briefly.

	Primary Outcome Measured: Prescription numbers for all prescribers were obtained from the Commonwealth Health Insurance Commission for the pre (March - May) and post detailing (August - September) periods.
Kronman et al, 2020 USA N = 19 practitioners	Participants: Paediatric clinicians. Intervention Category: Audit and feedback + Educational. Control: Usual care. Intervention: This stepped-wedge clinical trial ran from November 2015 to June 2018, the study randomly assigned 19 paediatric practices in the Paediatric Research in Office Settings Network or the NorthShore University Health System to 4 wedges. Visits for acute otitis media, bronchitis, pharyngitis, sinusitis, and upper respiratory infection for children 6 months to, 11 years old without recent antibiotic use were included. Clinicians received the intervention as 3 program modules containing online tutorials and webinars on evidence-based communication strategies and antibiotic prescribing, booster video vignettes, and individualized antibiotic prescribing feedback reports over 11 months. In module 1, clinicians viewed 25-minute online tutorials about best practices for both parent-clinician communication practices and antibiotic prescribing, participated in live or recorded 40-minute webinars on those topics, and received an individualized feedback report presenting antibiotic prescribing rates during ARTI visits in the baseline control period. The theory of planned behaviour underpinned development of the evidence-based communication tutorial, which aims to modify how providers frame treatment recommendations and follow-up plans for patients with ARTIs. The researchers implemented 2 main strategies: (1) building subjective norms, self-awareness, and changing attitudes among the clinicians supporting the targeted communication and prescribing behaviours and (2) developing the skills to achieve these goals through modelling, practice, feedback, reinforcement, and building self-confidence. In module 2, clinicians received two 5-minute online booster video vignettes recapping communication best practices and the second antibiotic prescribing feedback report, presenting prescribing rates during the module 1 participation period.

	In module 3, clinicians received 1 communication booster video vignette and the third and fourth antibiotic prescribing feedback reports, presenting prescribing rates during modules 2 and 3, respectively. All enrolled clinicians received links to the Web-based tutorials, webinars, booster video vignettes, and individualized antibiotic prescribing feedback reports via e-mail. Study staff tracked clinician participation in the Web-based intervention components by determining if clinicians opened each online tutorial and completed embedded quiz questions at a passing rate of 80%. All enrolled paediatricians were offered American Board of Paediatrics Maintenance of Certification Part 4 credit for completing the DART QI program. Primary Outcome Measured: Overall antibiotic prescribing rates for all ARTI visits.
Lagerlov et al, 2000 Norway N = 199 practitioners	Participants: General practitioners. Intervention Category: Audit and feedback + Educational. Control: Usual care. Intervention: 199 general practitioners in 32 groups were randomised to participate in peer review meetings related to either asthma or urinary tract infections. The dispensing by the participating doctors of anti-asthmatic drugs and antibiotics during the year before the intervention period provided the basis for prescription feedback. Rather than using guidelines alone or prescription feedback alone the study examined a combined intervention of providing individual feedback and deriving quality criteria using guideline recommendations in peer review groups. The intervention feedback was designed to describe the treatment given in relation to recommendations in the national guidelines. In each group the doctors agreed on quality criteria for their own treatment of the corresponding diseases based on these recommendations. Comparison of their prescription feedback with their own quality criteria gave each doctor the proportion of acceptable and unacceptable treatments.

	Primary Outcome Measured: Divergence in the prescribing behaviour between the year before and the year after the intervention.
Le Corvoisier et al, 2013 France N = 171 practitioners	Participants: General practitioners. Intervention Category: Educational. Control: GPs in the control group (n = 99) received no antibiotic prescription recommendation. Intervention: Intervention group GPs (n = 72) attended an interactive seminar presenting evidence-based guidelines on antibiotic prescription for respiratory infections. Primary Outcome Measured: The proportion of prescriptions containing an antibiotic in each group and related costs.
Legare et al, 2011 Canada N = 33 practitioners and 459 patients	Participants: Family medicine groups (practitioner and patients). Intervention Category: Decision support tools + Educational. Control: Delayed Decision support tools + Educational. Intervention: DECISION+ is a multiple component, continuing professional development program in shared decision making that addresses the use of antibiotics for ARIs. DECISION+ is up of three main components: (i) interactive workshops and related material; (ii) reminders of expected behaviours; and (iii) feedback to FPs on the agreement between their decisional conflict and that of their patients. The intervention group received immediate DECISION+ participation. Throughout the pilot trial, DECISION+ was adapted in response to participant feedback.

	Primary Outcome Measured: After the consultation, patients and Family Physicians independently self-reported the decision (immediate use, delayed use, or no use of antibiotics) and its quality.
Legare et al, 2012 Canada N = 149 practitioners and 359 patients	Participants: General practitioners. Intervention Category: Decision support tools + educational. Control: Usual care. Intervention: The study performed a randomized trial, clustered at the level of family practice teaching unit, with 2 study arms: DECISION+2 and control. The DECISION+2 training program included a 2-hour online tutorial followed by a 2-hour interactive seminar about shared decision-making. The online tutorial addressed key components of the clinical decision-making process about antibiotic treatment for acute respiratory infections in primary care. Participants (teachers and residents) had one month to complete the online tutorial. Facilitators who were trained during the DECISION+ pilot trial were updated on DECISION+2. These facilitators led the on-site interactive workshop, which aimed to help physicians review and integrate the concepts they acquired during the online training. Both the online tutorial and workshop included videos, exercises, and decision aids to help physicians communicate to their patients the probability of a bacterial acute respiratory infection and the benefits and harms associated with the use of antibiotics. As part of the intervention, research assistants verified that the decision aids were available in each of the walk-in consultation rooms in all the family practice teaching units in the intervention arm. Primary Outcome Measured: The proportion of patients who decided to use antibiotics immediately after consultation. Secondary Outcomes Measured: Patients' perception that shared decision-making had occurred. Two weeks after the initial consultation, the study assessed patients' adherence to the decision, repeat consultation, decisional regret, and quality of life.
Lemiengre et al, 2018	Participants: Family physicians (FPs).

Belgium N = 131 practitioners	Intervention Category: (1) Point of care testing, (2) Educational, (3) Point of care testing + Educational. Control: Usual care. Intervention: The participants were allocated to one of four intervention groups according to whether the FPs performed: (1) a point-of-care C-reactive protein test (POC CRP); (2) a brief intervention to elicit parental concern combined with safety net advice (BISNA). The brief intervention consisted of the following three questions for parents at the start of the consultation: 'Are you concerned [about the illness of your child]?', 'What exactly concerns you?', and 'Why does this concern you?' Apart from these questions, a parent information leaflet containing information about supportive treatment (for example, what to do in case of fever, how to use antipyretics) and when to re-consult was provided as safety net advice.; (3) both POC CRP and BISNA; or (4) usual care (UC). Primary Outcome measured: The immediate antibiotic prescribing rate.
Linder et al, 2010 USA N = 27 practices	Participants: Primary care practices. Intervention Category: Audit & feedback. Control: Usual care. Intervention: The study randomly assigned 27 primary care practices to receive the Acute Respiratory Infection (ARI) Quality Dashboard, an electronic health record (EHR)–based feedback system (e.g., the proportion of ARI visits at which antibiotics were prescribed, clinician's performance against his or her clinic peers and against national benchmarks) or usual care. Primary Outcome measured: Antibiotic prescribing rate for ARI visits. Secondary Outcome Measured: Antibiotic prescribing between ARI Quality Dashboard users and nonusers.
Little et al, 2013	Participants: General Practitioners in six European countries.

Multiple locations across Europe N = 246 practices	Intervention Category: (1) Point of care testing, (2) Communication training, (3) Communication training + point of care testing. Control: Usual care. Intervention: After a baseline audit, primary-care practices were cluster randomised to usual care, (1) training in the use of a C-reactive protein (CRP) test at point of care, (2) in enhanced communication skills, or (3) in both CRP and enhanced communication. The C-reactive protein (CRP) group received internet training on how to target testing and how to negotiate with the patient about management decisions. Training in enhanced communication skills focused on the gathering of information on patients' concerns and expectations, exchange of information on symptoms, natural disease course, and treatments, agreement of a management plan, summing up, and providing guidance about when to reconsult. Physicians were also provided with an interactive booklet to use during consultations that included information on symptoms, use of antibiotics and antibiotic resistance, self-help measures, and when to re-consult. The internet modules and materials were translated into the relevant national language and mainly addressed lower-respiratory-tract infections, although many of the issues were relevant to all respiratory-tract infections. Group practices were asked to appoint a lead physician to organise a structured meeting on prescribing issues. A survey was sent to all physicians after the study about approach to training and the format of any group meetings. Primary Outcome Measured: Antibiotic use, as documented on the case-report forms. Secondary Outcome Measured: Duration and severity of symptoms. Re-consultation for new or worsening symptoms within 4 weeks.
Little et al, 2019 Multiple locations across Europe N = 372 practitioners	Participants: General practitioners. Intervention Category: (1) Point-of-care testing, (2) Communication training, (3) Communication training + point of care testing. Control: Usual care. Intervention: A total of 246 general practices in 6 countries were cluster-randomized to usual care, (1) Internet-based training on C-reactive protein (CRP) point-of-care testing, (2) Internet based training on enhanced communication skills and interactive booklet, or (3) both interventions combined.

	Primary Outcome Measured: Antibiotic prescribing for RTIs after 12 months.
Llor et al, 2011 Spain N = 61 practitioners	Participants: General practitioners. Intervention Category: Point of care testing. Control: Usual care. Intervention: Participant physicians were randomly assigned to one of two study arms: an intervention group assigned to rapid antigen detection testing (RADT) and a control group which followed usual care and did not have RADT. Primary Outcome Measured: Antibiotic prescriptions. Secondary Outcome Measured: Inappropriate antibiotic prescription.
Macfarlane et al, 2002 UK N = 212 patients	Participants: Adult patients over 16 years of age presenting with acute bronchitis, who were previously well and not under supervision or management for an underlying disease. Intervention Category: Educational + Delayed prescription. Control: Patients in group A, who did no received the patient information leaflet. Intervention: Patients in group A were judged by their general practitioner not to need antibiotics that day but were given a prescription to use if they got worse and standard verbal reassurance. For all patients in group A the general practitioner provided verbal information based on a prompt card. These patients were then randomised by using permuted blocks of four to receive or not receive a patient information leaflet about the natural course of lower respiratory tract symptoms and the advantages and disadvantages of antibiotic use. The patient information leaflet was in the sealed envelope, blinded from the general practitioner by means of a blank leaflet, together with the diary card and return envelope. Patients were asked to open and read the contents of the envelope after the consultation. Patients in group B (47) were judged to need antibiotics and were given a prescription and encouraged to use it. Primary Outcome Measured: Antibiotic Consumption: Patients who took the antibiotics in the following two weeks.

	Secondary Outcome Measured: Re-consultation rates: Re-consultations for the same symptoms in the next month.
Mainous et al, 2000 USA N = 216 practitioners	Participants: General practitioners. Intervention Category: (1) Audit and feedback, (2) Education, (3) Audit and feedback + Educational Control: Usual care. Intervention: Based on Medicaid regions in Kentucky, primary care physicians managing paediatric respiratory infections in Medicaid were randomized into four groups. Groups received either 1) performance feedback only, 2) patient education materials only, 3) both feedback and education materials, or 4) no intervention. Primary Outcome Measured: Antibiotic prescribing.
McIsaac & Goel, 1998 Canada N = 450 practitioners	Participants: Family physicians. Intervention Category: Decision support tools. Control: Physicians received an information package, a score card, and a recording form to use during one sore-throat encounter. Intervention: The physicians randomly received either a control form, or an intervention form which required them to interact with the score during the clinical recording process. Half of the encounter forms (intervention form) included the items of the score' explicitly displayed in a box format identical to that on the laminated score card. The physician was asked to check off the presence of the four score items and circle the total score. The suggested appropriate management action to take was displayed next to the score. Thus, physicians using the intervention form would interact with the score and management recommendations during the clinical encounter as part of the recording process. The control forms followed the exact same checklist format except that the items constituting the score were simply listed along

	with other clinical signs or symptoms, and no management recommendations were made. Primary Outcome Measured: Antibiotic prescriptions.
McIsaac et al, 2002 Canada N= 621 practitioners	Participants: General practice physician. Intervention Category: Decision support tools. Control: Physicians completed a form like the intervention group, but the form did not include either the sticker or the chart prompts. Intervention: Physicians received, by mail, an article describing the clinical score management approach; a laminated pocket card summarizing the method; clinical encounter and patient consent forms; and a 1-page survey of practice characteristics. In the intervention group, physicians were provided with a sticker to apply to the encounter form that listed the score management approach. The sticker contained boxes to be checked by the physicians to calculate the score total and determine appropriate management. Physicians not wishing to use the sticker were prompted on the from to write the score total in a space provided. As a result, physicians in the intervention group received repeated prompts that reminded them to use the score approach each time they completed a clinical encounter form. Primary Outcome Measured: Rate of antibiotic use. Secondary Outcome Measured: Rate of unnecessary antibiotic prescriptions given to patients with a negative throat culture.
McIsaac et al, 2021 Canada N = 54 practitioners	Participants: Primary care practitioners. Intervention Category: Audit and feedback + Decision support tools + Educational. Control: Usual care. Intervention: Primary care practitioners from six primary care clinics in Toronto, Ontario were assigned to intervention or control groups to evaluate the effectiveness of a multi-faceted intervention for reducing antibiotic prescriptions to adults with respiratory and urinary tract infections. The intervention included provider education, clinical decision aids, and audit and feedback of antibiotic prescribing.

	Primary Outcome Measured: Total antibiotic prescriptions for these infections. Secondary Outcome Measured: Delayed prescriptions, prescriptions longer than 7 days, recommended antibiotic use, and outcomes for individual infections.
McNulty et al, 2018 UK N = 152 practices	Participants: General practices. Intervention Category: Educational. Control: Usual care. Intervention: General practices were stratified by clinical commissioning group, antibiotic dispensing rate and practice patient list size, then randomly allocated to intervention (TARGET workshop, 73 practices) or control (usual practice, 79 practices). The TARGET workshop incorporated a presentation, reflection on antibiotic data, promotion of patient and general practice (GP) staff resources, clinical scenarios, and action planning, Primary Outcome Measured: The primary outcome measure was total oral antibiotic items dispensed/1000 patients for the year after the workshop (or pseudo workshop date for controls), adjusted for the previous year's dispensing.
Meeker et al, 2014 USA N = 954 patients and 14 practitioners	Participants: Adults with acute respiratory infections. Intervention Category: Educational. Control: Usual care. Intervention: The intervention consisted of displaying poster-sized commitment letters in examination rooms for 12 weeks. These letters, featuring clinician photographs and signatures, stated their commitment to avoid inappropriate antibiotic prescribing for acute respiratory infections(i.e.,

	diagnoses of acute respiratory infection for which antibiotics are not recommended). Primary Outcome Measured: Antibiotic prescribing rates for antibiotic-inappropriate ARI diagnoses in baseline and intervention periods, adjusted for patient age, sex, and insurance status.
Meeker et al, 2016 USA N = 248 practitioners	Participants: Primary care physicians. Intervention Category: (1) Audit and feedback, (2) Decision support tools (Accountable Justification), (3) Decision support tools (Alternatives), (4) Audit and feedback + Decision support tools (Accountable Justification), (5) Audit and feedback + Decision support tools (Alternatives), (6) Audit and feedback + Decision support tools (Accountable Justification) and Audit and feedback + Decision support tools (Alternatives), (7) Decision support tools (Accountable Justification) + Decision support tools (Alternatives). Control: Usual care. Intervention: Three behavioural interventions, implemented alone or in combination as follows*: suggested alternatives* presented electronic order sets suggesting nonantibiotic treatments; *accountable justification* prompted clinicians to enter free-text justifications for prescribing antibiotics into patients' electronic health records; *peer comparison* sent emails to clinicians that compared their antibiotic prescribing rates with those of "top performers" (those with the lowest inappropriate prescribing rates). Primary Outcome Measured: Antibiotic prescribing rates for visits with antibiotic-inappropriate diagnoses (nonspecific upper respiratory tract infections, acute bronchitis, and influenza) from 18 months preintervention to 18 months afterward, adjusting each intervention's effects for co-occurring interventions and preintervention trends, with random effects for practices and clinicians.
O'Connell et al, 1999 Australia	Participants: General practitioners practising in non-urban areas. Intervention Category: Audit and feedback + Educational. Control: Received no information on their prescribing.

N = 2,440 practitioners	Intervention: Two sets of graphical displays (6 months apart) of their prescribing rates for 2 years, relative to those of their peers, were posted to participants. Data were provided for five main drug groups and were accompanied by educational newsletters. The control group received no information on their prescribing. In addition, prescribers were provided with a comparison of the age-sex profile of their patients compared with those attending the other general practices. The first material posted was the graphical displays and data, accompanied by an educational newsletter covering some general prescribing issues. The second material posted included 6 additional months of prescribing information, and the accompanying newsletter focused on specific issues relating to the prescribing of antibiotics. Primary Outcome Measured: Prescribing rates: Median prescribing rates per 100 Medicare services provided during the studied period.
Ostervall, 2017 Sweden N = 31 practices	Participants: Patients in 31 clinics during the flu season in Stockholm. Intervention Category: Educational Control: Usual care. Intervention: This study used a randomized controlled trial to test the effect on antibiotics use of reminders to primary care patients. The intervention in the treatment group is a questionnaire to fill out, with simple questions on antibiotic resistance and effectiveness of treatment with antibiotics. Two different versions of the treatment questionnaire are used. The reminder is given as a statement, inserted among the questions, to which the patients respond whether they are aware of this fact or not. The reminder is framed in terms of either the collective or the individual risk increase. The phrasings used are: - Are you aware that the risk of antibiotic resistance in society increases with the amount of antibiotics used? (T1) - Are you aware that the risk of you being affected by bacteria resistant to antibiotics increases with each course of antibiotics you take? (T2) Primary Outcome Measured: Antibiotic use.
Persell et al, 2016 USA	Participants: Primary care clinicians. Intervention Category: (1) Decision Support Tools (Accountable Justification), (2) Decision Support Tools (Alternatives), (3) Audit and feedback, (4) Decision Support Tools (Accountable Justification) + Decision Support Tools

N = 28 practitioners	(Alternatives), (5) Audit and feedback + Decision Support Tools (Alternatives), (6) Audit and feedback + Decision Support Tools (Accountable Justification), (7) Audit and feedback + Decision Support Tools (Alternatives) + Decision Support Tools (Accountable Justification). Control: Usual care. Intervention: Primary care clinicians were randomized in a 2 × 2 × 2 factorial experiment with 3 interventions: 1) Accountable Justifications; 2) Suggested Alternatives; and 3) Peer Comparison. Experiment participants received interventions alone: 1) Accountable Justifications; 2) Suggested Alternatives; and 3) Peer Comparison and combined (4) Decision Support Tools (Accountable Justification) + Decision Support Tools (Alternatives), (5) Audit and feedback + Decision Support Tools (Alternatives), (6) Audit and feedback + Decision Support Tools (Accountable Justification), (7) Audit and feedback + Decision Support Tools (Alternatives) + Decision Support Tools (Accountable Justification). Clinicians randomized to "Accountable Justifications" received EHR alerts in the course of e-prescribing an antibiotic for an ARI diagnosis. The alert briefly summarized the treatment guidelines corresponding to the ARI diagnosis for which the antibiotic was being written (e.g., "antibiotics are not indicated for non-specific upper respiratory infections"), prompted the clinician to enter a free-text justification for prescribing an antibiotic, and informed the clinician that the free-text justification provided would be included in the patient's medical record where it would be visible to other clinicians. Clinicians were also informed that if no free-text justification was entered, a default statement "No justification for prescribing antibiotics was given" would appear in the record. If the antibiotic order was cancelled, no justification was required, and no default text appeared. When clinicians assigned to the Suggested Alternatives intervention entered an ARI diagnosis for a patient visit, a computerized alert presented an order set containing multiple non-antibiotic prescription and non-prescription medication choices as well as educational materials that could be printed and given to the patient. Clinicians in the Peer Comparison Intervention group received emailed monthly performance feedback reports. These reports included the clinician's individual antibiotic prescribing rates for non-antibiotic-appropriate ARIs and as a benchmark, the antibiotic prescribing rate for clinicians who were at the

	10th percentile within the clinic (i.e., those with the lowest rates of inappropriate antibiotic prescribing). Primary Outcome Measured: Rates of antibiotic prescribing for: non-antibiotic-appropriate ARI (acute respiratory infections) diagnoses, acute sinusitis/pharyngitis, all other diagnoses/symptoms of respiratory infection, and all three ARI categories combined.
Pshetizky et al, 2003 Israel N= 81 patients	Participants: Parents of children aged 3 months to 4 years visiting the family practice clinics and diagnosed with acute otitis media. Intervention Category: Educational. Control: Received a prescription for antibiotics as part of the routine care, without a patient education component. Intervention: The randomization process included pre-prepared closed envelopes assigning each child to the different groups. One group received a prescription for antibiotics as part of the routine care, without a patient education component. The second group received a structured explanation and a prescription for antibiotics to be used if symptoms did not improve within 48 h. The explanation was short and included the following points: (i) AOM is part of an upper respiratory tract infection; (ii) it has been well established that in most cases children will recover regardless of antibiotic prescription; (iii) dangerous late complications from AOM unfortunately may occur regardless of whether antibiotics were or were not delivered in the course of the acute illness; and (iv) parents were recommended in cases of high fever or severe pain to administer paracetamol prescribed according to the child's weight. Primary Outcome Measured: Antibiotic consumption: where parents had administered the antibiotic to their child as prescribed up to 7 days after consultation.
Regev Yochay et al, 2011 Israel N = 52 practitioners	Participants: Primary care paediatric practitioners in solo practices. Intervention Category: Educational + Communication training + Audit and feedback. Control: Physicians in control practices had no trial intervention. Intervention: The intervention was led by local leaders and engaged the participating physicians. It included physician focus group meetings, workshops, seminars, and practice campaigns. These activities focused on self-developed guidelines, improving parent and physician knowledge, diagnostic skills, and parent-physician communication skills that promoted awareness of antibiotic resistance. An initial 2-day interactive workshop (held

	at the beginning of year 1 focused on defining the determinants for non-judicious antibiotic prescription and potential interventions to reduce non-judicious prescription. A second workshop (held at the beginning of year 2) focused on parent-physician communication, and a third workshop (held at the beginning of year 3) focused on APR feedback. The major emphases throughout the intervention activities were that antibiotics should be given only when bacterial infections are highly suspected (according to guidelines) and that the drugs of choice for most indications are penicillin or amoxicillin and that other antibiotic classes (particularly macrolides and cephalosporins) further promote antibiotic resistance and should be avoided. Primary Outcome Measured: Change in annual antibiotic prescription rates (APRs) of children treated by the intervention group physicians as compared with rates among those treated by control group physicians.
Samore et al, 2005 USA N = 50 practitioners	Participants: Inhabitants and primary care clinicians in rural communities in Utah and Idaho. Intervention Category: (1) Educational, (2) Decision support tools + Educational. Control: Received neither of the intervention arms. Intervention: Two different strategies to enhance appropriate use of antimicrobials for acute respiratory tract infections were compared. One arm of the randomized trial received (1) a community intervention alone, while the other received the (2) community intervention plus a direct intervention with primary care clinicians. The clinician intervention incorporated stand-alone decision support tools on paper or a handheld personal digital assistant (PDA) for the management of acute respiratory tract infection at the point-of-care. The community intervention focused on the topic of antimicrobial resistance and consisted of introductory meetings with community leaders, news releases in the print media, distribution of educational materials at pharmacies and physician offices, and a mailing to parents of children aged younger than 6 years. Primary Outcome Measured: Community-wide antimicrobial usage.
Schwartz et al, 2021 Canada N = 3,500 practitioners	Participants: High-prescribing primary care physicians (PCPs). Intervention Category: (1) Audit and feedback (Initiation) + Educational, (2) Audit and feedback (Duration) + Educational. Control: No letter.

	Intervention: Physicians were randomized to receive a mailed letter sent in December 2018 (1) addressing antibiotic treatment initiation (n = 1500), (2) a letter addressing prescribing duration (n = 1500), or no letter (control; n = 500). Each letter informed the primary care physicians recipient that they were in the highest 25th percentile compared with their peers for antibiotics prescribed based on their total number of antibiotic prescriptions. The initiation letter provided a table on appropriate antibiotic initiation for common respiratory infections, with recommendations and tools adapted from Choosing Wisely Canada resources. The duration letter provided recommendations on appropriate antibiotic prescribing durations. Outliers at the 99th percentile at baseline for each arm were excluded from analysis. Primary Outcome Measured: Total number of antibiotic prescriptions over 12 months postintervention. Secondary Outcome Measured: Number of prolonged-duration prescriptions (>7 days) and antibiotic drug costs (in Canadian dollars).
Sondergaard et al, 2003 Denmark N = 299 practitioners	Participants: GPs in the County of Funen, Denmark. Intervention Category: Audit and feedback. *(The intervention group received "Audit and feedback + Educational" but the control received an educational also – normal practice, so the intervention is classified as Audit and feedback, as that it what was tested.) Control: Received the guidelines only with no feedback on prescription patterns. Intervention: All GPs received a clinical guideline on the diagnosis and treatment of respiratory tract infections. The intervention group received clinical guidelines on the treatment of respiratory tract infections plus postal feedback with aggregated data on their prescribing patterns for antibiotics. Primary Outcome Measured: Prescriptions of antibiotics given by number of prescriptions per 1000 patients per month.
Taylor et al, 2005 USA	Participants: Healthy children younger than 24 months old enrolled at the time of an office visit. Intervention Category: Educational.

N = 499 patients	Control: Received brochures about injury prevention. Intervention: Parents of study children were randomized to receive either a pamphlet or videotape (featuring one of their child's paediatricians) promoting the judicious use of antibiotics. Primary Outcome Measured: The study compared the number of visits for upper respiratory tract infections (URIs), number of diagnoses and antibiotic prescriptions for otitis media and/or sinusitis and total number of antibiotics per patient among children in the intervention and control groups.
Vervloet et al, 2016 Netherlands N = 39 practitioners	Participants: Family physicians. Intervention Category: Communication training + Decision support tools + Audit and feedback. Control: Usual care. Intervention: The intervention consisted of FP communication skills training, including communication about delayed prescribing; implementation of antibiotic prescribing agreements in family physicians' Electronic Prescribing Systems; quarterly feedback figures for family physician's. The aim of this study was thus to evaluate the effect of a PTAM-based multifaceted intervention, which consisted of (1) FP communication skills training, including communication about delayed prescribing, (2) implementation of PTAM group's antibiotic prescribing agreements in the FPs' EPS and (3) providing quarterly feedback figures of RTI-related antibiotic prescriptions to the participating FPs, on the volume of RTI-related antibiotic prescriptions in family practice. The sequence of intervention delivery is described below. First, all participating FPs used the EPS. When the FP diagnosed an RTI, the EPS first suggested 'no prescription' and provided the FP with advice to give the patient. The next suggestion by the EPS, if the FP still wished to prescribe an antibiotic, was 'delayed prescription' together with information about for which patients in which situations such a prescription would be feasible. Only after these two suggestions, the FP could prescribe a 'normal prescription', if

	(s)he wished to. All FPs received technical support on how to work with the EPS to be able to adhere to antibiotic prescribing agreements made in a later stage. Hereafter, a PTAM was prepared on the two most common clinical presentations of RTI: acute cough and rhinosinusitis. During this PTAM, FPs were educated on treatment guidelines for both complaints and were trained in their communication skills. Agreements were made about antibiotic prescribing for RTI, which were implemented in their EPS. In the following PTAM, 3 months later, feedback figures on their antibiotic prescribing behaviour were discussed. The control groups did not receive any training, support or feedback on antibiotic prescribing during this period, they focused on a topic other than antibiotics. The control groups received the intervention once the study had finished. Primary Outcome Measured: The number of RTI-related antibiotic prescriptions after the intervention.
Welschen et al, 2004 Netherlands N = 89 practitioners and 1,892 patients	Participants: General practitioners with their collaborating pharmacists. Intervention Category: Audit and feedback + educational. Control: The control group did not receive any of these elements. Intervention: The first part of the intervention consisted of group education meeting with a consensus procedure on the indication for and first choice of antibiotics combined with communication skills training, which aimed to learn how to explore patients' worries and expectations and to inform patients about the natural course of the symptoms, self-medication, and alarm symptoms, concluded the meeting. The second component was monitoring, and feedback delivered to general practitioners on their prescribing behaviour. The third was a group education for assistants of general practitioners and pharmacists informing them about Dutch guidelines for general practitioners, followed by skills training in educating patient. And the fourth, education material for patients which consisted of a brochure and accompanying posters, which aimed to inform patients about the self-limiting character of most respiratory tract symptoms, self-medication, and serious symptoms ("alarm signals") necessitating a consultation with the general practitioners. It was available in waiting rooms of general practices, pharmacies, and municipal health services in the intervention group. Primary Outcome Measured: The proportion of practice encounters for acute symptoms of the respiratory tract for which antibiotics were prescribed. Secondary Outcome Measured: The mean number of antibiotic prescriptions per 1000 patients over time (practice level) in intervention and control group.

Zwar et al, 1999 Australia N = 157 practitioners.	Participants: General practitioner trainees in New South Wales. Intervention Category: Audit and feedback + educational. Control: Received an intervention on an unrelated topic. Intervention: The education intervention on antibiotic prescribing was delivered as a two-step process. The first step consisted of individual prescriber feedback for URTI and tonsillitis/streptococcal pharyngitis, specific management guidelines on acute sore throat, and patient handouts on symptomatic management of sore throat. These materials were mailed to the GP trainees following the first practice activity survey. The second step followed the second practice activity survey. Prescriber feedback and management guidelines were again mailed to GP trainees in the antibiotic intervention group. An educational visit was undertaken with those trainees who at survey 2 were prescribing an antibiotic on more than one occasion for every ten URTI problems managed or who were using other than the recommended antibiotic for tonsillitis or streptococcal pharyngitis. Trainees located in rural areas received the educational intervention by telephone. Primary Outcome Measured: The measure was total antibiotic prescriptions per 100 encounters for total indicators. Secondary Outcome Measured: Prescribing rate in agreement with accepted guidelines for tonsillitis/streptococcal pharyngitis.

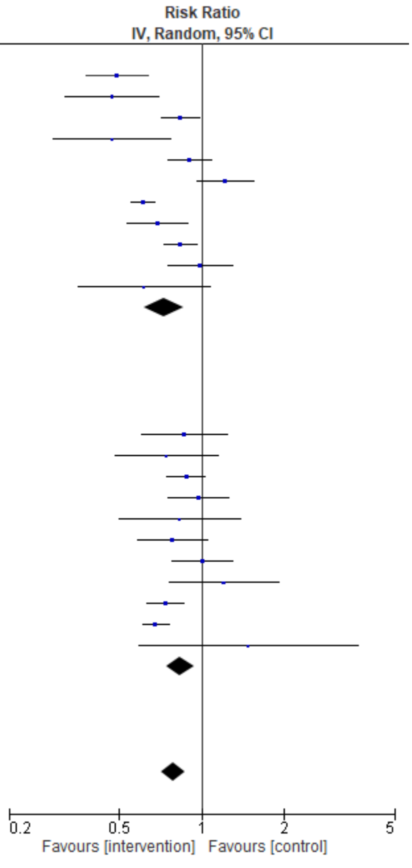
C. Subgroup Analysis Across Primary Outcome Measures

C.1 Prescribing Subgroup Analysis

Geography

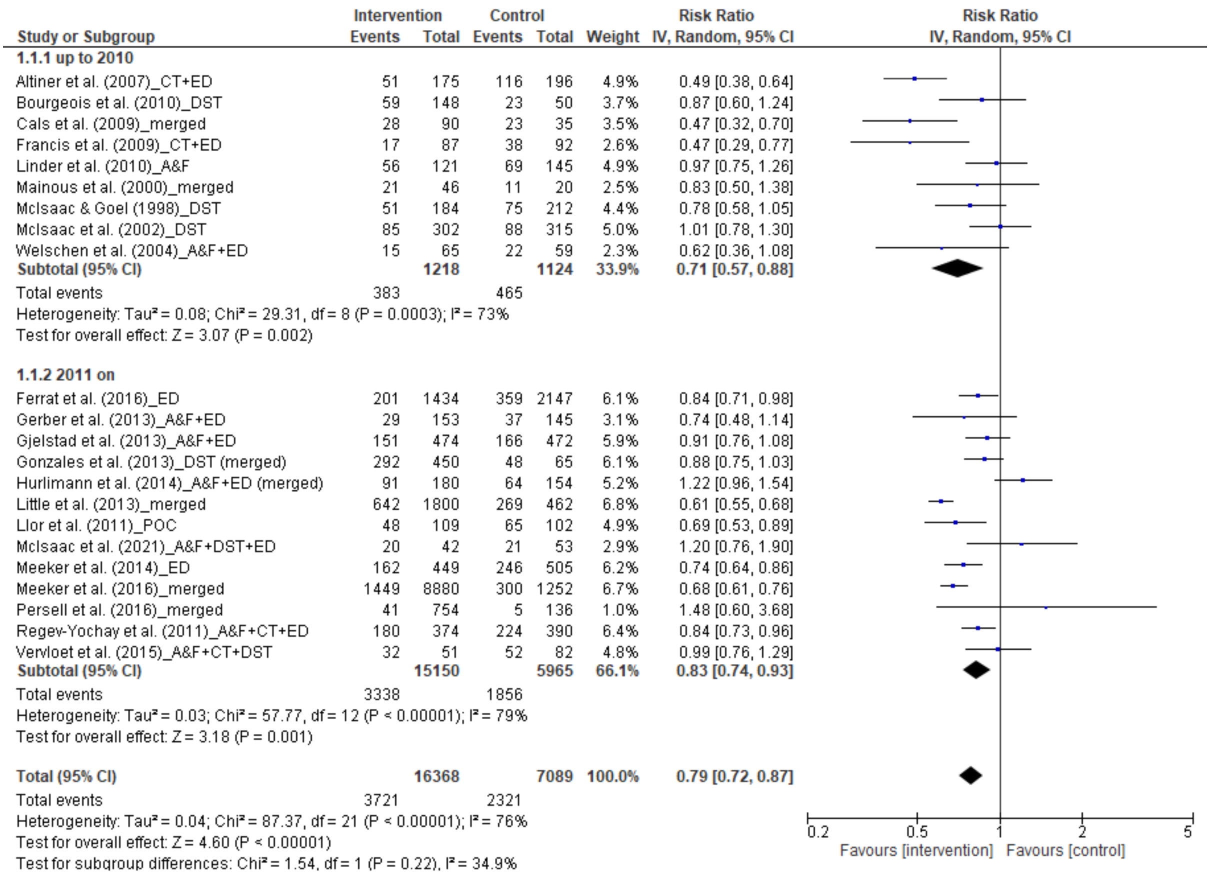
Subgroup analyses by continent indicated that studies published in Europe (27% reduced prescribing; RR = 0.73, 95%CI [0.62, 0.86]) and in North America (16% reduced prescribing; RR = 0.84, 95%CI [0.75, 0.94]) did not significantly differ and, thus, can be considered comparable in their reported intervention effect, χ^2 (1) = 1.75, p = .19, I^2 = 42.9%.

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Europe						
Altiner et al. (2007)_CT+ED	51	175	116	196	4.9%	0.49 [0.38, 0.64]
Cals et al. (2009)_merged	28	90	23	35	3.5%	0.47 [0.32, 0.70]
Ferrat et al. (2016)_ED	201	1434	359	2147	6.1%	0.84 [0.71, 0.98]
Francis et al. (2009)_CT+ED	17	87	38	92	2.6%	0.47 [0.29, 0.77]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	5.9%	0.91 [0.76, 1.08]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.2%	1.22 [0.96, 1.54]
Little et al. (2013)_merged	642	1800	269	462	6.8%	0.61 [0.55, 0.68]
Llor et al. (2011)_POC	48	109	65	102	4.9%	0.69 [0.53, 0.89]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	6.4%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	32	51	52	82	4.8%	0.99 [0.76, 1.29]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.3%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**4839**		**4191**	**53.3%**	**0.73 [0.62, 0.86]**
Total events	1456		1398			
Heterogeneity: Tau² = 0.06; Chi² = 64.33, df = 10 (P < 0.00001); I² = 84%						
Test for overall effect: Z = 3.72 (P = 0.0002)						
1.1.2 North America						
Bourgeois et al. (2010)_DST	59	148	23	50	3.7%	0.87 [0.60, 1.24]
Gerber et al. (2013)_A&F+ED	29	153	37	145	3.1%	0.74 [0.48, 1.14]
Gonzales et al. (2013)_DST (merged)	292	450	48	65	6.1%	0.88 [0.75, 1.03]
Linder et al. (2010)_A&F	56	121	69	145	4.9%	0.97 [0.75, 1.26]
Mainous et al. (2000)_merged	21	46	11	20	2.5%	0.83 [0.50, 1.38]
McIsaac & Goel (1998)_DST	51	184	75	212	4.4%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	5.0%	1.01 [0.78, 1.30]
McIsaac et al. (2021)_A&F+DST+ED	20	42	21	53	2.9%	1.20 [0.76, 1.90]
Meeker et al. (2014)_ED	162	449	246	505	6.2%	0.74 [0.64, 0.86]
Meeker et al. (2016)_merged	1449	8880	300	1252	6.7%	0.68 [0.61, 0.76]
Persell et al. (2016)_merged	41	754	5	136	1.0%	1.48 [0.60, 3.68]
Subtotal (95% CI)		**11529**		**2898**	**46.7%**	**0.84 [0.75, 0.94]**
Total events	2265		923			
Heterogeneity: Tau² = 0.02; Chi² = 20.93, df = 10 (P = 0.02); I² = 52%						
Test for overall effect: Z = 3.05 (P = 0.002)						
Total (95% CI)		**16368**		**7089**	**100.0%**	**0.79 [0.72, 0.87]**
Total events	3721		2321			
Heterogeneity: Tau² = 0.04; Chi² = 87.37, df = 21 (P < 0.00001); I² = 76%						
Test for overall effect: Z = 4.60 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.75, df = 1 (P = 0.19), I² = 42.9%						



Publication Year

When considering studies published up to and including 2010, relative to the subsequent decade, no significant differences were observed in the size of the intervention effect on prescribing rates. This suggests that the intervention effect holds over the respective periods of time, χ^2 (1) = 1.54, p = .22, I^2 = 34.9%.



Target Group

Subgroup analyses suggest that interventions targeting both the practitioner and patient (38% reduced prescribing; RR = 0.62, 95%CI [0.49, 0.79]) are more efficacious than those that just target the practitioner (16% reduced prescribing; RR = 0.84, 95%CI [0.75, 0.93]), χ^2 (1) = 5.00, p = .03, I^2 = 80%. Nonetheless, given the heterogeneity within the respective subgroups (practitioner: τ^2 = 0.04, I^2 = 78%; practitioner and patient: τ^2 = 0.04, I^2 = 59%) caution in the interpretation of findings is warranted.

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Practitioner						
Bourgeois et al. (2010)_DST	59	148	23	50	3.7%	0.87 [0.60, 1.24]
Cals et al. (2009)_merged	28	90	23	35	3.5%	0.47 [0.32, 0.70]
Ferrat et al. (2016)_ED	201	1434	359	2147	6.1%	0.84 [0.71, 0.98]
Gerber et al. (2013)_A&F+ED	29	153	37	145	3.1%	0.74 [0.48, 1.14]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	5.9%	0.91 [0.76, 1.08]
Gonzales et al. (2013)_DST (merged)	292	450	48	65	6.1%	0.88 [0.75, 1.03]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.2%	1.22 [0.96, 1.54]
Linder et al. (2010)_A&F	56	121	69	145	4.9%	0.97 [0.75, 1.26]
Little et al. (2013)_merged	642	1800	269	462	6.8%	0.61 [0.55, 0.68]
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McIsaac & Goel (1998)_DST	51	184	75	212	4.4%	0.78 [0.58, 1.05]
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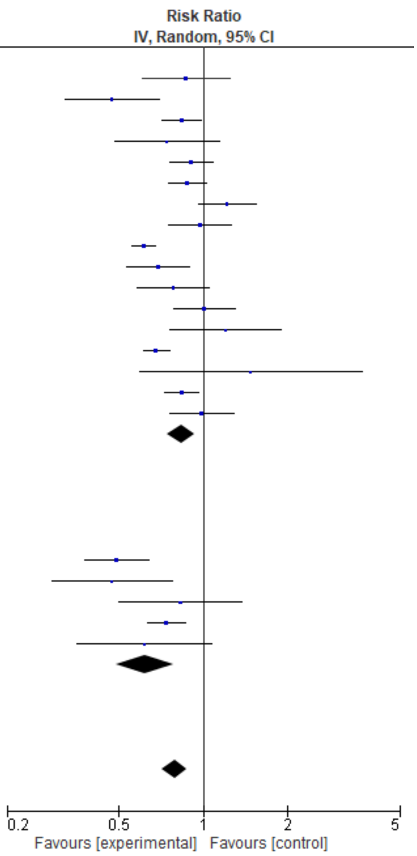
McIsaac et al. (2021)_A&F+DST+ED	20	42	21	53	2.9%	1.20 [0.76, 1.90]
Meeker et al. (2016)_merged	1449	8880	300	1252	6.7%	0.68 [0.61, 0.76]
Persell et al. (2016)_merged	41	754	5	136	1.0%	1.48 [0.60, 3.68]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	6.4%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	32	51	52	82	4.8%	0.99 [0.76, 1.29]
Subtotal (95% CI)		**15546**		**6217**	**81.4%**	**0.84 [0.75, 0.93]**
Total events	3455		1888			
Heterogeneity: Tau² = 0.04; Chi² = 71.55, df = 16 (P < 0.00001); I² = 78%						
Test for overall effect: Z = 3.19 (P = 0.001)						
1.1.2 Practitioner and patient						
Altiner et al. (2007)_CT+ED	51	175	116	196	4.9%	0.49 [0.38, 0.64]
Francis et al. (2009)_CT+ED	17	87	38	92	2.6%	0.47 [0.29, 0.77]
Mainous et al. (2000)_merged	21	46	11	20	2.5%	0.83 [0.50, 1.38]
Meeker et al. (2014)_ED	162	449	246	505	6.2%	0.74 [0.64, 0.86]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.3%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**822**		**872**	**18.6%**	**0.62 [0.49, 0.79]**
Total events	266		433			
Heterogeneity: Tau² = 0.04; Chi² = 9.74, df = 4 (P = 0.05); I² = 59%						
Test for overall effect: Z = 3.95 (P < 0.0001)						
Total (95% CI)		**16368**		**7089**	**100.0%**	**0.79 [0.72, 0.87]**
Total events	3721		2321			
Heterogeneity: Tau² = 0.04; Chi² = 87.37, df = 21 (P < 0.00001); I² = 76%						
Test for overall effect: Z = 4.60 (P < 0.00001)						
Test for subgroup differences: Chi² = 5.00, df = 1 (P = 0.03), I² = 80.0%						

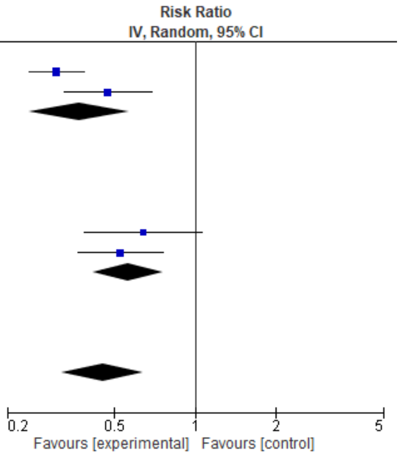


C.2 Consumption Subgroup Analysis

Geography

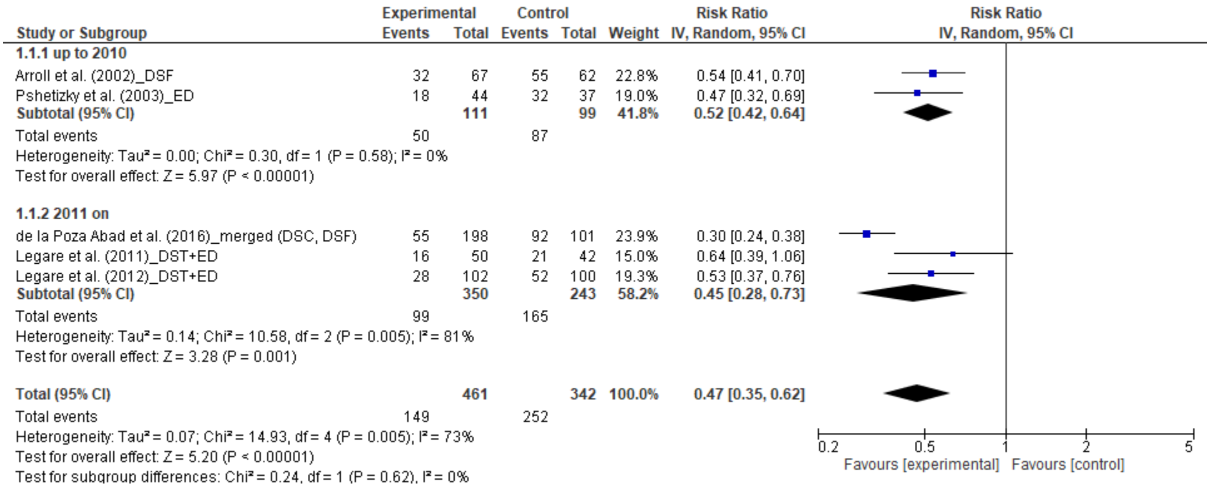
Irrespective of the study location (continent: Europe, North America), a behaviour change intervention was effective in reducing antimicrobial consumption, relative to a control, χ^2 (1) = 2.53, p = .11, I^2 = 60.5%.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Europe						
de la Poza Abad et al. (2016)_merged (DSC, DSF)	55	198	92	101	30.1%	0.30 [0.24, 0.38]
Pshetizky et al. (2003)_ED	18	44	32	37	24.7%	0.47 [0.32, 0.69]
Subtotal (95% CI)		**242**		**138**	**54.8%**	**0.37 [0.24, 0.57]**
Total events	73		124			
Heterogeneity: Tau² = 0.07; Chi² = 3.77, df = 1 (P = 0.05); I² = 73%						
Test for overall effect: Z = 4.56 (P < 0.00001)						
1.1.2 North America						
Legare et al. (2011)_DST+ED	16	50	21	42	20.1%	0.64 [0.39, 1.06]
Legare et al. (2012)_DST+ED	28	102	52	100	25.1%	0.53 [0.37, 0.76]
Subtotal (95% CI)		**152**		**142**	**45.2%**	**0.56 [0.42, 0.76]**
Total events	44		73			
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.55); I² = 0%						
Test for overall effect: Z = 3.78 (P = 0.0002)						
Total (95% CI)		**394**		**280**	**100.0%**	**0.45 [0.32, 0.64]**
Total events	117		197			
Heterogeneity: Tau² = 0.09; Chi² = 11.50, df = 3 (P = 0.009); I² = 74%						
Test for overall effect: Z = 4.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 2.53, df = 1 (P = 0.11), I² = 60.5%						



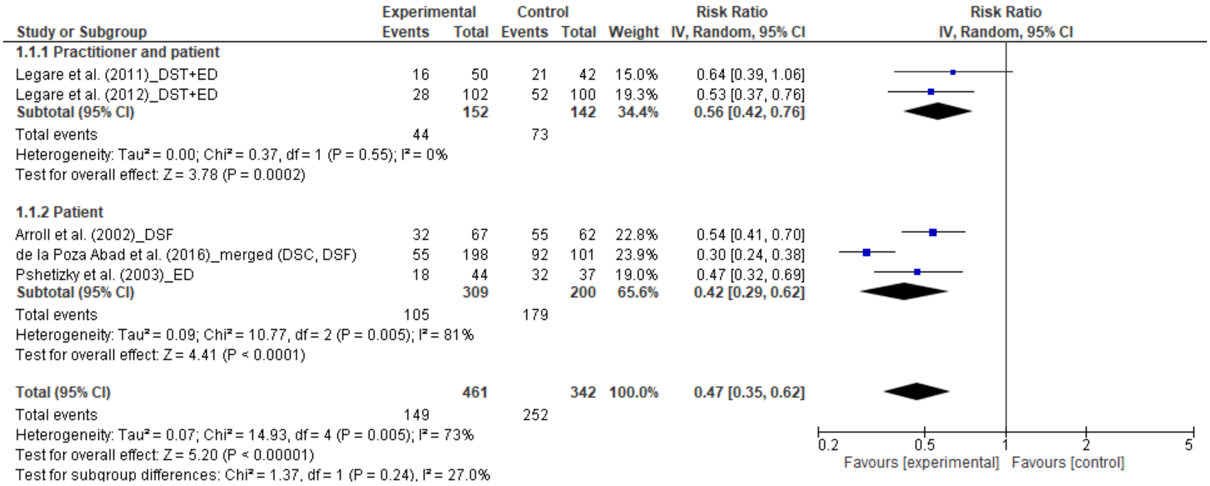
Publication Year

No publication year effects were observed on the efficacy of a behaviour change intervention to reduce antimicrobial consumption, relative to a control, χ^2 (1) = 0.24, p = .62, I2 = 0%.



Target Group

Intervention target (patient alone or in combination with the practitioner) did not influence the efficacy of a behaviour change intervention to reduce antimicrobial consumption, χ^2 (1) = 1.37, p = .24, I^2 = 27%.



D. Sensitivity Analyses for Antimicrobial Prescribing

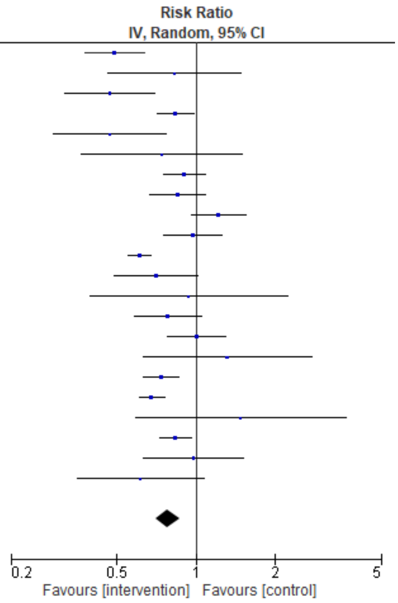
Due to the inclusion of cluster randomised controlled trials in the meta-analysis, the size of the trial was reduced to it's 'effective sample size', whereby the original sample size per trial arm is divided by the design effect, 1 + (M – 1) x ICC. Where reported in a study, the study-specific intraclass correlation coefficient (ICC) was used in calculations of the effect size. Elsewhere, an estimate of 0.06 was inputted based on Adams et al. (2004). In order to explore how this estimate may have impacted the findings, sensitivity analyses were conducted whereby the effect sizes generated from cluster randomised controlled trials were recalculated assuming an ICC = 0.16 unless otherwise reported in the study. This is informed by the high-quality cluster RCT conducted by Little et al., (2013), where an ICC=0.16 was used for sample size calculations, determined by the mean ICC for prescribing at practice level across three trials (Cals et al., 2009; Coenen et al., 2004; Welschen et al., 2004; ICC at practice level = 0.12, 0.17, and 0.18 respectively).

Results from the sensitivity analyses indicated that all findings for the prescription outcome remained consistent.

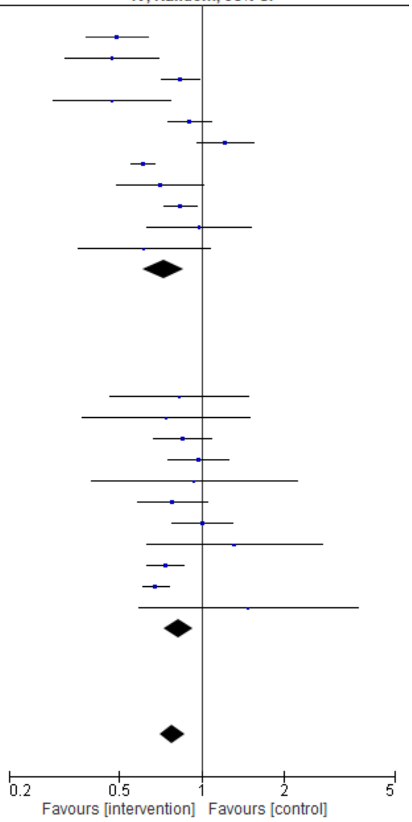
	Intervention		Control			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**IV, Random, 95% CI**
Altiner et al. (2007)_CT+ED	51	175	116	196	5.4%	0.49 [0.38, 0.64]
Bourgeois et al. (2010)_DST	22	56	9	19	2.4%	0.83 [0.47, 1.47]
Cals et al. (2009)_merged	28	90	23	35	3.8%	0.47 [0.32, 0.70]
Ferrat et al. (2016)_ED	201	1434	359	2147	6.8%	0.84 [0.71, 0.98]
Francis et al. (2009)_CT+ED	17	87	38	92	2.9%	0.47 [0.29, 0.77]
Gerber et al. (2013)_A&F+ED	11	58	14	55	1.8%	0.75 [0.37, 1.50]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	6.5%	0.91 [0.76, 1.08]
Gonzales et al. (2013)_merged (DST print, comp.)	114	176	19	25	5.6%	0.85 [0.67, 1.09]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.7%	1.22 [0.96, 1.54]
Linder et al. (2010)_A&F	56	121	69	145	5.5%	0.97 [0.75, 1.26]
Little et al. (2013)_merged	642	1800	269	462	7.5%	0.61 [0.55, 0.68]
Llor et al. (2011)_POC	24	54	32	51	4.1%	0.71 [0.49, 1.02]
Mainous et al. (2000)_merged	8	17	4	8	1.3%	0.94 [0.40, 2.22]
McIsaac & Goel (1998)_DST	51	184	75	212	4.9%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	5.5%	1.01 [0.78, 1.30]
McIsaac et al. (2021)_A&F+DST+ED	8	16	8	21	1.6%	1.31 [0.63, 2.73]
Meeker et al. (2014)_ED	162	449	246	505	6.9%	0.74 [0.64, 0.86]
Meeker et al. (2016)_merged	1449	8880	300	1252	7.4%	0.68 [0.61, 0.76]
Persell et al. (2016)_merged	41	754	5	136	1.1%	1.48 [0.60, 3.68]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	7.1%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	12	19	20	31	3.4%	0.98 [0.64, 1.51]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.5%	0.62 [0.36, 1.08]
Total (95% CI)		**15765**		**6782**	**100.0%**	**0.78 [0.70, 0.87]**
Total events	3419		2170			

Heterogeneity: Tau² = 0.04; Chi² = 79.76, df = 21 (P < 0.00001); I² = 74%

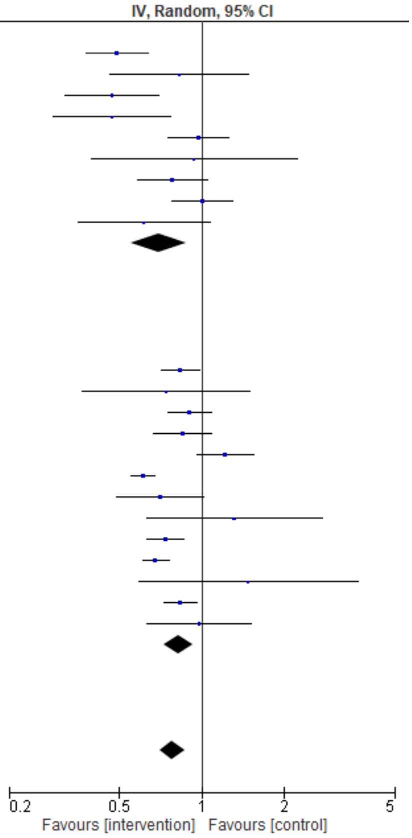
Test for overall effect: Z = 4.57 (P < 0.00001)



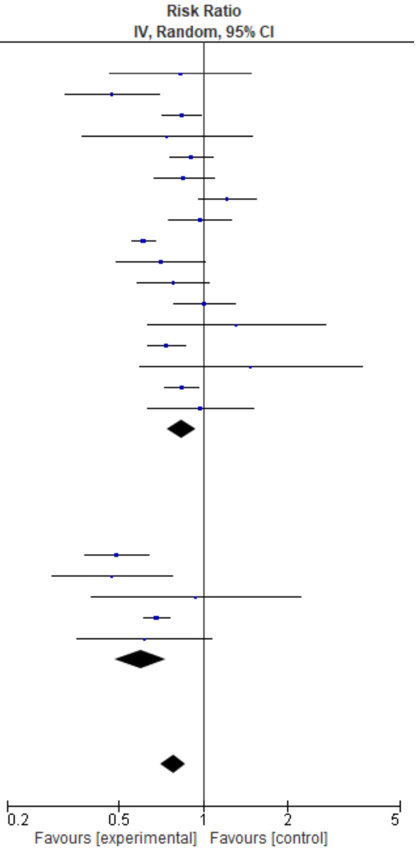
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Europe						
Altiner et al. (2007)_CT+ED	51	175	116	196	5.4%	0.49 [0.38, 0.64]
Cals et al. (2009)_merged	28	90	23	35	3.8%	0.47 [0.32, 0.70]
Ferrat et al. (2016)_ED	201	1434	359	2147	6.8%	0.84 [0.71, 0.98]
Francis et al. (2009)_CT+ED	17	87	38	92	2.9%	0.47 [0.29, 0.77]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	6.5%	0.91 [0.76, 1.08]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.7%	1.22 [0.96, 1.54]
Little et al. (2013)_merged	642	1800	269	462	7.5%	0.61 [0.55, 0.68]
Llor et al. (2011)_POC	24	54	32	51	4.1%	0.71 [0.49, 1.02]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	7.1%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	12	19	20	31	3.4%	0.98 [0.64, 1.51]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.5%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**4752**		**4089**	**56.0%**	**0.73 [0.62, 0.86]**
Total events	1412		1333			
Heterogeneity: Tau² = 0.06; Chi² = 61.13, df = 10 (P < 0.00001); I² = 84%						
Test for overall effect: Z = 3.69 (P = 0.0002)						
1.1.2 North America						
Bourgeois et al. (2010)_DST	22	56	9	19	2.4%	0.83 [0.47, 1.47]
Gerber et al. (2013)_A&F+ED	11	58	14	55	1.8%	0.75 [0.37, 1.50]
Gonzales et al. (2013)_DST (merged)	114	176	19	25	5.6%	0.85 [0.67, 1.09]
Linder et al. (2010)_A&F	56	121	69	145	5.5%	0.97 [0.75, 1.26]
Mainous et al. (2000)_merged	8	17	4	8	1.3%	0.94 [0.40, 2.22]
McIsaac & Goel (1998)_DST	51	184	75	212	4.9%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	5.5%	1.01 [0.78, 1.30]
McIsaac et al. (2021)_A&F+DST+ED	8	16	8	21	1.6%	1.31 [0.63, 2.73]
Meeker et al. (2014)_ED	162	449	246	505	6.9%	0.74 [0.64, 0.86]
Meeker et al. (2016)_merged	1449	8880	300	1252	7.4%	0.68 [0.61, 0.76]
Persell et al. (2016)_merged	41	754	5	136	1.1%	1.48 [0.60, 3.68]
Subtotal (95% CI)		**11013**		**2693**	**44.0%**	**0.83 [0.73, 0.93]**
Total events	2007		837			
Heterogeneity: Tau² = 0.01; Chi² = 17.58, df = 10 (P = 0.06); I² = 43%						
Test for overall effect: Z = 3.15 (P = 0.002)						
Total (95% CI)		**15765**		**6782**	**100.0%**	**0.78 [0.70, 0.87]**
Total events	3419		2170			
Heterogeneity: Tau² = 0.04; Chi² = 79.76, df = 21 (P < 0.00001); I² = 74%						
Test for overall effect: Z = 4.57 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.42, df = 1 (P = 0.23), I² = 29.5%						



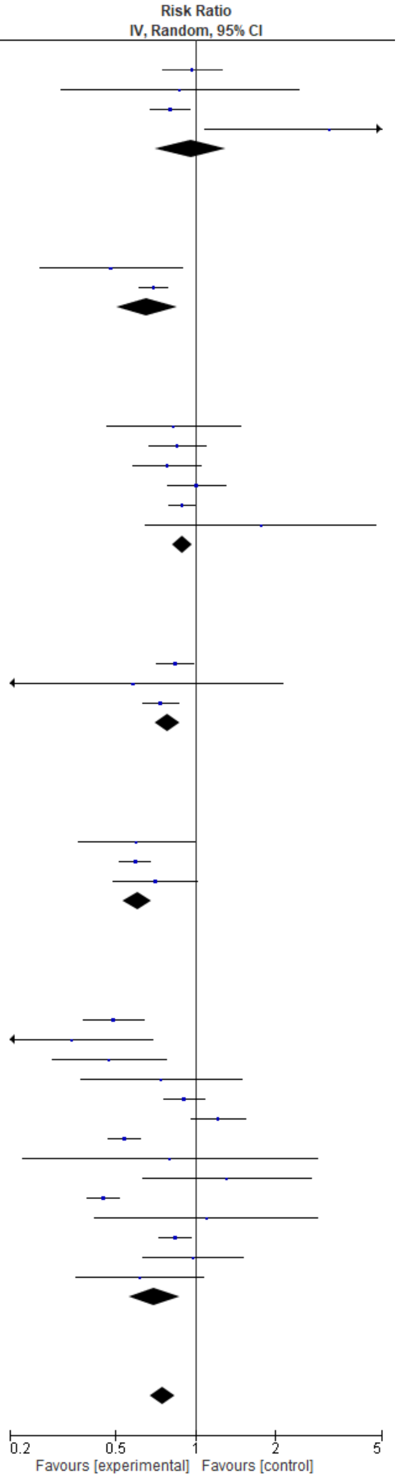
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 up to 2010						
Altiner et al. (2007)_CT+ED	51	175	116	196	5.4%	0.49 [0.38, 0.64]
Bourgeois et al. (2010)_DST	22	56	9	19	2.4%	0.83 [0.47, 1.47]
Cals et al. (2009)_merged	28	90	23	35	3.8%	0.47 [0.32, 0.70]
Francis et al. (2009)_CT+ED	17	87	38	92	2.9%	0.47 [0.29, 0.77]
Linder et al. (2010)_A&F	56	121	69	145	5.5%	0.97 [0.75, 1.26]
Mainous et al. (2000)_merged	8	17	4	8	1.3%	0.94 [0.40, 2.22]
McIsaac & Goel (1998)_DST	51	184	75	212	4.9%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	5.5%	1.01 [0.78, 1.30]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.5%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**1097**		**1081**	**34.2%**	**0.70 [0.55, 0.89]**
Total events	333		444			
Heterogeneity: Tau² = 0.09; Chi² = 28.76, df = 8 (P = 0.0003); I² = 72%						
Test for overall effect: Z = 2.97 (P = 0.003)						
1.1.2 2011 on						
Ferrat et al. (2016)_ED	201	1434	359	2147	6.8%	0.84 [0.71, 0.98]
Gerber et al. (2013)_A&F+ED	11	58	14	55	1.8%	0.75 [0.37, 1.50]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	6.5%	0.91 [0.76, 1.08]
Gonzales et al. (2013)_DST (merged)	114	176	19	25	5.6%	0.85 [0.67, 1.09]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.7%	1.22 [0.96, 1.54]
Little et al. (2013)_merged	642	1800	269	462	7.5%	0.61 [0.55, 0.68]
Llor et al. (2011)_POC	24	54	32	51	4.1%	0.71 [0.49, 1.02]
McIsaac et al. (2021)_A&F+DST+ED	8	16	8	21	1.6%	1.31 [0.63, 2.73]
Meeker et al. (2014)_ED	162	449	246	505	6.9%	0.74 [0.64, 0.86]
Meeker et al. (2016)_merged	1449	8880	300	1252	7.4%	0.68 [0.61, 0.76]
Persell et al. (2016)_merged	41	754	5	136	1.1%	1.48 [0.60, 3.68]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	7.1%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	12	19	20	31	3.4%	0.98 [0.64, 1.51]
Subtotal (95% CI)		**14668**		**5701**	**65.8%**	**0.82 [0.73, 0.93]**
Total events	3086		1726			
Heterogeneity: Tau² = 0.03; Chi² = 50.77, df = 12 (P < 0.00001); I² = 76%						
Test for overall effect: Z = 3.19 (P = 0.001)						
Total (95% CI)		**15765**		**6782**	**100.0%**	**0.78 [0.70, 0.87]**
Total events	3419		2170			
Heterogeneity: Tau² = 0.04; Chi² = 79.76, df = 21 (P < 0.00001); I² = 74%						
Test for overall effect: Z = 4.57 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.42, df = 1 (P = 0.23), I² = 29.7%						



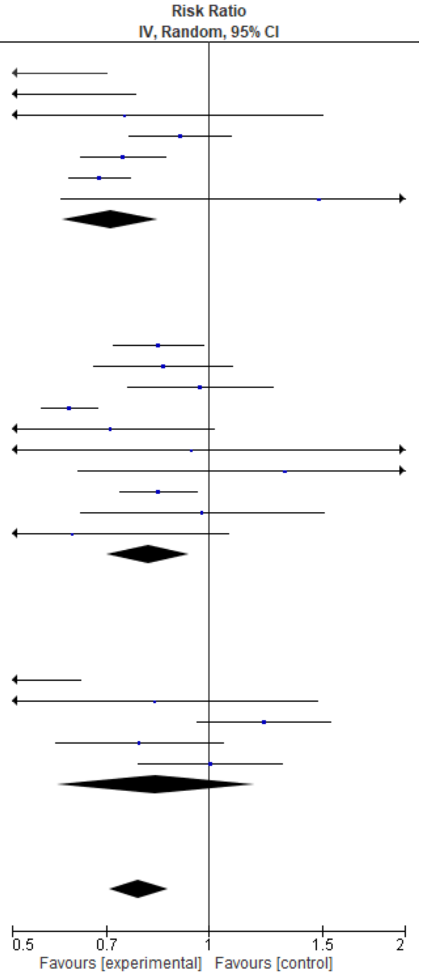
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Patient						
Bourgeois et al. (2010)_DST	22	56	9	19	2.4%	0.83 [0.47, 1.47]
Cals et al. (2009)_merged	28	90	23	35	3.8%	0.47 [0.32, 0.70]
Ferrat et al. (2016)_ED	201	1434	359	2147	6.8%	0.84 [0.71, 0.98]
Gerber et al. (2013)_A&F+ED	11	58	14	55	1.8%	0.75 [0.37, 1.50]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	6.5%	0.91 [0.76, 1.08]
Gonzales et al. (2013)_DST (merged)	114	176	19	25	5.6%	0.85 [0.67, 1.09]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.7%	1.22 [0.96, 1.54]
Linder et al. (2010)_A&F	56	121	69	145	5.5%	0.97 [0.75, 1.26]
Little et al. (2013)_merged	642	1800	269	462	7.5%	0.61 [0.55, 0.68]
Llor et al. (2011)_POC	24	54	32	51	4.1%	0.71 [0.49, 1.02]
McIsaac & Goel (1998)_DST	51	184	75	212	4.9%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	5.5%	1.01 [0.78, 1.30]
McIsaac et al. (2021)_A&F+DST+ED	8	16	8	21	1.6%	1.31 [0.63, 2.73]
Meeker et al. (2014)_ED	162	449	246	505	6.9%	0.74 [0.64, 0.86]
Persell et al. (2016)_merged	41	754	5	136	1.1%	1.48 [0.60, 3.68]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	7.1%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	12	19	20	31	3.4%	0.98 [0.64, 1.51]
Subtotal (95% CI)		**6541**		**5175**	**80.4%**	**0.84 [0.74, 0.94]**
Total events	1879		1690			
Heterogeneity: Tau² = 0.04; Chi² = 60.18, df = 16 (P < 0.00001); I² = 73%						
Test for overall effect: Z = 2.99 (P = 0.003)						
1.1.2 Patient and practitioner						
Altiner et al. (2007)_CT+ED	51	175	116	196	5.4%	0.49 [0.38, 0.64]
Francis et al. (2009)_CT+ED	17	87	38	92	2.9%	0.47 [0.29, 0.77]
Mainous et al. (2000)_merged	8	17	4	8	1.3%	0.94 [0.40, 2.22]
Meeker et al. (2016)_merged	1449	8880	300	1252	7.4%	0.68 [0.61, 0.76]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.5%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**9224**		**1607**	**19.6%**	**0.60 [0.49, 0.73]**
Total events	1540		480			
Heterogeneity: Tau² = 0.02; Chi² = 7.43, df = 4 (P = 0.12); I² = 46%						
Test for overall effect: Z = 4.90 (P < 0.00001)						
Total (95% CI)		**15765**		**6782**	**100.0%**	**0.78 [0.70, 0.87]**
Total events	3419		2170			
Heterogeneity: Tau² = 0.04; Chi² = 79.76, df = 21 (P < 0.00001); I² = 74%						
Test for overall effect: Z = 4.57 (P < 0.00001)						
Test for subgroup differences: Chi² = 7.73, df = 1 (P = 0.005), I² = 87.1%						



Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Audit and Feedback						
Linder et al. (2010)_A&F	56	121	69	145	4.1%	0.97 [0.75, 1.26]
Mainous et al. (2000)_A&F	3	6	4	7	0.9%	0.88 [0.31, 2.44]
Meeker et al. (2016)_A&F	175	910	282	1177	4.7%	0.80 [0.68, 0.95]
Persell et al. (2016)_A&F	8	68	5	136	0.9%	3.20 [1.09, 9.41]
Subtotal (95% CI)		**1105**		**1465**	**10.5%**	**0.96 [0.71, 1.30]**
Total events	242		360			
Heterogeneity: Tau² = 0.05; Chi² = 7.21, df = 3 (P = 0.07); I² = 58%						
Test for overall effect: Z = 0.26 (P = 0.79)						
1.1.2 Communication training						
Cals et al. (2009)_CT	8	25	24	36	2.0%	0.48 [0.26, 0.89]
Little et al. (2013)_CT	251	618	268	459	4.9%	0.70 [0.62, 0.79]
Subtotal (95% CI)		**643**		**495**	**6.9%**	**0.66 [0.50, 0.85]**
Total events	259		292			
Heterogeneity: Tau² = 0.02; Chi² = 1.34, df = 1 (P = 0.25); I² = 25%						
Test for overall effect: Z = 3.13 (P = 0.002)						
1.1.3 Decision support tool						
Bourgeois et al. (2010)_DST	22	56	9	19	2.1%	0.83 [0.47, 1.47]
Gonzales et al. (2013)_DST (merged)	114	176	19	25	4.1%	0.85 [0.67, 1.09]
McIsaac & Goel (1998)_DST	51	184	75	212	3.8%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	4.1%	1.01 [0.78, 1.30]
Meeker et al. (2016)_DST (merged)	860	4029	311	1299	5.0%	0.89 [0.80, 1.00]
Persell et al. (2016)_DST (merged)	14	216	5	136	1.0%	1.76 [0.65, 4.78]
Subtotal (95% CI)		**4963**		**2006**	**20.1%**	**0.89 [0.82, 0.98]**
Total events	1146		507			
Heterogeneity: Tau² = 0.00; Chi² = 3.61, df = 5 (P = 0.61); I² = 0%						
Test for overall effect: Z = 2.49 (P = 0.01)						
1.1.4 Education						
Ferrat et al. (2016)_ED	201	1434	359	2147	4.7%	0.84 [0.71, 0.98]
Mainous et al. (2000)_ED	2	6	4	7	0.6%	0.58 [0.16, 2.14]
Meeker et al. (2014)_ED	162	449	246	505	4.8%	0.74 [0.64, 0.86]
Subtotal (95% CI)		**1889**		**2659**	**10.1%**	**0.78 [0.70, 0.87]**
Total events	365		609			
Heterogeneity: Tau² = 0.00; Chi² = 1.41, df = 2 (P = 0.49); I² = 0%						
Test for overall effect: Z = 4.35 (P < 0.0001)						
1.1.5 Point of care testing						
Cals et al. (2009)_POC	12	30	22	33	2.5%	0.60 [0.36, 0.99]
Little et al. (2013)_POC	202	583	279	478	4.9%	0.59 [0.52, 0.68]
Llor et al. (2011)_POC	24	54	32	51	3.3%	0.71 [0.49, 1.02]
Subtotal (95% CI)		**667**		**562**	**10.7%**	**0.61 [0.54, 0.68]**
Total events	238		333			
Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 2 (P = 0.67); I² = 0%						
Test for overall effect: Z = 8.01 (P < 0.00001)						
1.1.6 Multiple						
Altiner et al. (2007)_CT+ED	51	175	116	196	4.1%	0.49 [0.38, 0.64]
Cals et al. (2009)_CT+POC	7	31	21	32	1.7%	0.34 [0.17, 0.69]
Francis et al. (2009)_CT+ED	17	87	38	92	2.6%	0.47 [0.29, 0.77]
Gerber et al. (2013)_A&F+ED	11	58	14	55	1.7%	0.75 [0.37, 1.50]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	4.6%	0.91 [0.76, 1.08]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	4.2%	1.22 [0.96, 1.54]
Little et al. (2013)_CT+POC	200	634	277	475	4.8%	0.54 [0.47, 0.62]
Mainous et al. (2000)_A&F+ED	2	5	4	8	0.6%	0.80 [0.22, 2.87]
McIsaac et al. (2021)_A&F+DST+ED	8	16	8	21	1.6%	1.31 [0.63, 2.73]
Meeker et al. (2016)_A&F+DST (merged)	417	3864	288	1200	4.9%	0.45 [0.39, 0.51]
Persell et al. (2016)_A&F+DST(account.just+altern)	19	470	5	136	1.0%	1.10 [0.42, 2.89]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	4.9%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	12	19	20	31	2.9%	0.98 [0.64, 1.51]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.2%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**6452**		**3321**	**41.7%**	**0.70 [0.56, 0.87]**
Total events	1181		1267			
Heterogeneity: Tau² = 0.12; Chi² = 106.28, df = 13 (P < 0.00001); I² = 88%						
Test for overall effect: Z = 3.20 (P = 0.001)						
Total (95% CI)		**15719**		**10508**	**100.0%**	**0.75 [0.68, 0.84]**
Total events	3431		3368			
Heterogeneity: Tau² = 0.06; Chi² = 167.90, df = 31 (P < 0.00001); I² = 82%						
Test for overall effect: Z = 5.04 (P < 0.00001)						
Test for subgroup differences: Chi² = 29.37, df = 5 (P < 0.0001), I² = 83.0%						



Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Low						
Cals et al. (2009)_merged	28	90	23	35	3.8%	0.47 [0.32, 0.70]
Francis et al. (2009)_CT+ED	17	87	38	92	2.9%	0.47 [0.29, 0.77]
Gerber et al. (2013)_A&F+ED	11	58	14	55	1.8%	0.75 [0.37, 1.50]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	6.5%	0.91 [0.76, 1.08]
Meeker et al. (2014)_ED	162	449	246	505	6.9%	0.74 [0.64, 0.86]
Meeker et al. (2016)_merged	1449	8880	300	1252	7.4%	0.68 [0.61, 0.76]
Persell et al. (2016)_merged	41	754	5	136	1.1%	1.48 [0.60, 3.68]
Subtotal (95% CI)		**10792**		**2547**	**30.6%**	**0.71 [0.60, 0.84]**
Total events	1859		792			
Heterogeneity: Tau² = 0.03; Chi² = 17.06, df = 6 (P = 0.009); I² = 65%						
Test for overall effect: Z = 4.01 (P < 0.0001)						
1.1.2 Some concerns						
Ferrat et al. (2016)_ED	201	1434	359	2147	6.8%	0.84 [0.71, 0.98]
Gonzales et al. (2013)_DST (merged)	114	176	19	25	5.6%	0.85 [0.67, 1.09]
Linder et al. (2010)_A&F	56	121	69	145	5.5%	0.97 [0.75, 1.26]
Little et al. (2013)_merged	642	1800	269	462	7.5%	0.61 [0.55, 0.68]
Llor et al. (2011)_POC	24	54	32	51	4.1%	0.71 [0.49, 1.02]
Mainous et al. (2000)_merged	8	17	4	8	1.3%	0.94 [0.40, 2.22]
McIsaac et al. (2021)_A&F+DST+ED	8	16	8	21	1.6%	1.31 [0.63, 2.73]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	7.1%	0.84 [0.73, 0.96]
Vervloet et al. (2015)_A&F+CT+DST	12	19	20	31	3.4%	0.98 [0.64, 1.51]
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.5%	0.62 [0.36, 1.08]
Subtotal (95% CI)		**4076**		**3339**	**45.5%**	**0.81 [0.70, 0.94]**
Total events	1260		1026			
Heterogeneity: Tau² = 0.03; Chi² = 29.89, df = 9 (P = 0.0005); I² = 70%						
Test for overall effect: Z = 2.85 (P = 0.004)						
1.1.3 High						
Altiner et al. (2007)_CT+ED	51	175	116	196	5.4%	0.49 [0.38, 0.64]
Bourgeois et al. (2010)_DST	22	56	9	19	2.4%	0.83 [0.47, 1.47]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.7%	1.22 [0.96, 1.54]
McIsaac & Goel (1998)_DST	51	184	75	212	4.9%	0.78 [0.58, 1.05]
McIsaac et al. (2002)_DST	85	302	88	315	5.5%	1.01 [0.78, 1.30]
Subtotal (95% CI)		**897**		**896**	**24.0%**	**0.83 [0.59, 1.18]**
Total events	300		352			
Heterogeneity: Tau² = 0.13; Chi² = 27.97, df = 4 (P < 0.0001); I² = 86%						
Test for overall effect: Z = 1.04 (P = 0.30)						
Total (95% CI)		**15765**		**6782**	**100.0%**	**0.78 [0.70, 0.87]**
Total events	3419		2170			
Heterogeneity: Tau² = 0.04; Chi² = 79.76, df = 21 (P < 0.00001); I² = 74%						
Test for overall effect: Z = 4.57 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.56, df = 2 (P = 0.46), I² = 0%						



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Welschen, I., Kuyvenhoven, M. M., Hoes, A. W., & Verheij, T. J. (2004). Effectiveness of a multiple intervention to reduce antibiotic prescribing for respiratory tract symptoms in primary care: randomised controlled trial. *BMJ*, 329(7463), 431. https://doi.org/10.1136/bmj.38182.591238.EB

E. Risk of Bias Assessment

E.1 Overview

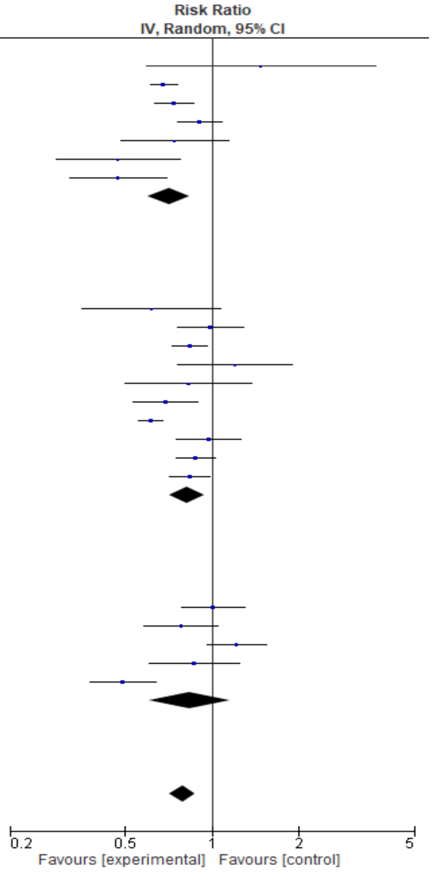
Estimates of the effect of an intervention on prescribing and on consumption by risk of bias are presented in the next two sub-sections. This is followed by risk of bias traffic light pots for each study.

E.2 Prescribing

Subgroup analyses suggest that the intervention effect on prescribing rates does not significantly differ depending on the risk of bias assessment, χ^2 (2) = 1.99, p = .37, I^2 = 0%. Studies assessed as low overall risk and of some concern show that behaviour change initiatives reduce antibiotic prescribing by 18% and 29%, respectively, relative to control (RR = 0.71, 95% CI[0.60, 0.84], Z = 4.13, p < .001, τ^2 = .02, I^2 = 65%; RR = 0.82, 95% CI[0.71, 0.94], Z = 2.80, p = .005, τ^2 = .03, I^2 = 76%). On average, studies assessed as high risk of bias did not show a significant intervention effect, relative to control, RR = 0.84, 95% CI [0.60, 1.16], Z =1.06, p = .29, τ^2 = .12, I^2 = 86% albeit caution is required as non-significant subgroup findings suggested that study bias alone could not explain the variance in effects across studies.

Effect of intervention on prescribing rates by risk of bias assessment

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Low						
Persell et al. (2016)_merged	41	754	5	136	1.0%	1.48 [0.60, 3.68]
Meeker et al. (2016)_merged	1449	8880	300	1252	6.7%	0.68 [0.61, 0.76]
Meeker et al. (2014)_ED	162	449	246	505	6.2%	0.74 [0.64, 0.86]
Gjelstad et al. (2013)_A&F+ED	151	474	166	472	5.9%	0.91 [0.76, 1.08]
Gerber et al. (2013)_A&F+ED	29	153	37	145	3.1%	0.74 [0.48, 1.14]
Francis et al. (2009)_CT+ED	17	87	38	92	2.6%	0.47 [0.29, 0.77]
Cals et al. (2009)_merged	28	90	23	35	3.5%	0.47 [0.32, 0.70]
Subtotal (95% CI)		**10887**		**2637**	**29.0%**	**0.71 [0.60, 0.84]**
Total events	1877		815			
Heterogeneity: Tau² = 0.02; Chi² = 17.07, df = 6 (P = 0.009); I² = 65%						
Test for overall effect: Z = 4.13 (P < 0.0001)						
1.1.2 Some concerns						
Welschen et al. (2004)_A&F+ED	15	65	22	59	2.3%	0.62 [0.36, 1.08]
Vervloet et al. (2015)_A&F+CT+DST	32	51	52	82	4.8%	0.99 [0.76, 1.29]
Regev-Yochay et al. (2011)_A&F+CT+ED	180	374	224	390	6.4%	0.84 [0.73, 0.96]
McIsaac et al. (2021)_A&F+DST+ED	20	42	21	53	2.9%	1.20 [0.76, 1.90]
Mainous et al. (2000)_merged	21	46	11	20	2.5%	0.83 [0.50, 1.38]
Llor et al. (2011)_POC	48	109	65	102	4.9%	0.69 [0.53, 0.89]
Little et al. (2013)_merged	642	1800	269	462	6.8%	0.61 [0.55, 0.68]
Linder et al. (2010)_A&F	56	121	69	145	4.9%	0.97 [0.75, 1.26]
Gonzales et al. (2013)_DST (merged)	292	450	48	65	6.1%	0.88 [0.75, 1.03]
Ferrat et al. (2016)_ED	201	1434	359	2147	6.1%	0.84 [0.71, 0.98]
Subtotal (95% CI)		**4492**		**3525**	**47.7%**	**0.82 [0.71, 0.94]**
Total events	1507		1140			
Heterogeneity: Tau² = 0.03; Chi² = 37.07, df = 9 (P < 0.0001); I² = 76%						
Test for overall effect: Z = 2.80 (P = 0.005)						
1.1.3 High						
McIsaac et al. (2002)_DST	85	302	88	315	5.0%	1.01 [0.78, 1.30]
McIsaac & Goel (1998)_DST	51	184	75	212	4.4%	0.78 [0.58, 1.05]
Hurlimann et al. (2014)_A&F+ED (merged)	91	180	64	154	5.2%	1.22 [0.96, 1.54]
Bourgeois et al. (2010)_DST	59	148	23	50	3.7%	0.87 [0.60, 1.24]
Altiner et al. (2007)_CT+ED	51	175	116	196	4.9%	0.49 [0.38, 0.64]
Subtotal (95% CI)		**989**		**927**	**23.2%**	**0.84 [0.60, 1.16]**
Total events	337		366			
Heterogeneity: Tau² = 0.12; Chi² = 27.98, df = 4 (P < 0.0001); I² = 86%						
Test for overall effect: Z = 1.06 (P = 0.29)						
Total (95% CI)		**16368**		**7089**	**100.0%**	**0.79 [0.72, 0.87]**
Total events	3721		2321			
Heterogeneity: Tau² = 0.04; Chi² = 87.37, df = 21 (P < 0.00001); I² = 76%						
Test for overall effect: Z = 4.60 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.99, df = 2 (P = 0.37), I² = 0%						

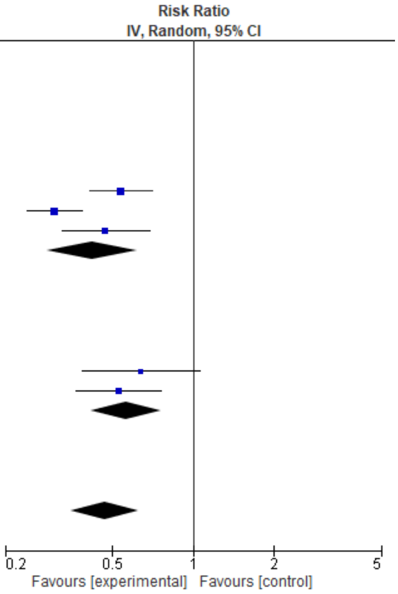


E.3 Consumption

Irrespective of studies assessed as overall at some concern or at high risk of bias, findings suggested that the intervention effect on rates of antimicrobial consumption were consistent accounting for a 38% and 44% reduction, respectively (RR = 0.42, 95% CI[0.29, 0.62], Z = 4.41, p <.001, τ^2 = .09, I^2 = 81%; RR = 0.56, 95% CI[0.42, 0.76], Z = 3.78, p < .001, τ^2 = .00, I^2 = 0%).

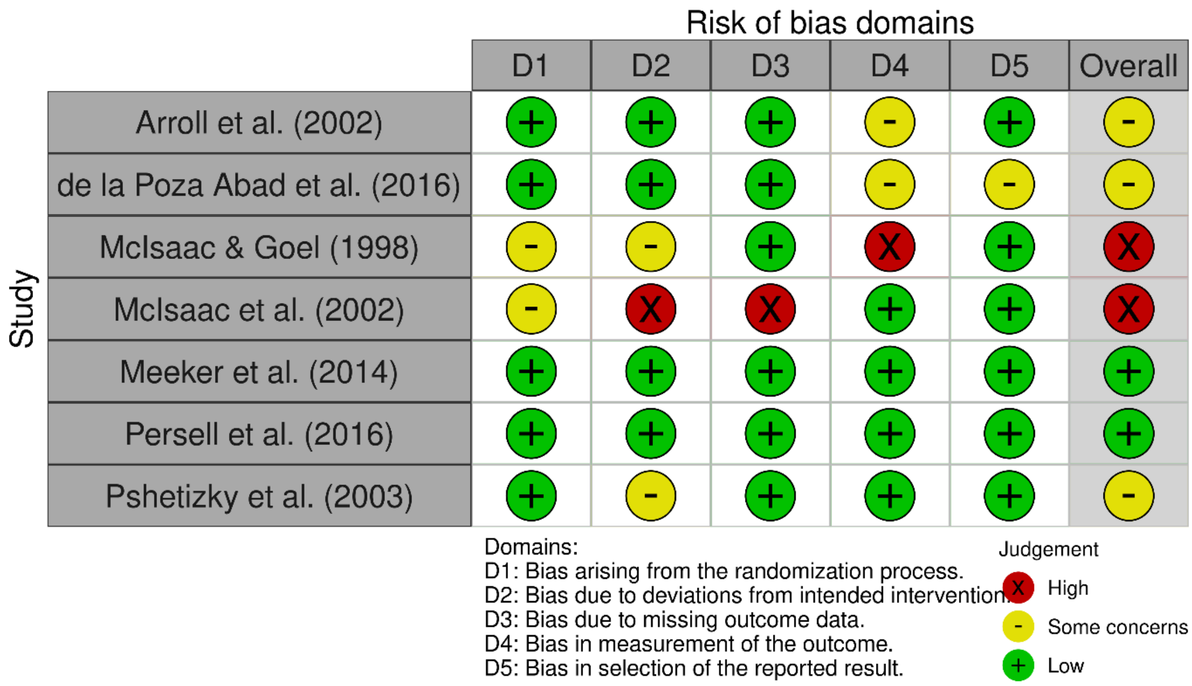
Effect of intervention on antimicrobial consumption rates by risk of bias assessment

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Low						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.1.2 Some concerns						
Arroll et al. (2002)_DSF	32	67	55	62	22.8%	0.54 [0.41, 0.70]
de la Poza Abad et al. (2016)_merged (DSC, DSF)	55	198	92	101	23.9%	0.30 [0.24, 0.38]
Pshetizky et al. (2003)_ED	18	44	32	37	19.0%	0.47 [0.32, 0.69]
Subtotal (95% CI)		**309**		**200**	**65.6%**	**0.42 [0.29, 0.62]**
Total events	105		179			
Heterogeneity: Tau² = 0.09; Chi² = 10.77, df = 2 (P = 0.005); I² = 81%						
Test for overall effect: Z = 4.41 (P < 0.0001)						
1.1.3 High						
Legare et al. (2011)_DST+ED	16	50	21	42	15.0%	0.64 [0.39, 1.06]
Legare et al. (2012)_DST+ED	28	102	52	100	19.3%	0.53 [0.37, 0.76]
Subtotal (95% CI)		**152**		**142**	**34.4%**	**0.56 [0.42, 0.76]**
Total events	44		73			
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.55); I² = 0%						
Test for overall effect: Z = 3.78 (P = 0.0002)						
Total (95% CI)		**461**		**342**	**100.0%**	**0.47 [0.35, 0.62]**
Total events	149		252			
Heterogeneity: Tau² = 0.07; Chi² = 14.93, df = 4 (P = 0.005); I² = 73%						
Test for overall effect: Z = 5.20 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.37, df = 1 (P = 0.24), I² = 27.0%						



E.4 Risk of Bias (2.0) Traffic Light Plots

E.4.1 Randomised Controlled Trials



E.4.2 Cluster Randomised Controlled Trials

Risk of bias domains

Study	D1	D1b	D2	D3	D4	D5	Overall
Altiner et al. (2007)	-	X	+	-	-	+	X
Bourgeouis et al. (2010)	-	+	X	+	+	+	X
Briel et al. (2006)	+	-	-	+	+	+	-
Cals et al. (2009)	+	+	+	+	+	+	+
Ferrat et al. (2016)	+	+	+	-	+	+	-
Francis et al. (2009)	+	+	+	+	+	+	+
Gerber et al. (2013)	+	+	+	+	+	+	+
Gjelstad et al. (2013)	+	+	+	+	+	+	+
Gonzales et al. (2013)	-	+	+	+	+	+	-
Hoye et al. (2013)	X	+	+	X	+	+	X
Hurlimann et al. (2015)	+	+	X	+	+	+	X
Legare et al. (2011)	+	+	X	+	X	-	X
Legare et al. (2012)	+	-	X	-	X	-	X
Linder et al. (2010)	-	+	-	+	+	+	-
Little et al. (2013)	+	+	+	+	-	+	-
Llor et al. (2011)	+	+	-	+	-	+	-
Mainous et al. (2000)	-	+	-	-	-	+	-
McIsaac et al. (2021)	-	+	-	+	+	+	-
Meeker et al. (2016)	+	+	+	+	+	+	+
Regev-Yochay et al. (2011)	-	+	+	+	+	+	-
Vervloet et al. (2016)	-	+	-	+	+	+	-
Welschen et al. (2004)	-	+	+	+	+	+	-

Domains:
D1 : Bias arising from the randomization process.
D1b: Bias arising from the timing of identification and recruitment of Individual participants in relation to timing of randomization.
D2 : Bias due to deviations from intended intervention.
D3 : Bias due to missing outcome data.
D4 : Bias in measurement of the outcome.
D5 : Bias in selection of the reported result.

Judgement
X High
- Some concerns
+ Low

F. Primary Studies' Conclusions on Intervention Effectiveness

Studies	Intervention Category	Did it Work?	Authors Comment
Altiner et al, 2007	CT + ED	Yes	An interventional strategy that focused on doctor–patient communication and patient empowerment is an effective concept to reduce antibiotic prescriptions in primary care.
Arroll et al, 2002	DP	Yes	Delayed prescriptions are a safe and effective means at reducing antibiotic consumption.
Bourgeois et al, 2010	DST	No	The low overall use of computerized decision support (CDS) resulted in an ineffective intervention. However, use of the CDS significantly reduced antibiotic prescriptions among visits compared with those eligible visits where it was not used.
Breil et al, 2006	CT + ED	No	Patient-centred communication training did not reduce the rate of antibiotic prescriptions below an already unusually low level.
Breil et al, 2006	ED	No	No significant differences were seen
Butler et al, 2012	ED	Yes	The STAR educational programme led to reductions in all cause oral antibiotic dispensing over the subsequent year.
Cals et al, 2009	POC	Yes	Both general practitioners' use of point of care testing for C reactive protein and training in enhanced communication skills significantly reduced antibiotic prescribing for lower respiratory tract infection.
Cals et al, 2009	CT	Yes	
Cals et al, 2009	CT + POC	Yes	Our results did not show interaction effects between the C reactive protein test and the enhanced communication skills strategy—that is, the combined effect of the test and training was neither synergistic nor antagonistic [Both interventions individually showed a statistically significant effect on antibiotic prescribing, the combined intervention did not show any further effect greater than that of the individual effects]
Chappell et al, 2021	A&F	Yes	A targeted intervention using social norms reduced prescribing of antibiotics by high prescribing GP's.
Christakis et al, 2001	A&F	Yes	A point-of-care information system integrated into outpatient pediatric care can significantly influence provider behavior for a common condition.
Curtis et al, 2021	A&F	No	The primary outcome, the mean proportion of antibiotics which were broad-spectrum, reduced by 1.42% for the intervention group compared with 1.12% for controls . . . However, our regression model indicated this was not statistically significant at $P < 0.05$.
Curtis et al, 2021	A&F	Yes	The behavioural impact group reduced their broad-spectrum prescribing by 1.63% compared with 1.20% for plain feedback representing an additional reduction of approximately 1700 (2.1%) broad-spectrum prescriptions. . . This difference was significant at $P < 0.05$.
De la Poza Abad et al, 2016	DP	Yes	Patients randomized to the no prescription strategy or to either of the delayed strategies used fewer antibiotics and less frequently believed in antibiotic effectiveness.

Studies	Intervention Category	Did it Work?	Authors Comment
De la Poza Abad et al, 2016	DP	Yes	Patients randomized to the no prescription strategy or to either of the delayed strategies used fewer antibiotics and less frequently believed in antibiotic effectiveness.
D'Hulster et al, 2022	CT + ED	Yes	Inviting GPs to complete an online communication skill training course and providing them with the linked patient information booklets did not reduce antibiotic prescribing. However, GPs who completed TRACE prescribed 7% fewer antibiotics, especially during winter.
Dowell et al, 2001	DP	Yes	Delayed prescribing is effective at reducing the use of antibiotics for self-limiting cough.
Ferrat et al, 2016	ED	Yes	A single, standardized and interactive educational seminar targeting GPs significantly decreased antibiotic use for RTIs after 4.5 years. [the measure used was prescribing].
Figueiras et al, 2020	DST + ED	Yes	Interventions designed on the basis of gaps in physicians' knowledge of and attitudes to mis prescription can improve antibiotic prescribing.
Finkelstein et al, 2001(1)	ED	Yes	A limited simultaneous educational outreach intervention for parents and providers reduced antibiotic use among children.
Finkelstein et al, 2001(1)	ED	Yes	
Francis et al, 2009	CT + ED	Yes	Use of a booklet on respiratory tract infections in children within primary care consultations led to important reductions in antibiotic prescribing.
Gerber et al, 2013	A&F + ED	Yes	In this large paediatric primary care network, clinician education coupled with audit and feedback, compared with usual practice, improved adherence to prescribing guidelines for common bacterial ARTIs, and the intervention did not affect antibiotic prescribing for viral infections.
Gjelstad et al, 2013	A&F + ED	Yes	The intervention led to improved antibiotic prescribing for respiratory tract infections.
Gold et al, 2021(2)	A&F	No	A social-norms-feedback letter to practices whose prescribing was increasing did not decrease prescribing compared to no letter.
Gold et al, 2022	A&F	No	Our broad-spectrum feedback letters had no effect on broad-spectrum prescribing; adding a bar chart to a text-only letter had no effect on overall antibiotic prescribing.
Gonzales et al, 2013	DST	Yes	Implementation of a decision support strategy for acute bronchitis can help reduce the overuse of antibiotics in primary care settings. The effect of printed vs computer-assisted decision support strategies for providing decision support was equivalent.
Gonzales et al, 2013	DST	Yes	
Hallsworth et al, 2016	A&F + ED	Yes	Social norm feedback from a high-profile messenger can substantially reduce antibiotic prescribing at low cost and at national scale.
Hallsworth et al, 2016	ED	No	The patient-focused intervention did not significantly affect the primary outcome measure.
Hoffman et al, 2022	DST + ED	No	A brief shared decision-making intervention provided to GPs did not reduce antibiotic dispensing more than usual care.

Studies	Intervention Category	Did it Work?	Authors Comment
Hoye et al, 2013	ED	Yes	Promoting delayed prescribing among GPs results in a small decrease in antibiotic dispensing.
Hoye et al, 2013	DST + ED	Yes	The pop-up intervention produced a small but statistically significant decrease in dispensing rate.
Hurlimann et al, 2014	A&F + ED	No	In our setting, implementing guidelines, coupled with sustained individual feedback, was not able to reduce the proportion of sinusitis and other upper RTIs treated with antibiotics, but increased the use of recommended antibiotics for RTIs and UTIs.
Hurlimann et al, 2014	A&F + ED	No	
Hurlimann et al, 2014	A&F + ED	No	
Ilett et al, 1999(4)	ED	Yes	We conclude that the academic detailing process was successful in modifying prescribing patterns and that it also decreased prescription numbers.
Kronman et al, 2020(5)	A&F + ED	Yes	This program reduced antibiotic prescribing during outpatient ARTI visits.
Lagerlov et al, 2000(6)	A&F + ED	Yes	The educational intervention used in this study improved the prescribing behaviour of doctors in accordance with guideline recommendations.
Le Corvoisier et al, 2013	ED	Yes	This randomised trial shows that a standardised and interactive educational seminar results in a long-term reduction in antibiotic prescribing.
Legare et al, 2011	DST + ED	Yes	DECISION+ was developed successfully and appears to reduce the use of antibiotics.
Legare et al, 2012	DST + ED	Yes	The shared decision-making program DECISION+2 enhanced patient participation in decision-making and led to fewer patients deciding to use antibiotics.
Lemiengre et al, 2018	POC	No	Systematic POC CRP testing without guidance is not an effective strategy to reduce antibiotic prescribing.
Lemiengre et al, 2018	ED	No	
Lemiengre et al, 2018	ED + POC	No	
Linder et al, 2010	A&F	No	The ARI Quality Dashboard was not associated with an overall change in antibiotic prescribing for ARIs.
Little et al, 2013	POC	Yes	The antibiotic prescribing rate was lower with CRP training than without.
Little et al, 2013	CT	Yes	[The antibiotic prescribing rate was lower] with enhanced-communication training than without.
Little et al, 2013	CT + POC	Yes	The combined intervention was associated with the greatest reduction in prescribing rate.
Little et al, 2019	POC	Yes	[Yes at 3 months but] CRP training did not [remain more efficacious at 12-month follow-up].
Little et al, 2019	CT	Yes	Internet-based training in enhanced communication skills remains effective in the longer term for reducing antibiotic prescribing. / Communication training remained more efficacious at [12-month follow-up].
Little et al, 2019	CT + POC	Yes	Internet-based training in enhanced communication skills remains effective in the longer term for reducing antibiotic prescribing.

Studies	Intervention Category	Did it Work?	Authors Comment
Llor et al, 2011	POC	Yes	Even though more than 30% of negative RADT results resulted in antibiotic prescribing, the study findings support the use of RADT in the consultation. This strategy has an important impact on reducing antibiotic prescription among adults with acute pharyngitis.
Mainous et al, 2000	A&F	No	These interventions demonstrate little if any impact on promoting appropriate antibiotic prescribing.
Mainous et al, 2000	ED	No	
Mainous et al, 2000	A&F + ED	No	The interventions investigated here to encourage judicious use of antibiotics for presumably viral upper respiratory infections in children show little if any effect on promoting appropriate prescribing.
McIsaac & Goel, 1998	DST	Yes	There was a trend towards a reduction in antibiotic prescriptions (21%, p = 0.09) in the physicians using the intervention form.
McIsaac et al, 2002	DST	No	Chart prompts during clinical encounters to use a clinical score in the assessment of patients with a sore throat did not reduce unnecessary antibiotic prescribing by family physicians.
McIsaac et al, 2021(7)	A&F + DST + ED	Yes	A community-based, primary care provider-focused antimicrobial stewardship intervention was associated with a reduced likelihood of antibiotic prescriptions.
McNulty et al, 2018	ED	Yes	This study within usual service provision found that TARGET antibiotic workshops can help improve antibiotic use.
Meeker et al, 2014	ED	Yes	Displaying poster-sized commitment letters in examination rooms decreased inappropriate antibiotic prescribing for ARIs.
Meeker et al, 2016	DST	Yes	Among primary care practices, the use of accountable justification and peer comparison as behavioural interventions resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections.
Meeker et al, 2016	DST	No	Suggested alternatives, which lacked a social component, had no statistically significant effect.
Meeker et al, 2016	A&F	Yes	Peer comparison resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections.
Meeker et al, 2016	A&F + DST	Yes	Among primary care practices, the use of accountable justification and peer comparison as behavioural interventions resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections.
Meeker et al, 2016	A&F + DST	Yes	
Meeker et al, 2016	DST	Yes	Peer comparison resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections.
Meeker et al, 2016	A&F + DST	Yes	Among primary care practices, the use of accountable justification and peer comparison as behavioural interventions resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections.
O'Connell et al, 1999	A&F + ED	No	The form of feedback evaluated here—mailed, unsolicited, centralised, government sponsored, and based on aggregate data—had no impact on the prescribing levels of general practitioners.

Studies	Intervention Category	Did it Work?	Authors Comment
Ostervall, 2017	ED	Yes	With reminders antibiotics use fell by 12.6 per cent relative to the control clinics.
Persell et al, 2016	DST	No	We observed large reductions in antibiotic prescribing regardless of whether study participants received an intervention, suggesting an overriding Hawthorne effect or possibly clinician-to-clinician contamination.
Persell et al, 2016	DST	No	
Persell et al, 2016	A&F	No	
Persell et al, 2016	DST (Accountable Justification) + DST (Alternatives)	No	
Persell et al, 2016	A&F + DST (Alternatives)	No	
Persell et al, 2016	A&F + DST (Accountable Justification)	No	
Persell et al, 2016	A&F +DST (Accountable Justification) + DST (Alternatives)	No	
Pshetizky et al, 2003	ED	Yes	In children with AOM, a brief explanation by the family physician to the child's parents about the disease and the expected spontaneous recovery could decrease antibiotic use by ~50%.
Regev Yochay et al, 2011	ED + CT + AF	Yes	Multifaceted intervention that engages the physicians in an educational process is effective in reducing APRs and can be sustained.
Samore et al, 2005	ED	Yes	CDSS implemented in rural primary care settings reduced overall antimicrobial use.
Samore et al, 2005	DST + ED	Yes	Clinical decision support systems implemented in rural primary care settings reduced overall antimicrobial use and improved appropriateness of antimicrobial selection for acute respiratory tract infection.
Schwartz et al, 2021(8)	A&F + ED	Yes	In this randomized clinical trial, a single mailed letter to the highest-prescribing PCPs in Ontario, Canada providing peer-comparison feedback, including messaging on limiting antibiotic-prescribing durations, led to statistically significant reductions in total and prolonged-duration antibiotic prescriptions.
Schwartz et al, 2021(8)	A&F + ED	Yes	
Sondergaard et al, 2003(9)	A&F	No	No influence on GP prescribing.
Taylor et al, 2005(10)	ED	No	An educational intervention aimed at parents did not result in a decrease in the number of antibiotic prescriptions in their children.

Studies	Intervention Category	Did it Work?	Authors Comment
Vervloet et al, 2016	A&F + CT + DST	Yes	This multifaceted peer-group-based intervention was effective in reducing the number of RTI-related antibiotic prescriptions for adolescents and adults.
Welschen et al, 2004	A&F + ED	Yes	A multiple intervention reduced prescribing rates of antibiotics for respiratory tract symptoms.
Zwar et al, 1999	A&F + ED	Yes	Antibiotic prescribing by the Intervention group declined over three occasions.

A&F = Audit and Feedback; C = Communication focused intervention; CT = Communication Training; DP = Delayed prescription; DP + E = Delayed prescription used in conjunction with an educational element; DST = Decision Support Tool; ED + CT = Educational plus communication training; ED = Educational; M = Multifaceted programme with 3 or more intervention elements; POC = Point of care testing and training for certain illnesses;
RR = Risk Ratio; OR = Odds Ratio; IRR = Incidence rate ratio; RE = Relative intervention effect; CI = Confidence interval;
(1) The rate of antibiotic courses dispensed per person-year; (2) Results displayed are from an autoregressive and moving average model of first order ARMA (1,1) correlation structure; (3) Adjusted Medication Appropriateness Index (MAI) scores per person; (4) Average no. prescriptions per GP; (5) Results displayed as probability of antibiotic prescription; (6) Results reported as mean proportion of acceptably treated patients; (7) Results displayed as probability of antibiotic prescription after adjustment for characteristics associated with antibiotic prescriptions; (8) Total number of antibiotic prescriptions over 12 months postintervention.; (9) Prescriptions per 1000 patients per month; (10) Total no. of prescriptions for antibiotics per patient; (11) Percentage of antibiotics prescribed/consumed from all visits, unless stated otherwise, (12) Percentage points unless otherwise stated.