

Review

Effectiveness of interventions aiming to reduce inappropriate drug prescribing: an overview of interventions

Daniëlle Kroon^{1,*}, Nina F. Steutel^{2,3,†}, Hester Vermeulen^{1,4},
Merit M. Tabbers³, Marc A. Benninga³, Miranda W. Langendam² and
Simone A. van Dulmen¹

¹Radboud University Medical Center, Radboud Institute of Health Sciences, IQ healthcare, Nijmegen, The Netherlands

²Department of Clinical Epidemiology, Bioinformatics and Biostatistics, Amsterdam UMC, University of Amsterdam, Amsterdam Public Health institute, The Netherlands

³Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Pediatric Gastroenterology, Amsterdam, The Netherlands

⁴Faculty of Health and Social Studies, HAN University of Applied Sciences, Nijmegen, The Netherlands

[†]These authors contributed equally to this work.

*Correspondence: Daniëlle Kroon, Radboud University Medical Center, 114 IQ healthcare, PO Box 9101, 6500 HB Nijmegen, the Netherlands. Phone: 0031 24 3615305, Fax: 031 24 35 40166. Email: Danielle.Kroon@radboudumc.nl.

Received December 14, 2020; Accepted June 15, 2021.

Abstract

Objective Inappropriate prescribing of drugs is associated with unnecessary harms for patients and healthcare costs. Interventions to reduce these prescriptions are widely studied, yet the effectiveness of different types of interventions remains unclear. Therefore, we provide an overview regarding the effectiveness of intervention types that aim to reduce inappropriate drug prescriptions, unrestricted by target drugs, population or setting.

Methods For this overview, systematic reviews (SRs) were used as the source for original studies. EMBASE and MEDLINE were searched from inception to August 2018. All SRs aiming to evaluate the effectiveness of interventions to reduce inappropriate prescribing of drugs were eligible for inclusion. The SRs and their original studies were screened for eligibility. Interventions of the original studies were categorized by type of intervention. The percentage of interventions showing a significant reduction of inappropriate prescribing were reported per intervention category.

Key findings Thirty-two SRs were included, which provided 319 unique interventions. Overall, 61.4% of these interventions showed a significant reduction in inappropriate prescribing of drugs. Strategies that were most frequently effective in reducing inappropriate prescribing were multifaceted interventions (73.2%), followed by interventions containing additional diagnostic tests (antibiotics) (70.4%), computer interventions (69.2%), audit and feedback (66.7%), patient-mediated interventions (62.5%) and multidisciplinary (team) approach (57.1%). The least frequently effective intervention was an education for healthcare professionals (50.0%).

Conclusion The majority of the interventions were effective in reducing inappropriate prescribing of drugs. Multifaceted interventions most frequently showed a significant reduction of inappropriate prescribing. Education for healthcare professionals is the most frequently included intervention in this overview, yet this category is least frequently effective.

Keywords: inappropriate prescribing, interventions, strategies, effectiveness

Introduction

Inappropriate prescribing of drugs is associated with unnecessary healthcare costs and risk of side effects for patients.^[1] These side effects can lead to harmful consequences such as falls, hospitalization and an increased one-year mortality rate.^[2] The prevalence of inappropriate prescribing of drugs is high. For example, 18.5% of elderly and up to 46.5% of the people living in long-term care facilities received one or more potentially inappropriate drug.^[3, 4] Avoiding these inappropriate prescriptions can have a large impact on patient outcomes and lead to a substantial reduction in healthcare costs.^[5, 6] Inappropriate prescribing is defined as the prescription of medication where risk outweighs the benefit, failure to use a safer alternative drug, the misuse of a drug including incorrect dosage and duration of treatment, use of drugs with significant drug-drug and drug-disease interactions and finally the omission of beneficial drugs.^[7]

The presence of inappropriate prescribing indicates that the existence of a clinical practice guideline does not necessarily lead to guideline adherence.^[8, 9] An example is the increasing prescription of acid suppressant medication in children with infant colic and gastro-oesophageal reflux (disease).^[10, 11] Research indicates that proton pump inhibitors should not be prescribed in infants, given the lack of evidence for its effectiveness, the side effects and the lack of studies that prove its safety in the longer term.^[12] This is clearly described in (inter)national guidelines and by the U.S. Food and Drug Administration.^[13–16]

Another example is overprescribing antimicrobial drugs. Inappropriate use of antibiotic drugs is correlated to antibiotic resistance.^[17] The harm of antibiotic resistance is underlined by a recent study, which estimated that antibiotic resistance contributed to the death of 33 110 people in the European Union.^[17] Of all antibiotic prescriptions, 8.8–23.1% could be considered as inappropriate in primary care in England,^[18] whereas this is estimated to be up to 76% for some medical conditions in the United States.^[19]

Many different barriers for reducing inappropriate prescribing have been identified, such as patient expectations, clinical uncertainty, inadequate information management, administrative complaints, financial disincentives, negative staff attitudes and anxiety to change practice.^[20] Numerous interventions have been developed to overcome these perceived barriers. The impact of these interventions is described in various systematic reviews (SRs), focusing on specific settings, interventions or patient populations.^[21–24] However, the comparative effectiveness of interventions for reducing inappropriate prescribing is unclear. Therefore, we aimed to identify effective intervention types for reducing inappropriate prescribing, without restrictions regarding setting, type of drugs or targeted population. This could guide healthcare professionals and policymakers towards the most suitable approach for their own initiatives in reducing inappropriate prescribing of drugs.

Method

For this overview, SRs were used as a source for original studies. The review protocol was registered in the PROSPERO database (registration number CRD42016038131). In addition to the protocol, original studies of the SRs were included for analyses of the effectiveness of interventions. Results are reported based on PRISMA guidelines.^[25]

Data sources and search strategy

In collaboration with a medical information specialist, we developed a search strategy for EMBASE and MEDLINE. The search strategy consisted of synonyms for inappropriate prescribing combined with a filter for systematic reviews. The full search strategy is described in [Supplementary Appendix 1](#). The databases were searched from inception to August 2018. In addition, the reference lists of included SRs were checked for eligible articles.

Eligibility criteria

SRs were eligible for inclusion if the aim of the review was to evaluate the effectiveness of interventions to reduce inappropriate prescribing, or potentially inappropriate prescribing. This had to be stated in the objectives or method section. All types of interventions were eligible if targeted at healthcare professionals, patients or the general public, either at an individual or organizational level. All types of outcomes regarding unnecessary or inappropriate prescribing were accepted, but outcomes of individual interventions had to be reported. No restrictions were made concerning patient characteristics, medical conditions and settings. We defined SRs as literature reviews written by more than one author, in which the authors reported the search terms, searched in two or more databases and reported a table of included studies. Reviews that did not fulfil these criteria and reviews of low methodological quality (AMSTAR score 3 or less) were excluded.^[26–28] No language restrictions were applied.

Subsequently, we screened the original studies that were included in the SRs, following the PICO structure as presented in [Table 1](#). The aim of the original studies had to be the implementation of one or more intervention(s) to reduce (potentially) inappropriate prescribing of medication. The intervention had to be explicitly described, and outcomes had to be reported as the prevalence of (potentially) inappropriate prescribing before and after the intervention, or compared to a control group. The study was excluded if the intervention or outcomes were not clearly described in the SR, and the original study was not available to clarify this. There were no restrictions regarding the study design of the original studies.

Selection of the SRs and original studies

Duplicate references were removed, and the title and abstract of the remaining references were screened for potential relevance. The inclusion criteria were applied to the full texts of the SRs.

Table 1 PICO structure

P	All patients, unrestricted by characteristics, medical conditions or setting
I	All types of interventions aiming to reduce (potentially) inappropriate prescribing of all types of drugs
C	Any control group or pre-intervention group
O	All types of outcomes regarding unnecessary or inappropriate prescribing

The selection process was carried out by a team of reviewers; each article was checked by at least two independent reviewers (NS, HV, ML, DK, SVD). Inclusion of the original studies was conducted by two reviewers (DK and SVD) after duplicate studies were removed. Disagreement was resolved by discussion.

Methodological quality of the SRs

The methodological quality of the SRs was assessed using the AMSTAR instrument by at least two reviewers independently (NS, HV, ML, DK, SVD).^[26, 27] Consensus was reached by discussion between the reviewers.

Data extraction

For each included SR the following information was extracted by one reviewer and checked for accuracy by a second reviewer: objective, inclusion criteria, search date, population, setting, type of interventions, outcomes, number of included studies and participants, risk of bias of the included SR, results of the studies, quality of the evidence and conclusion. All original studies of the SRs were extracted. Subsequently, the interventions of original studies and their outcomes were listed.

Data analysis

In order to compare the effectiveness of different types of interventions, we used the results of the included studies of the systematic reviews. If the intervention showed a significant ($P < 0.05$) reduction in inappropriate prescribing, it was defined as effective and therefore successful. The significance had to be stated in numbers or described by the authors, otherwise, the effect was labelled as 'not reported'. All studies that did not include statistical analysis, were considered as 'not significant' in the analysis. All interventions were categorized by type, which was based on the EPOC taxonomy^[29]: additional diagnostic testing, audit and feedback, computer interventions, education for healthcare professionals, patient-mediated interventions, multidisciplinary (team) approach, multifaceted interventions and other interventions. Interventions including both education for healthcare professionals and feedback were classified in the intervention category 'Audit and feedback' because we considered education an integral part of audit and feedback. Computer interventions included computerized alerts, recommendations and decision support systems. The setting of the intervention was categorized by type: hospital, outpatient setting and long-term care facility. Outpatient settings included primary care, care provided in medical clinics and community pharmacies. Long-term care facilities included health-care homes, elderly homes, nursing homes and residential homes.

Results

Our search resulted in 4066 references after de-duplication. Out of 134 articles that were assessed in full-text, 32 systematic reviews met our inclusion criteria. A flow diagram is presented in [Figure 1](#). The included systematic reviews are listed in [Table 2](#) and, with

more detail, in [Supplementary Appendix 2](#). The results of the methodological quality assessment of the SRs with the AMSTAR instrument are presented in [Supplementary Appendix 3](#). We extracted 513 original studies from the systematic reviews, which studied 546 interventions. After removing duplicate interventions ($n = 167$) and interventions of studies that did not meet our inclusion criteria ($n = 59$), we were able to identify 319 unique interventions ([Figure 2](#)). All interventions are listed in more detail in [Supplementary Appendix 4](#). The significance was reported for 299 interventions, 20 interventions that did not report a statistical analysis were considered as not significant. The results per intervention category are presented in [Table 3](#) and [Figure 3](#).

Overall, 61.4% (196/319) of the interventions significantly reduced inappropriate prescribing, 32.3% (103/319) of the interventions did not lead to a significant reduction, and there was no significance reported for 6.3% (20/319) of the interventions. Intervention types that most often significantly reduced inappropriate prescribing were multifaceted interventions (73.2%, 30/41) and interventions containing an additional diagnostic test (70.4%, 19/27). In the other categories, percentages of interventions that significantly reduced inappropriate prescribing were 69.2% (36/52) for computer interventions, 66.7% (16/24) for audit and feedback, 62.5% (20/32) for patient-mediated interventions, 57.1% (32/56) for a multidisciplinary (team) approach, and 50.0% (35/70) for education for healthcare professionals. In the category of other interventions, various types of interventions were placed, which resulted in small numbers of intervention types and mixed results. This is further explained in the description below.

In a hospital setting, 76.6% (59/77) of the interventions were significantly effective, compared to 57.7% (112/194) of the interventions in an outpatient setting and 52.1% (25/48) of the interventions conducted in long-term care facilities. Antibiotics were the most frequently targeted drugs with 140 interventions in outpatient settings, 26 interventions in hospitals, and four interventions in a long-term care facility. There was some variation in the percentage of significantly effective interventions over time: 58.8% (30/51) for interventions published before 2000, 62.0% (103/166) for intervention published between 2000–2010, and 61.8% (63/102) for interventions published after 2010. Details per intervention category are described below.

Multifaceted interventions ($n = 41$)

Multifaceted interventions included two or more aspects in the applied strategy. Thirty-nine interventions contained an educational facet, targeted at patients and/or healthcare professionals. One intervention consisted of a change in disease management, including extended visits of a physician and a pharmacist visit, and one intervention was a utilization control program. Inappropriate antibiotic prescribing was targeted in 31 interventions. The most common combination was patient education and education for healthcare professionals ($n = 14$). Thirty-seven interventions were conducted in an outpatient setting, two interventions were conducted in a long-term care facility and two in a hospital. In 73.2%

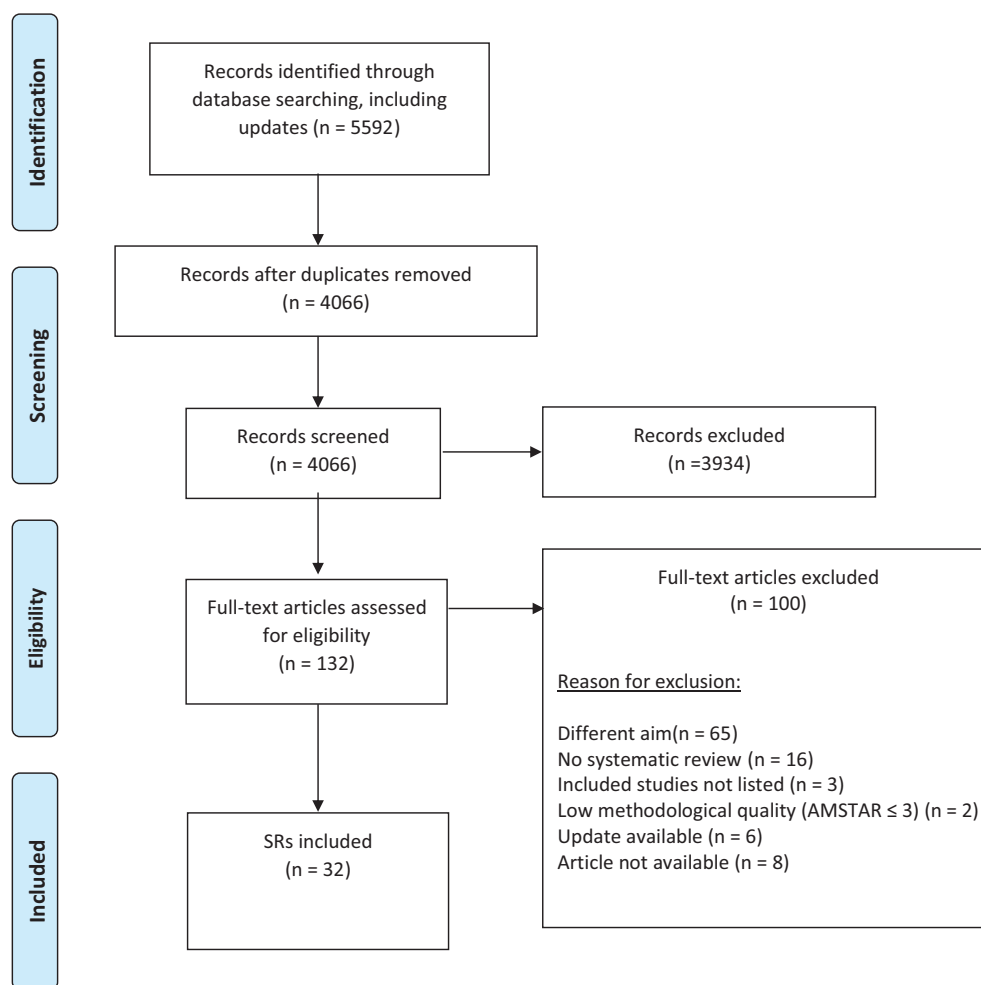


Figure 1 Flow diagram inclusion of systematic reviews

(30/41) of the multifaceted interventions, a significant reduction of inappropriate prescribing was measured. Thirty interventions were targeted at both patients and healthcare professionals, of which 76.7% (23/30) showed a significant reduction of inappropriate prescribing. The combination of patient education and education for healthcare professionals were significantly effective in 64.3% (9/14) of the interventions. Providing feedback as one aspect of a strategy was significantly effective in 72.7% (8/11) of the interventions.

Additional diagnostic testing (n = 27)

All interventions in this category targeted inappropriate antibiotic prescribing, either by starting antibiotic treatment less often or shortening the duration of the treatment. All interventions included tests for one or more infection parameter(s) or implemented rapid testing for influenza or streptococcus. In 70.4% (19/27) of the interventions with additional diagnostic testing, a significant reduction of inappropriate antibiotic prescribing was reported. In outpatient settings, this was in 66.7% (10/15) of the interventions and in hospital settings in 75.0% (9/12) of the interventions.

Computer interventions (n = 52)

Interventions in this category included computerized alerts and recommendations and computer decision support systems. A total of 52 computer interventions were studied and of which 69.2% (36/52)

significantly reduced inappropriate prescribing. Of 30 interventions that were applied in hospitals, 16 interventions were computerized alerts, eight interventions were computer-generated recommendations and six interventions contained a computer decision support system that was studied. Computer interventions were mainly implemented to reduce inappropriate prescribing due to drug-drug interactions, double prescriptions, inappropriate dosing and drug-allergy interactions. In hospital settings, 80.0% (24/30) of the interventions were reported to significantly reduce inappropriate prescriptions. In outpatient settings, 20 interventions were studied, of which 15 interventions concerned the implementation of a computer decision support system and five interventions implementation of computerized alerts or recommendations. Of all computer interventions in outpatient settings, 50.0% (10/20) was significantly effective in reducing inappropriate prescribing. Two interventions were conducted in long-term care facilities and both significantly reduced inappropriate prescribing.

Audit and feedback (n = 24)

Audit and feedback were used in 24 interventions, of which 22 interventions were combined with education for clinicians. Twenty-two interventions were conducted in an outpatient setting, one in a hospital and one in a long-term care facility. Twenty-one interventions were targeted at antibiotic treatment. Of all interventions,

Table 2 Details of the included systematic reviews

First author, year of publication	Focus	Multifaceted intervention	Additional diagnostic testing	Patient-mediated interventions	Audit and feedback	Computer interventions	Multidisciplinary approach	Education for healthcare professionals	Other	Excluded	Total number of interventions
Aldred 2016 ^[30]	LTC						6	2	2	1	12
Arnold 2005 ^[31]	Outpatient, antibiotics	8		5	12	1		10	3	11	50
Arroll 2003 ^[32]	Outpatient, antibiotics			5							5
Birkenhager 2018 ^[24]	LTC, psychotropic drugs							5	1	5	11
Castelino 2009 ^[33]	Elderly	2				1	7	14		1	11
Chhina 2013 ^[34]	Outpatient	1									15
Cross 2016 ^[35]	Antibiotics	3		6	2	1				2	14
Dalton 2018 ^[36]	Elderly, hospital					8					8
Davey 2017 ^[23]	Hospital, antibiotics		12		1	2	3	5		6	29
Diep 2018 ^[37]	Hospital, intravenous Immunoglobulin								3		3
Forsetlund 2011 ^[38]	Elderly, LTC	1					7	11	1		20
Haastrup 2014 ^[39]	Primary care, proton pump inhibitors			2					3	1	6
Hill-Taylor 2016 ^[40]	Elderly						1		3		4
Holstiege 2015 ^[41]	Outpatient, antibiotics					8					8
Johansson 2016 ^[22]	Elderly, polypharmacy			1			19	2	2	1	25
Lainer 2013 ^[42]	Outpatient					8	1			1	10
Lane 2018 ^[43]	Outpatient, antimicrobial prescribing	1							1	1	3
Loganathan 2011 ^[44]	LTC					2	6	7		1	16
Marcum 2010 ^[45]	LTC				1	2	7	7		1	18
McDonagh 2018 ^[46]	Outpatient, antibiotics for respiratory tract infection	1	2	1	2	2		4		2	14
McDonagh 2016 ^[21]	Outpatient, antibiotics for respiratory tract infection	15	13	10	6	7		13	1	4	69
Ostini 2011 ^[47]	Pre-existing inappropriate prescriptions	1		5	1	1	2			2	12
Page 2017 ^[48]	Hospital					23					23
Patterson 2014 ^[49]	Elderly, polypharmacy			1		1	8		1	1	12
Ranji 2008 ^[50]	Outpatient, antibiotics	6		18	12	3		12	2	2	55
Saha 2018 ^[51]	Outpatient, antibiotics				4			3			7
Tesfaye 2017 ^[52]	Chronic kidney disease					6	8	1	2	5	22
Thillainadesan 2018 ^[53]	Elderly, hospital						6		3		9
Thompson Coon 2014 ^[54]	Long-term care facilities						3	12		7	22
Vodicka 2013 ^[55]	Outpatient, antibiotics	2	1	1	1	3		4		5	17
Walsh 2016 ^[56]	Elderly, hospital						5				5
Yourman 2008 ^[57]	Elderly	2				4	3			1	10

*This table includes interventions that were included in more than one systematic review

66.7% (16/24) resulted in a significant reduction of inappropriate prescribing. Both interventions that provided feedback without education did not significantly reduce inappropriate prescribing of antimicrobial drugs.

Patient-mediated interventions ($n = 32$)

This category included patient education, mass media campaigns and delayed prescribing. All patient-mediated interventions were targeted at outpatients or the general public. The majority of the interventions focused on reducing antibiotic use ($n = 27$). Of all patient-mediated interventions, 62.5% (20/32) showed a significant reduction in inappropriate prescribing of drugs. Patient education resulted in a significant reduction of drug prescription in 52.9% (9/17) of the interventions. Mass media campaigns were all targeted at antibiotics and were significantly effective in 71.4% (5/7) of the interventions. Delayed prescribing is defined as providing the patient with a prescription with advice on when to use it. All delayed prescriptions were prescriptions for antibiotic treatment. In 75.0% (6/8) of the interventions using delayed prescribing, a significant reduction was seen in antimicrobial drugs usage.

Multidisciplinary (team) approach ($n = 56$)

In this category, interventions consisted of a specialist (e.g. pharmacist or specialist geriatric care) performing a medication review or forming or re-forming a multidisciplinary team. Overall, a multidisciplinary approach showed a significant reduction in inappropriate prescribing in 57.1% (32/56) of the interventions. A team approach resulted in a significant reduction of inappropriate prescribing in 68.8% (11/16) of the interventions and a medication review by a specialist in 52.5% (21/40) of the interventions. In most interventions in outpatient settings, a pharmacist conducted the medication review to reduce polypharmacy. This led to a significant reduction of inappropriate prescriptions in 27.8% (5/18) of the interventions. In long-term care facilities and hospitals, both forming a multidisciplinary team and a pharmacist reviewing medication were studied. In respectively 58.8% (10/17) and 81.0% (17/21) of the multidisciplinary interventions a significant reduction of inappropriate prescribing was observed.

Education for healthcare professionals ($n = 70$)

The category education for healthcare professionals contains the most interventions ($n = 70$) of all categories. Education for healthcare professionals was significantly effective in reducing inappropriate prescribing in 50.0% (35/70) of the interventions. In long-term care facilities, education for healthcare professionals was effective in 36.4% (8/22) of the interventions, in outpatient settings in 52.4% (22/42) and in hospital settings in 83.3% (5/6). Educational interventions for healthcare professions working in hospitals and outpatient were mostly targeted at antibiotic prescribing, respectively 6/6 and 28/42.

Other ($n = 17$)

Seventeen interventions could not be listed in the defined categories. Medication review tools as intervention resulted in a significant reduction of inappropriate prescribing in 80.0% (4/5). Interventions in which a decision support tool was used, reduced prescription of inappropriate drugs in 33.3% (2/6). Other significantly effective interventions were the introduction of a request form for intravenous immunoglobulin ($n = 1$), and extra patient administration ($n = 1$). Interventions without a significant reduction were: tapering

medication ($n = 1$), feedback with epidemiological data ($n = 1$) and reporting renal function ($n = 2$).

Discussion

In this study, we presented an overview of the effectiveness of interventions aiming to reduce inappropriate prescribing of medication. Overall, 61.4% of the included interventions were reported to result in a significant reduction of inappropriate prescribing. Most frequently effective were multifaceted interventions and interventions with additional diagnostic testing. Educational interventions solely targeted at healthcare professionals were most studied, yet those resulted least frequently in a significant reduction of inappropriate prescribing.

For antimicrobial drugs, additional diagnostic testing and multifaceted interventions showed to be most frequently effective in reducing inappropriate prescriptions. These strategies could therefore be used to tackle the growing problem of antibiotic resistance. This is also reflected in another review for additional diagnostic testing.^[58] However, the overuse of diagnostic tests should be taken into consideration, since some medical conditions are clinical diagnoses, and consequently laboratory testing is not recommended by guidelines.^[59, 60] Therefore, in some cases in outpatient settings, multifaceted interventions may be preferred. It should be noted that our data did not include multifaceted interventions targeting antibiotic prescribing in hospitals. Additional diagnostic testing, however, did show positive results for reducing inappropriate antibiotic prescription in hospitals.

Education for healthcare professionals is the most applied intervention in our results, nevertheless, only 50.0% of the interventions in this category was successful. The limited effectiveness of this intervention is in accordance with an earlier study^[61] and could be explained by different mechanisms. For example, the lack of knowledge may not be the main underlying problem for inappropriate prescribing, other factors are more dominant in the context of inappropriate prescribing,^[62] the education was of low quality or was not repeated sufficiently.^[24, 50, 61] However, if education targeted at healthcare professionals is combined with feedback, it tends to be effective more often. This may be explained by the theory that feedback provides insight into one's own routines, which is, after awareness, the next step towards behavioural change.^[63]

Furthermore, our results suggested that patients are an important factor in inappropriate prescribing. To illustrate, interventions targeted at patients are more often successful than education for healthcare professionals. Moreover, interventions targeting both patients and healthcare professionals are more frequently effective in reducing inappropriate prescribing, compared to interventions that are not targeted at patients. The finding that patients have an important role is supported by other literature as well.^[64–66] Therefore, we suggest considering targeting patients as a facet of an intervention to reduce inappropriate prescribing.

Notable differences were reported in the effectiveness of interventions between interventions conducted in hospitals, outpatient settings and long-term care facilities in all intervention categories. Interventions in hospitals tend to be successful more often compared to interventions conducted in outpatient settings. Contributable factors could include study design (including sample size), quality of the study, design of the intervention or defined outcome measures. For example, studies in long-term care facilities relatively often had a randomized controlled design, compared to studies performed in a hospital setting (Supplementary Appendix 4). The differences in effectiveness between settings may also be explained by the degree

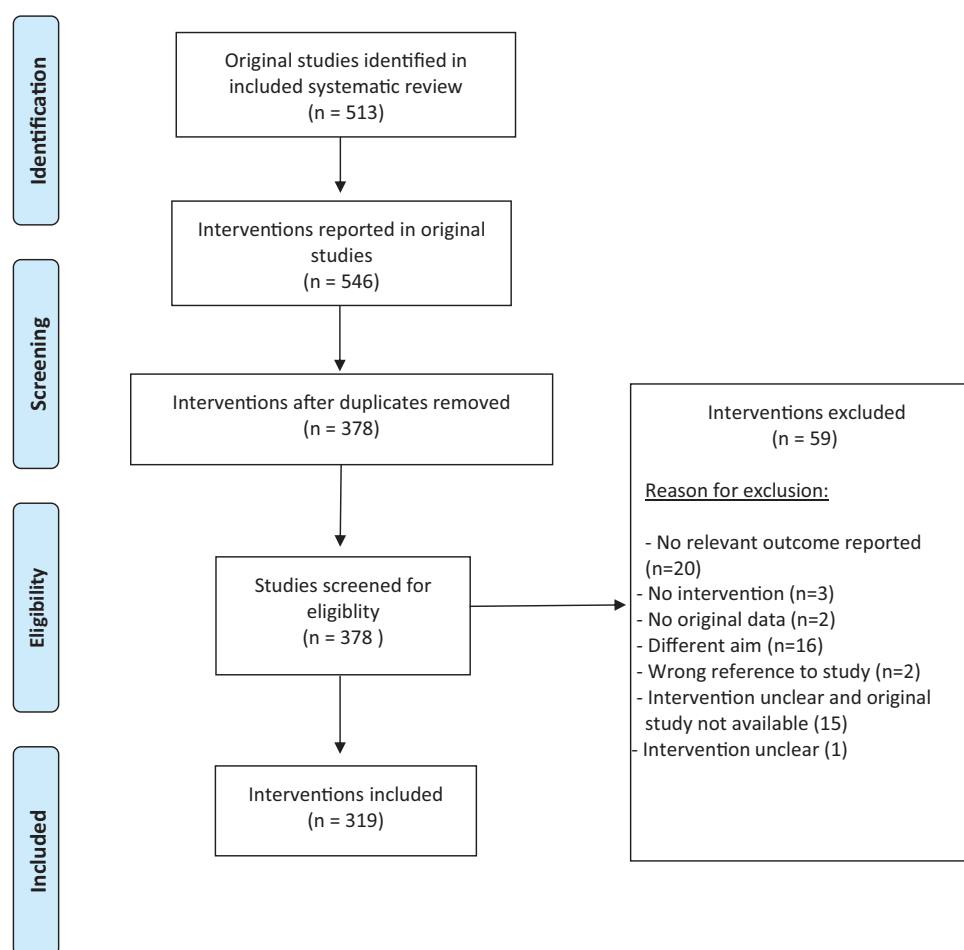


Figure 2 Flow diagram inclusion of interventions

to which the intervention was integrated into the daily practice of healthcare professionals.^[40] Interventions in outpatient settings often demanded more effort and/or extra steps of the healthcare professionals.^[55] For example, in interventions with a multidisciplinary approach in an outpatient setting often a pharmacist participated as a medication reviewer. This collaboration was not further integrated into the daily activities,^[67] whereas in hospital settings integration was often enhanced by the use of pre-existing routine meetings.^[68, 69] This also applied to computer interventions: in hospital settings, alerts automatically popped up, contrary to the manually controlled systems often used in outpatient settings.^[55, 70, 71]

Implications for practice

This review provides an overview of different types of interventions to reduce inappropriate prescribing. We did not find an intervention type that was effective in all settings. This suggests that interventions should be tailored to the context, by targeting barriers and facilitators. However, based on our results, we do suggest conducting interventions with multiple facets. Moreover, we suggest to only use education for healthcare professionals as part of a multifaceted strategy.

Strengths and limitations

To our knowledge, this is the first review presenting an overview of interventions to reduce inappropriate prescribing of drugs, unrestricted by target drugs, population or setting. A few limitations

should be reported. First, this paper reports whether the intervention in the original study significantly reduced inappropriate prescribing of drugs. Due to heterogeneity in reported outcome measures, a meta-analysis could not be performed. By defining an intervention as 'successful' if it significantly reduced inappropriate prescribing, some nuances about the clinical impact of the effect are likely overlooked. In addition, whether an intervention significantly reduces inappropriate prescribing, depends on the sample size and the choice of outcome measures. Second, the inclusion of the original studies in this review depended on the inclusion criteria of the systematic reviews. This resulted in sets of included studies based on a specific intervention, patient population or drug. Although we may have missed interventions that are not included in systematic reviews, this review presents a wide range of intervention types and many interventions. Therefore, this may not influence representativeness. Third, the methodological quality was only assessed for systematic reviews and not for underlying studies.

Conclusion

This study showed that 61.4% of the interventions reported a significant reduction in inappropriate prescribing of drugs. The most frequently effective interventions were multifaceted strategies and additional diagnostic testing. Education for healthcare professionals is the most frequently included intervention in this overview, yet this category is least frequently effective in reducing inappropriate prescribing. Further research should focus on defining favourable

Table 3 Interventions per category and reduction of inappropriate prescribing

Intervention category	Focus of inappropriate prescribing	Description of interventions	Interventions with significant reduction/total (%)	Interventions with significant reduction/total (%) per setting
Multifaceted interventions (<i>n</i> = 41)	Antibiotic prescribing (<i>n</i> = 31) Other (<i>n</i> = 10)	One or more educational aspect(s) in the intervention (<i>n</i> = 39) Organizational interventions (<i>n</i> = 2) Most common combination: Patient education and education for healthcare professionals (<i>n</i> = 14)	30/41 (73.2%)	Hospital: 1/2 (50.0%) Outpatient: 28/37 (75.7%) LTC: 1/2 (50.0%)
Additional diagnostic testing (<i>n</i> = 27)	Antibiotic prescribing (<i>n</i> = 27)	Testing one or more infection parameter(s) (<i>n</i> = 22) Rapid testing: influenza (<i>n</i> = 1) Rapid testing: streptococcus (<i>n</i> = 4)	19/27 (70.4%)	Hospital: 9/12 (75%) Outpatient: 10/15 (66.7%) LTC: None
Computer interventions (<i>n</i> = 52)	Drug interactions, allergies, dosing, double prescriptions, contraindications (<i>n</i> = 38) Antibiotic prescribing (<i>n</i> = 14)	Computer alerts and recommendations (<i>n</i> = 29) Computer decision support (<i>n</i> = 23)	36/52 (69.2%)	Hospital: 24/30 (80.0%) Outpatient: 10/20 (50.0%) LTC: 2/2 (100%)
Audit and feedback (<i>n</i> = 24)	Antibiotic prescribing (<i>n</i> = 21) Polypharmacy (<i>n</i> = 1) Benzodiazepine (<i>n</i> = 2)	Audit and feedback with education clinician (<i>n</i> = 22) Audit and feedback (<i>n</i> = 2)	16/24 (66.7%)	Hospital: 0/1 (0.0%) Outpatient: 15/22 (68.2%) LTC: 1/1 (100%)
Patient-mediated interventions (<i>n</i> = 32)	Antibiotic prescribing (<i>n</i> = 27) Other (<i>n</i> = 5)	Patient education (<i>n</i> = 17) Mass media campaigns (<i>n</i> = 7) Delayed prescribing (<i>n</i> = 8)	20/32 (62.5%)	Hospital: None Outpatient: 20/32 (62.5%) LTC: None
Multidisciplinary (team) approach (<i>n</i> = 56)	Various	(re)forming a multidisciplinary team (<i>n</i> = 16) Medical review by specialist (e.g. pharmacist, geriatrician) other than prescriber (<i>n</i> = 40)	32/56 (57.1%)	Hospital: 17/21 (81.0%) Outpatient: 5/18 (27.8%) LTC: 10/17 (58.8%)
Education for healthcare professionals (<i>n</i> = 70)	Antibiotic prescribing (<i>n</i> = 38) Other (<i>n</i> = 32)	Various types of educational meetings and trainings (<i>n</i> = 70)	35/70 (50.0%)	Hospital: 5/6 (83.3%) Outpatient: 22/42 (52.4%) LTC: 8/22 (36.4%)
Other (<i>n</i> = 17)	Various	Review tools (<i>n</i> = 5) Decision support (<i>n</i> = 6) Tapering PPI (<i>n</i> = 1) Request form (<i>n</i> = 1) Providing epidemiological data (<i>n</i> = 1) Extra notes in medical record (<i>n</i> = 1) Reporting renal function (<i>n</i> = 2)	8/17 (47.1%)	Hospital: 3/5 (60.0%) Outpatient: 2/8 (25.0%) LTC: 3/4 (75.0%)

CRP, C-reactive protein; LTC, long term care facility; PPI, proton pump inhibitor

contexts for interventions to improve the effectiveness of these interventions.

Supplementary Material

Supplementary data are available at *Journal of Pharmaceutical Health Services Research* online.

Acknowledgements

We would like to thank René Spijker, medical information specialist, for his contribution to this review.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary material.

Conflict of interest

The authors have no conflict of interest to declare.

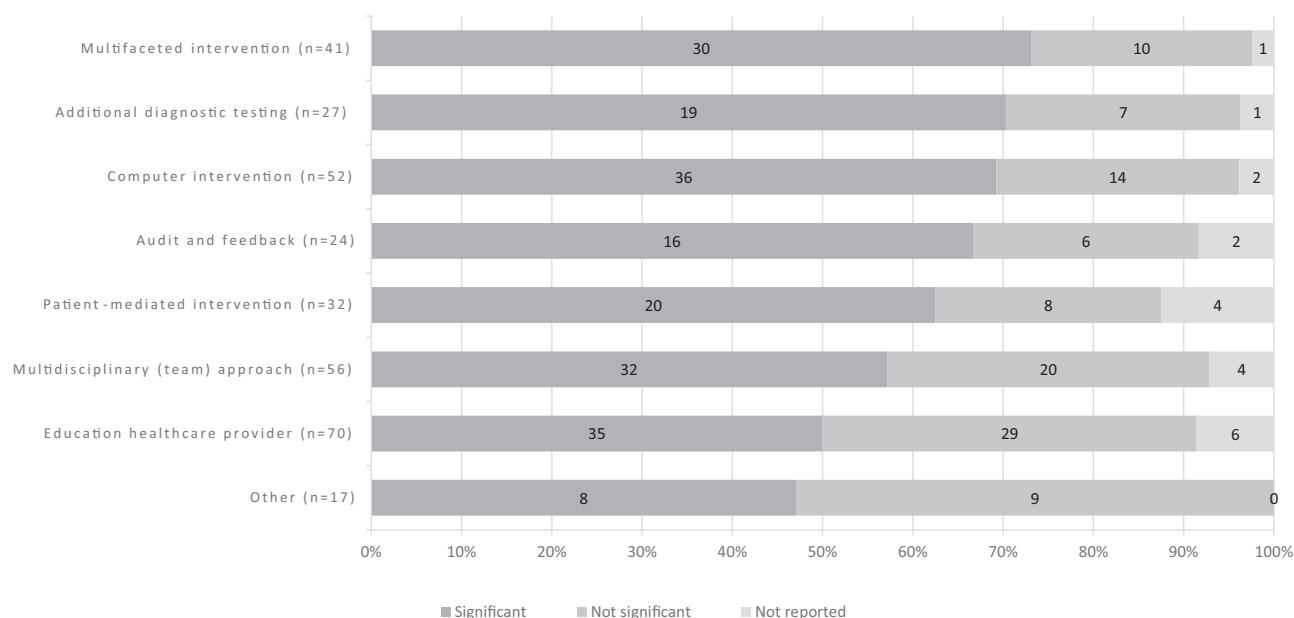


Figure 3 Amount of interventions per category, reported as significantly reducing inappropriate prescribing, no significant reduction or significance not reported

References

- Jano E, Aparasu RR. Healthcare outcomes associated with beers' criteria: a systematic review. *Ann Pharmacother* 2007; 41: 438–47. <https://doi.org/10.1345/aph.1H473>
- Dedhiya SD, Hancock E, Craig BA *et al.* Incident use and outcomes associated with potentially inappropriate medication use in older adults. *Am J Geriatr Pharmacother* 2010; 8: 562–70. [https://doi.org/10.1016/S1543-5946\(10\)80005-4](https://doi.org/10.1016/S1543-5946(10)80005-4)
- Perri M 3rd, Menon AM, Deshpande AD *et al.* Adverse outcomes associated with inappropriate drug use in nursing homes. *Ann Pharmacother* 2005; 39: 405–11. <https://doi.org/10.1345/aph.1E230>
- Li G, Andrews HF, Chihuri S *et al.*; LongROAD Research Team. Prevalence of potentially inappropriate medication use in older drivers. *BMC Geriatr* 2019; 19: 260. <https://doi.org/10.1186/s12877-019-1287-8>
- Stockl KM, Le L, Zhang S *et al.* Clinical and economic outcomes associated with potentially inappropriate prescribing in the elderly. *Am J Manag Care* 2010; 16: e1–10.
- Tommelein E, Mehuys E, Petrovic M *et al.* Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. *Eur J Clin Pharmacol* 2015; 71: 1415–27. <https://doi.org/10.1007/s00228-015-1954-4>
- Spinewine A, Schmader KE, Barber N *et al.* Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet* 2007; 370: 173–84. [https://doi.org/10.1016/S0140-6736\(07\)61091-5](https://doi.org/10.1016/S0140-6736(07)61091-5)
- Flodgren G, Hall AM, Goulding L, *et al.* Tools developed and disseminated by guideline producers to promote the uptake of their guidelines. *Cochrane Database Syst Rev* 2016; 8:CD010669. <https://doi.org/10.1002/14651858.CD010669.pub2>
- Cabana MD, Rand CS, Powe NR *et al.* Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; 282: 1458–65. <https://doi.org/10.1001/jama.282.15.1458>
- De Bruyne P, Christiaens T, Vander Stichele R *et al.* Changes in prescription patterns of acid-suppressant medications by Belgian pediatricians: analysis of the national database, [1997–2009]. *J Pediatr Gastroenterol Nutr* 2014; 58: 220–5. <https://doi.org/10.1097/MPG.0b013e3182a3b04e>
- Blank ML, Parkin L. National study of off-label proton pump inhibitor use among New Zealand infants in the first year of life (2005–2012). *J Pediatr Gastroenterol Nutr* 2017; 65: 179–84. <https://doi.org/10.1097/MPG.0000000000001596>
- van der Pol RJ, Smits MJ, van Wijk MP *et al.* Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: a systematic review. *Pediatrics* 2011; 127: 925–35. <https://doi.org/10.1542/peds.2010-2719>
- Vandenplas Y, Rudolph CD, Di Lorenzo C *et al.* Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). *J Pediatr Gastroenterol Nutr* 2009; 49: 498–547. <https://doi.org/10.1097/MPG.0b013e3181b7f563>
- Chen IL, Gao WY, Johnson AP *et al.* Proton pump inhibitor use in infants: FDA reviewer experience. *J Pediatr Gastroenterol Nutr* 2012; 54: 8–14. <https://doi.org/10.1097/MPG.0b013e31823890b4>
- Quitadamo P, Papadopolou A, Wenzl T *et al.* European pediatricians' approach to children with GER symptoms: survey of the implementation of 2009 NASPGHAN-ESPGHAN guidelines. *J Pediatr Gastroenterol Nutr* 2014; 58: 505–9. <https://doi.org/10.1097/MPG.0b013e3182a69912>
- Rosen R, Vandenplas Y, Singendonk M *et al.* Pediatric Gastroesophageal reflux clinical practice guidelines: Joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr* 2018; 66: 516–54. <https://doi.org/10.1097/MPG.0000000000001889>
- Cassini A, Högberg LD, Plachouras D *et al.*; Burden of AMR Collaborative Group. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *Lancet Infect Dis* 2019; 19: 56–66. [https://doi.org/10.1016/S1473-3099\(18\)30605-4](https://doi.org/10.1016/S1473-3099(18)30605-4)
- Smieszek T, Pouwels KB, Dolck FCK, *et al.* Potential for reducing inappropriate antibiotic prescribing in English primary care. *J Antimicrob Chemother* 2018; 73: ii36–ii43. <https://doi.org/10.1093/jac/dkx500>
- Shively NR, Buehrle DJ, Clancy CJ, *et al.* Prevalence of inappropriate antibiotic prescribing in primary care clinics within a veterans affairs health care system. *Antimicrob Agents Chemother* 2018; 62: e00337–18. <https://doi.org/10.1128/AAC.00337-18>
- Baker R, Camosso-Stefinovic J, Gillies C, *et al.* Tailored interventions to overcome identified barriers to change: effects on professional practice and

- health care outcomes. *Cochrane Database Syst Rev* 2010; 3: CD005470. <https://doi.org/10.1002/14651858.CD005470.pub2>
21. McDonagh M, Peterson K, Winthrop K, *et al.* Improving Antibiotic Prescribing for Uncomplicated Acute Respiratory Tract Infections. Comparative Effectiveness Review No. 163. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2012-00014-I.) AHRQ Publication No. 15(16)-EHC033- EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.
 22. Johansson T, Abuzahra ME, Keller S *et al.* Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2016; 82: 532–48. <https://doi.org/10.1111/bcp.12959>
 23. Davey P, Marwick CA, Scott CL *et al.* Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2017; 2: CD003543. <https://doi.org/10.1002/14651858.CD003543.pub4>
 24. Birkenhäger-Gillesse EG, Kollen BJ, Achterberg WP *et al.* Effects of psychosocial interventions for behavioral and psychological symptoms in dementia on the prescription of psychotropic drugs: a systematic review and meta-analyses. *J Am Med Dir Assoc* 2018; 19: 276.e1–9. <https://doi.org/10.1016/j.jamda.2017.12.100>
 25. Liberati A, Altman DG, Tetzlaff J *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009; 6: e1000100. <https://doi.org/10.1371/journal.pmed.1000100>
 26. Shea BJ, Grimshaw JM, Wells GA *et al.* Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Med Res Methodol* 2007; 7: 10. <https://doi.org/10.1186/1471-2288-7-10>
 27. Shea BJ, Hamel C, Wells GA *et al.* AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. *J Clin Epidemiol* 2009; 62: 1013–20. <https://doi.org/10.1016/j.jclinepi.2008.10.009>
 28. Ryan RE, Kaufman CA, Hill SJ. Building blocks for meta-synthesis: data integration tables for summarising, mapping, and synthesising evidence on interventions for communicating with health consumers. *BMC Med Res Methodol* 2009; 9: 16. <https://doi.org/10.1186/1471-2288-9-16>
 29. Effective Practice and Organisation of Care (EPOC). EPOC Taxonomy. 2015. epoc.cochrane.org/epoc-taxonomy (26 April 2018, date last accessed).
 30. Alldred DP, Kennedy MC, Hughes C *et al.* Interventions to optimise prescribing for older people in care homes. *Cochrane Database Syst Rev* 2016; 2: CD009095. <https://doi.org/10.1002/14651858.CD009095.pub3>
 31. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database Syst Rev* 2005; 2005: CD003539. <https://doi.org/10.1002/14651858.CD003539.pub2>
 32. Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce antibiotic use in respiratory tract infections? A systematic review. *Br J Gen Pract* 2003; 53: 871–7.
 33. Castellino RL, Bajorek BV, Chen TF. Targeting suboptimal prescribing in the elderly: a review of the impact of pharmacy services. *Ann Pharmacother* 2009; 43: 1096–106. <https://doi.org/10.1345/aph.1L700>
 34. Chhina HK, Bhole VM, Goldsmith C *et al.* Effectiveness of academic detailing to optimize medication prescribing behaviour of family physicians. *J Pharm Pharm Sci* 2013; 16: 511–29. <https://doi.org/10.18433/j3kk6c>
 35. Cross EL, Tolfree R, Kipping R. Systematic review of public-targeted communication interventions to improve antibiotic use. *J Antimicrob Chemother* 2017; 72: 975–87. <https://doi.org/10.1093/jac/dkw520>
 36. Dalton K, O'Brien G, O'Mahony D *et al.* Computerised interventions designed to reduce potentially inappropriate prescribing in hospitalised older adults: a systematic review and meta-analysis. *Age Ageing* 2018; 47: 670–8. <https://doi.org/10.1093/ageing/afy086>
 37. Diep C, Shih AW, Jamula E *et al.* Impact of organizational interventions on reducing inappropriate intravenous immunoglobulin (IVIG) usage: a systematic review and meta-analysis. *Transfus Apher Sci* 2018; 57: 215–21. <https://doi.org/10.1016/j.transci.2018.01.008>
 38. Forsetlund L, Eike MC, Gjerberg E *et al.* Effect of interventions to reduce potentially inappropriate use of drugs in nursing homes: a systematic review of randomised controlled trials. *BMC Geriatr* 2011; 11: 16. <https://doi.org/10.1186/1471-2318-11-16>
 39. Haastrup P, Paulsen MS, Begtrup LM *et al.* Strategies for discontinuation of proton pump inhibitors: a systematic review. *Fam Pract* 2014; 31: 625–30. <https://doi.org/10.1093/fampra/cmu050>
 40. Hill-Taylor B, Walsh KA, Stewart S *et al.* Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/ Screening Tool to alert doctors to the right treatment) criteria: systematic review and meta-analysis of randomized controlled studies. *J Clin Pharm Ther* 2016; 41: 158–69. <https://doi.org/10.1111/jcpt.12372>
 41. Holstiege J, Mathes T, Pieper D. Effects of computer-aided clinical decision support systems in improving antibiotic prescribing by primary care providers: a systematic review. *J Am Med Inform Assoc* 2015; 22: 236–42. <https://doi.org/10.1136/amiajnl-2014-002886>
 42. Lainer M, Mann E, Sönnichsen A. Information technology interventions to improve medication safety in primary care: a systematic review. *Int J Qual Health Care* 2013; 25: 590–8. <https://doi.org/10.1093/intqhc/mzt043>
 43. Lane I, Bryce A, Ingle SM *et al.* Does locally relevant, real-time infection epidemiological data improve clinician management and antimicrobial prescribing in primary care? A systematic review. *Fam Pract* 2018; 35: 542–50. <https://doi.org/10.1093/fampra/cmy008>
 44. Loganathan M, Singh S, Franklin BD *et al.* Interventions to optimise prescribing in care homes: systematic review. *Age Ageing* 2011; 40: 150–62. <https://doi.org/10.1093/ageing/afq161>
 45. Marcum ZA, Handler SM, Wright R *et al.* Interventions to improve suboptimal prescribing in nursing homes: A narrative review. *Am J Geriatr Pharmacother* 2010; 8: 183–200. <https://doi.org/10.1016/j.amjopharm.2010.05.004>
 46. McDonagh MS, Peterson K, Winthrop K *et al.* Interventions to reduce inappropriate prescribing of antibiotics for acute respiratory tract infections: summary and update of a systematic review. *J Int Med Res* 2018; 46: 3337–57. <https://doi.org/10.1177/0300060518782519>
 47. Ostini R, Jackson C, Hegney D *et al.* How is medication prescribing ceased? A systematic review. *Med Care* 2011; 49: 24–36. <https://doi.org/10.1097/MLR.0b013e3181ef9a7e>
 48. Page N, Baysari MT, Westbrook JL. A systematic review of the effectiveness of interruptive medication prescribing alerts in hospital CPOE systems to change prescriber behavior and improve patient safety. *Int J Med Inform* 2017; 105: 22–30. <https://doi.org/10.1016/j.ijmedinf.2017.05.011>
 49. Patterson SM, Hughes C, Kerse N, *et al.* Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev* 2012; 5: CD008165. <https://doi.org/10.1002/14651858.CD008165.pub3>
 50. Ranji SR, Steinman MA, Shojania KG *et al.* Interventions to reduce unnecessary antibiotic prescribing: a systematic review and quantitative analysis. *Med Care* 2008; 46: 847–62. <https://doi.org/10.1097/MLR.0b013e318178eabd>
 51. Saha SK, Hawes L, Mazza D. Effectiveness of interventions involving pharmacists on antibiotic prescribing by general practitioners: a systematic review and meta-analysis. *J Antimicrob Chemother* 2019; 74: 1173–81. <https://doi.org/10.1093/jac/dky572>
 52. Tesfaye WH, Castellino RL, Wimmer BC, *et al.* Inappropriate prescribing in chronic kidney disease: a systematic review of prevalence, associated clinical outcomes and impact of interventions. *Int J Clin Pract* 2017; 71: e12960. <https://doi.org/10.1111/ijcp.12960>
 53. Thillainadesan J, Gnjdic D, Green S *et al.* Impact of deprescribing interventions in older hospitalised patients on prescribing and clinical outcomes: A systematic review of randomised trials. *Drugs Aging* 2018; 35: 303–19. <https://doi.org/10.1007/s40266-018-0536-4>
 54. Thompson Coon J, Abbott R, Rogers M *et al.* Interventions to reduce inappropriate prescribing of antipsychotic medications in people with dementia resident in care homes: a systematic review. *J Am Med Dir Assoc* 2014; 15: 706–18. <https://doi.org/10.1016/j.jamda.2014.06.012>
 55. Vodicka TA, Thompson M, Lucas P *et al.*; TARGET Programme team. Reducing antibiotic prescribing for children with respiratory tract

- infections in primary care: a systematic review. *Br J Gen Pract* 2013; 63: e445–54. <https://doi.org/10.3399/bjgp13X669167>
56. Walsh KA, O’Riordan D, Kearney PM *et al.* Improving the appropriateness of prescribing in older patients: a systematic review and meta-analysis of pharmacists’ interventions in secondary care. *Age Ageing* 2016; 45: 201–9. <https://doi.org/10.1093/ageing/afv190>
 57. Yourman L, Concato J, Agostini JV. Use of computer decision support interventions to improve medication prescribing in older adults: a systematic review. *Am J Geriatr Pharmacother* 2008; 6: 119–29. <https://doi.org/10.1016/j.amjopharm.2008.06.001>
 58. Tonkin-Crine SK, Tan PS, van Hecke O *et al.* Clinician-targeted interventions to influence antibiotic prescribing behaviour for acute respiratory infections in primary care: an overview of systematic reviews. *Cochrane Database Syst Rev* 2017; 9: CD012252. <https://doi.org/10.1002/14651858.CD012252.pub2>
 59. Dagnelie CF DJE, Lemmen WH, Opstelten W, *et al.* NHG-Standaard Acute keelpijn (Derde herziening). <https://www.nhg.org/standaarden/volledig/nhg-standaard-acute-keelpijn> (20 September 2020, date last accessed).
 60. NICE. Sore throat (acute): antimicrobial prescribing. ©NICE. 2018. www.nice.org.uk/guidance/NG84 (20 September 2020, date last accessed).
 61. Soong C, Shojania KG. Education as a low-value improvement intervention: often necessary but rarely sufficient. *BMJ Qual Saf* 2020; 29: 353–7. <https://doi.org/10.1136/bmjqs-2019-010411>
 62. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 2011; 6: 42. <https://doi.org/10.1186/1748-5908-6-42>
 63. Grol RP, Bosch MC, Hulscher ME *et al.* Planning and studying improvement in patient care: the use of theoretical perspectives. *Milbank Q* 2007; 85: 93–138. <https://doi.org/10.1111/j.1468-0009.2007.00478.x>
 64. Britten N, Ukoumunne O. The influence of patients’ hopes of receiving a prescription on doctors’ perceptions and the decision to prescribe: a questionnaire survey. *BMJ* 1997; 315: 1506–10. <https://doi.org/10.1136/bmj.315.7121.1506>
 65. Reeve E, To J, Hendrix I *et al.* Patient barriers to and enablers of deprescribing: a systematic review. *Drugs Aging* 2013; 30: 793–807. <https://doi.org/10.1007/s40266-013-0106-8>
 66. Scott JG, Cohen D, DiCicco-Bloom B *et al.* Antibiotic use in acute respiratory infections and the ways patients pressure physicians for a prescription. *J Fam Pract* 2001; 50: 853–8.
 67. Allard J, Hébert R, Rioux M *et al.* Efficacy of a clinical medication review on the number of potentially inappropriate prescriptions prescribed for community-dwelling elderly people. *CMAJ* 2001; 164: 1291–6.
 68. Spinewine A, Swine C, Dhillon S *et al.* Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. *J Am Geriatr Soc* 2007; 55: 658–65. <https://doi.org/10.1111/j.1532-5415.2007.01132.x>
 69. Bergkvist A, Midlöv P, Höglund P *et al.* A multi-intervention approach on drug therapy can lead to a more appropriate drug use in the elderly. LMM-Landskrona Integrated Medicines Management. *J Eval Clin Pract* 2009; 15: 660–7. <https://doi.org/10.1111/j.1365-2753.2008.01080.x>
 70. Bourgeois FC, Linder J, Johnson SA *et al.* Impact of a computerized template on antibiotic prescribing for acute respiratory infections in children and adolescents. *Clin Pediatr (Phila)* 2010; 49: 976–83. <https://doi.org/10.1177/0009922810373649>
 71. Galanter WL, Polikaitis A, DiDomenico RJ. A trial of automated safety alerts for inpatient digoxin use with computerized physician order entry. *J Am Med Inform Assoc* 2004; 11: 270–7. <https://doi.org/10.1197/jamia.M1500>