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ANTIBIOTIC PRESCRIPTIONS FOR ACUTE RESPIRATORY TRACT INFECTIONS IN PRIMARY CARE, MEDICAL, SURGICAL AND PAEDIATRIC WARDS: A REVIEW 2020

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Abstract:

Background: Although most respiratory tract infections (RTIs) are due to viral infections, they cause the majority of antibiotic (Abx) prescriptions in primary care. This systematic review summarises the evidence on the effectiveness of interventions in primary care aiming to reduce Abx prescriptions in patients ≥ 13 years for acute RTI.

Methods: *We searched the databases "MEDLINE/PubMed" and "Cochrane Library" for the period from January 1, 2005, to August 31, 2016, for randomised controlled trials (RCTs) in primary care aiming at the reduction of Abx prescriptions for patients suffering from RTI. Out of 690 search results, 67 publications were retrieved and 17 RCTs were included. We assumed an absolute change of 10% as minimal important change.*

Results: *Twelve out of 17 included RCTs showed statistically significant lower Abx prescription rates in the intervention groups, but only six of them reported a clinically relevant reduction according to our definition. Communication skills training (CST) and point-of-care testing (POCT) were the most effective interventions. Pre-intervention Abx prescription rates varied between 13.5% and 80% and observed reductions ranged from 1.5 to 23.3%. Studies with post-intervention rates lower than 20% had no significant effects. Post-intervention observation periods ranged from 2 weeks up to 3.5 years. The design of the trials was heterogeneous precluding calculation of pooled effect size. The reporting of many RCTs was poor.*

Conclusions: *CST and POCT alone or as adjunct can reduce antibiotic prescriptions for RTI. Eleven out of 17 trials were not successfully reducing Abx prescription rates according to our definition of minimal important change. However, five of them reported a statistically significant reduction. Trials with initially lower prescription rates were less likely to be successful. Future trials should investigate sustainability of intervention effects for a longer time period. The generalisability of findings was limited due to heterogeneous designs and outcome measures. Therefore, a consensus of designing and reporting of studies aiming at reducing antibiotic prescriptions is urgently needed to generate meaningful evidence.*

Keywords: *Acute respiratory tract infections, Antibiotics, Primary care*

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INTRODUCTION:

Although most respiratory tract infections (RTIs) are due to viral infections, they cause the majority of antibiotic prescriptions in primary care [1]. Most patients suffering from RTI do not benefit from an antibiotic treatment since severity and duration of the disease are not relevantly altered. On the contrary, many patients experience side effects such as diarrhoea and rash [2]. Additionally, unnecessary antibiotic prescriptions contribute to increasing bacterial resistance to standard antibiotics [3].

Various interventions have been evaluated to reduce antibiotic prescribing for RTI, e.g. public campaigns, distribution of printed educational material or group education meetings [4–6]. A recent systematic review found moderate short-term effects on antibiotic prescribing of interventions facilitating shared decision-making [7]. Another global review summarised the effects of antimicrobial stewardship programs in ambulatory care including interventions for all infectious conditions and children. This review found low-strength evidence for interventions including provider and/or patient education, guidelines, delayed prescribing (DP) and computerised clinical decision support systems (CDSS) [8]. It is expected that within the next years, antibiotic stewardship programs will need to be established worldwide [9]. So far, there is still a discussion and uncertainty about which specific elements of interventions lead to high effectiveness and sustainability [10]. Therefore, this review aims to update and summarise current evidence of various interventions in primary care on reducing antibiotic prescription rates (Abx prescription rates) due to acute RTIs in patients ≥ 13 years.

METHODS:

This is a systematic review reported according to the PRISMA Statement [11]. This systematic review was not registered.

Search methods for identification of trials

The systematic literature search was carried out in MEDLINE/PubMed and the Cochrane Library using the following search terms:

((antibiotic*) AND (“respiratory tract infection” OR “respiratory tract infections” OR “res-piratory infection”) AND (communication OR training OR “point of care test” OR “rapid strep test” OR “delayed prescribing” OR intervention* OR “electronic decision support” OR “clinical decision support system” OR “clinical decision support systems” OR “shared decision making”) AND (“primary care” OR “primary health care” OR “medical care”)) OR ((“Anti-Bacterial Agents”[Mesh]) AND (“Respiratory Tract Infections”[Mesh]) AND (“Primary Health Care”[Mesh] OR “Physicians, Primary Care”[Mesh]))

Additionally, the bibliographies of the included trials were screened for relevant intervention trials. We could not search further databases like EMBASE due to limited access and lack of funding.

RESULTS:

Study selection

We searched databases on the 31st of July in 2016 and identified 690 publications. Reviewers independently screened for potentially relevant publications and categorised 215 publications as potentially relevant. After removal of duplicates (n = 84), the remaining 151 titles and abstracts were screened for eligibility and discussed by the reviewers. Disagreements between reviewers were resolved by consensus. Major reasons for exclusion were different trial populations, e.g. including children, trials carried out in non-primary care settings and non-randomised study designs. We excluded 84 out of 151 publications. A total of 67 potentially relevant articles were fully screened for inclusion and exclusion criteria

All cluster-randomised trials performed cluster-adjusted data analyses. The number of participating physicians ranged from 6 to 573. Most trials were conducted in Europe [13, 14, 20–22, 27, 28, 31], six trials in North America [15, 23–25, 30, 32] and one in Asia [33]. One trial was a multinational project carried

out in six European countries (Belgium, Spain, Wales, England, Poland and the Netherlands) [26]. Published baseline data was available for seven trials [14, 20, 23, 26–29]. Eleven trials assessed the Abx prescription rate right after patients' initial consultation [13, 20, 22, 23, 26–31, 33].

Primary endpoints

Data on Abx prescription rates was collected directly by physicians [20, 21, 26, 27, 31], by pharmacists using faxed or mailed prescriptions [21, 32], by field researchers [33] or by electronic medical records [13, 15, 22–25, 28, 29]. Four trials used special documentation software [14, 23–25].

The time period for registration of Abx prescriptions ranged from right after the initial consultation up to 28 days after initial consultation.

Six trials assessed effectiveness of the intervention after a longer period of time, within 1 year [15, 29] or within 18 months after the intervention [30], after 1 year [13, 20] or after 3.5 years

Description of participating physicians

Ten trials recruited primary care physicians in private practices [13, 14, 20–22, 26–29, 32], and seven trials recruited physicians from primary care clinics [15, 23–25, 30, 31, 33].

Description of patient population

Patients ≥ 13 years with acute upper and lower RTIs were included. The average age of patients was similar across trials and ranged from 40 to 53 years. The number of registered consultations varied from 149 to 1,115,359 [28, 32].

Description of interventions

Multifaceted interventions

Twelve RCTs used multifaceted interventions [13, 14, 20–26, 28–30]. Multifaceted interventions contain two or more components and address the different aspects of inadequate antibiotic prescribing. Due to the multifaceted interventions of the included trials, some of them are discussed repeatedly in the following subsections. For example, the factorial study design of Cals et al. allows reporting of the effect of the CST or POCT alone or combined [22].

Intervention elements addressing physicians

Twelve trials used interventions that addressed physicians [13, 14, 20–24, 26, 28–30, 32]. Four different types of interventions were evaluated:

A "classic" knowledge transfer approach using interactive seminars [13, 14, 21] and distribution of printed teaching and information materials [21, 23] as well as feedback on individual Abx prescription rates [13, 14, 21, 22, 24, 29]. Themes discussed included diagnosis-making and therapy of RTIs in accordance with guidelines as well as the challenge of increasing bacterial resistance.

A CST dealing with perceived pressure to prescribe where physicians learnt how to communicate with patients about their expectations on antibiotic prescribing and how to respond to patients' concerns. In three trials, physicians were trained in seminars [20–22]. One trial provided an Internet-based CST [26].

Physicians were introduced to the concept of DP. This implies advising patients with low probability of bacterial RTI to use a prescription for antibiotics only in case symptoms do not resolve or get worse up to a pre-defined point in time. Cals et al. combined this strategy with C-reactive protein (CRP) POCT [30]. POCT are simple diagnostic tests and allow measuring CRP directly in the practice. CRP is an acute-phase protein with increasing plasma concentration during inflammatory processes. The measurement of CRP with a POCT has been proved accurate and can increase diagnostic certainty if combined with clinical examination—especially for identifying patients at high risk of pneumonia [35, 36]. Gjelstad et al. implemented additional software applications that asked physicians to specify whether the concept of DP was used and to document the number of days agreed to postpone antibiotic use [14]. Worrall et al. compared two DP procedures—one of them employing a ready-to-use prescription and the other applying a post-dated prescription usable only up to 48 h after initial consultation [32]. Gulliford implemented information about DP within a CDSS [28].

Electronic health records (EHR) asked physicians to justify their treatment decision if an antibiotic was ordered and provided alternative treatment interventions [29].

Intervention elements addressing patients

Five trials implemented interventions addressing patients [20, 23, 25, 28, 33]. Four trials used patient brochures with information about RTIs as adjunct [20, 23, 25, 28]. One trial used an additional waiting room poster addressing increasing bacterial resistance and prescribing pressure as one of the main reasons for inadequate prescribing [20]. Linder et al. and Gulliford et al. implemented documentation software with the possibility to print patient information leaflets [25,

28]. In the RCT of Linder et al., it remained unclear how many physicians used this possibility [25]. In the trial of Gulliford et al., the number of printed leaflets was low among the physicians with the highest utilisation of the CDSS (25 leaflets per 1000 consultations for RTI) [28]. In the trial of Hui Min Lee et al., patients in the IG were educated on the aetiology of upper RTIs by trained field researchers prior to the consultation [33].

Intervention elements addressing improved diagnosis-making

Twelve trials implemented interventions addressing diagnosis-making [13, 15, 22–31]. In one trial, the POCT was combined with a CST [22]. Another trial combined POCT with the strategy of DP [30]. Little et al. provided CRP-POCT training via the Internet [26]. Andreeva et al. used the CRP-POCT as a single intervention [27]. Bjerrum et al. employed a rapid antigen detection test for identifying group A streptococcal infections (RADT) in combination with feedback on personal prescribing rates [13]. Llor et al. used the RADT by itself [31]. The RADT is a fast pathogen identification test and can assist a physician in differentiating between a bacterial pharyngitis caused by group A streptococci or a viral infection. In combination with clinical scores such as the McIsaac score, it can raise diagnostic certainty and help to avoid unnecessary antibiotic prescriptions [37].

Six trials made use of CDSS [15, 23–25, 28, 29]. Linder et al. [24, 25] and McGinn et al. [15] provided assistance for estimating the likelihood of a bacterial RTI [24, 25] or a pneumonia/streptococcal pharyngitis [15]. Gulliford et al. provided evidence from research for antibiotic prescribing when a RTI was coded in an electronic medical record [28]. Andreeva et al. compared two different methods of diagnostic assistance: a computer-based system and a poster with a clinical algorithm [23]. Meeker et al. asked their participating physicians to justify their entered diagnosis and treatment [29].

CONCLUSIONS AND DISCUSSION:

CST and POCT alone or in combination have the potential to reduce antibiotic prescriptions for RTIs. Electronic decision support tools showed only mixed results. Eleven out of 17 trials were not successful in reducing Abx prescription rates according to our definition of minimal important change [13–40]. However, six of them reported a statistically significant reduction [13–15, 20, 28, 29]. Trials with low initial Abx prescription rates were less likely to be successful. Despite a number of noteworthy current studies, the generated evidence remains disappointingly limited. Only moderate evidence which interventional strategies are successful and how these findings could be generalised beyond the actual setting and the observational period of the trial exist.

We conclude that there is a need to develop a consensus for designing and reporting of trials aiming to reduce inappropriate Abx prescriptions in the near future. It should address (among others) the measurement of pre-intervention prescribing rates, adjustment for seasonal and temporal trends, (minimal) follow-up time, data analysis and reporting.

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REFERENCES:

1. Holmes WF, Macfarlane JT, Macfarlane RM, Hubbard R. Symptoms, signs, and prescribing for acute lower respiratory tract illness. Br J Gen Pract. 2001;51:177–181. [PMC free article] [PubMed] [Google Scholar]
2. Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. Cochrane Database Syst Rev. 2013;11:CD000023. [PMC free article] [PubMed]
3. Roca I, Akova M, Baquero F, Carlet J, Cavaleri M, Coenen S, et al. The global threat of antimicrobial resistance: science for intervention. New Microbes New Infect. 2015;6:22–29. doi: 10.1016/j.nmni.2015.02.007. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
4. Sabuncu E, David J, Bernède-Bauduin C, Pépin S, Leroy M, Boëlle P-Y, et al. Significant reduction of antibiotic use in the community after a nationwide campaign in France, 2002–2007. PLoS Med. 2009;6:e1000084. doi: 10.1371/journal.pmed.1000084. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
5. Rautakorpi U-M, Huikko S, Honkanen P, wKlaukka T, Mäkelä M, Palva E, et al. The Antimicrobial Treatment Strategies (MIKSTRA) Program: a 5-year follow-up of infection-specific antibiotic use in primary health care and the effect of implementation of treatment guidelines. Clin Infect Dis 2006; 42:1221–1230. [PubMed]
6. Welschen I, Kuyvenhoven MM, Hoes AW, Verheij TJM. Effectiveness of a multiple intervention to reduce antibiotic prescribing for respiratory tract symptoms in primary care: randomised controlled trial. BMJ. 2004;329:431. doi: 10.1136/bmj.38182.591238.EB. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

7. Coxeter P, Del Mar CB, McGregor L, Beller EM, Hoffmann TC. Interventions to facilitate shared decision making to address antibiotic use for acute respiratory infections in primary care. Cochrane Database Syst Rev. 2015;11:CD010907. [PMC free article] [PubMed]
8. Drekonja DM, Filice GA, Greer N, Olson A, MacDonald R, Rutks I, et al. Antimicrobial stewardship in outpatient settings: a systematic review. Infect Control Hosp Epidemiol. 2015;36:142–152. doi: 10.1017/ice.2014.41. [PubMed] [CrossRef] [Google Scholar]
9. World Health Organization . Global action plan on antimicrobial resistance. 2015. [Google Scholar]
10. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev. 2005;4:CD003539. [PMC free article] [PubMed]
11. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA Statement. J Clin Epidemiol. 2009;62:1006–1012. doi: 10.1016/j.jclinepi.2009.06.005. [PubMed] [CrossRef] [Google Scholar]
12. Tates K, Meeuwesen L. Doctor–parent–child communication. A (re)view of the literature. Soc Sci Med. 2001;52:839–851. doi: 10.1016/S0277-9536(00)00193-3. [PubMed] [CrossRef] [Google Scholar]
13. Bjerrum L, Cots JM, Llor C, Molist N, Munck A. Effect of intervention promoting a reduction in antibiotic prescribing by improvement of diagnostic procedures: a prospective, before and after study in general practice. Eur J Clin Pharmacol. 2006;62:913–918. doi: 10.1007/s00228-006-0187-y. [PubMed] [CrossRef] [Google Scholar]
14. Gjelstad S, Høye S, Straand J, Brekke M, Dalen I, Lindbæk M. Improving antibiotic prescribing in acute respiratory tract infections: cluster randomised trial from Norwegian general practice (prescription peer academic detailing (Rx-PAD) study) BMJ. 2013;347:f4403. doi: 10.1136/bmj.f4403. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
15. McGinn TG, McCullagh L, Kannry J, Knaus M, Sofianou A, Wisnivesky JP, et al. Efficacy of an evidence-based clinical decision support in primary care practices: a randomized clinical trial. JAMA Intern Med. 2013;173:1584–1591. doi: 10.1001/jamainternmed.2013.8980. [PubMed] [CrossRef] [Google Scholar]
16. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;d5928:343. [PMC free article] [PubMed] [Google Scholar]
17. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale: Taylor & Francis Inc; 1988. [Google Scholar]
18. Manager HCTPCT. Antibiotic use in outpatient settings [Internet]. [cited 2017 Nov 1]. Available from: http://pew.org/1N89p4C.
19. de With K, Schröder H, Meyer E. Antibiotikaanwendung in Deutschland im europäischen Vergleich. Dtsch Med Wochenschr. 2004;129:1987–92.
20. Altiner A, Brockmann S, Sielk M, Wilm S, Wegscheider K, Abholz H-H. Reducing antibiotic prescriptions for acute cough by motivating GPs to change their attitudes to communication and empowering patients: a cluster-randomized intervention study. J Antimicrob Chemother. 2007;60:638–644. doi: 10.1093/jac/dkm254. [PubMed] [CrossRef] [Google Scholar]
21. Briel M, Langewitz W, Tschudi P, Young J, Hugenschmidt C, Bucher HC. Communication training and antibiotic use in acute respiratory tract infections. A cluster randomised controlled trial in general practice. Swiss Med Wkly. 2006;136:241–247. [PubMed] [Google Scholar]
22. Cals JWL, Butler CC, Hopstaken RM, Hood K, Dinant G-J. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. BMJ. 2009;338:b1374. doi: 10.1136/bmj.b1374. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
23. Gonzales R, Anderer T, McCulloch CE, Maselli JH, Bloom FJ, Graf TR, et al. A cluster-randomized trial of decision support strategies for reducing antibiotic use for acute bronchitis. JAMA Intern Med. 2013;173:267–273. doi: 10.1001/jamainternmed.2013.1589. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
24. Linder JA, Schnipper JL, Tsurikova R, Yu T, Volk LA, Melnikas AJ, et al. Electronic health record feedback to improve antibiotic prescribing for acute respiratory infections. Am J Manag Care [Internet]. 2010;16. [cited 2017 Mar 14]. Available from: http://www.ajmc.com/journals/supplement

/2010/ajmc_10dec_hit/ajmc_10hitdeclinder_exclu_e311 [PubMed]
25. Linder JA, Schnipper JL, Tsurikova R, Yu T, Volk LA, Melnikas AJ, et al. Documentation-based clinical decision support to improve antibiotic prescribing for acute respiratory infections in primary care: a cluster randomised controlled trial. Inform Prim Care. 2009;17:231–240. [PubMed] [Google Scholar]
26. Little P, Stuart B, Francis N, Douglas E, Tonkin-Crine S, Anthierens S, et al. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. Lancet Lond Engl. 2013;382:1175–1182. doi: 10.1016/S0140-6736(13)60994-0. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
27. Andreeva E, Melbye H. Usefulness of C-reactive protein testing in acute cough/respiratory tract infection: an open cluster-randomized clinical trial with C-reactive protein testing in the intervention group. BMC Fam Pract. 2014;15:80. doi: 10.1186/1471-2296-15-80. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
28. Gulliford MC, van Staa T, Dregan A, McDermott L, McCann G, Ashworth M, et al. Electronic health records for intervention research: a cluster randomized trial to reduce antibiotic prescribing in primary care (eCRT study) Ann Fam Med. 2014;12:344–351. doi: 10.1370/afm.1659. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
29. Meeker D, Linder JA, Fox CR, Friedberg MW, Persell SD, Goldstein NJ, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. JAMA. 2016;315:562–570. doi: 10.1001/jama.2016.0275. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
30. Cals JWL, Schot MJC, de Jong SAM, Dinant G-J, Hopstaken RM. Point-of-care C-reactive protein testing and antibiotic prescribing for respiratory tract infections: a randomized controlled trial. Ann Fam Med. 2010;8:124–133. doi: 10.1370/afm.1090. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
31. Llor C, Madurell J, Balagué M, Gómez M, Cots JM. Impact of rapid antigen detection testing on antibiotic prescription in acute pharyngitis in adults. A multicentric randomized controlled trial. Br J Gen Pract. 2011;61:e244–e251. doi: 10.3399/bjgp11X572436. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
32. Worrall G, Kettle A, Graham W, Hutchinson J. Postdated versus usual delayed antibiotic prescriptions in primary care: reduction in antibiotic use for acute respiratory infections? Can Fam Physician Med Fam Can. 2010;56:1032–1036. [PMC free article] [PubMed] [Google Scholar]
33. Hui Min Lee M, Shaw Teng Pan D, Huixin Huang J, I-Cheng Chen M, Hui Goh E, Jiang L. Efficacy of a patient-based health education intervention in reducing antibiotic use for acute upper respiratory tract infections in the private sector primary care setting in Singapore. Antimicrob Agents Chemother. 2017;61(5). [PMC free article] [PubMed]
34. Cals JWL, de Bock L, Beckers P-JHW, Francis NA, Hopstaken RM, Hood K, et al. Enhanced communication skills and C-reactive protein point-of-care testing for respiratory tract infection: 3.5-year follow-up of a cluster randomized trial. Ann Fam Med. 2013;11:157–164. doi: 10.1370/afm.1477. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
35. Chalmers JD, Singanayagam A, Hill AT. C-reactive protein is an independent predictor of severity in community-acquired pneumonia. Am J Med. 2008;121:219–225. doi: 10.1016/j.amjmed.2007.10.033. [PubMed] [CrossRef] [Google Scholar]
36. Hopstaken RM, Muris JW, Knottnerus JA, Kester AD, Rinkens PE, Dinant GJ. Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection. Br J Gen Pract. 2003;53:358–364. [PMC free article] [PubMed] [Google Scholar]
37. Tanz RR, Gerber MA, Kabat W, Rippe J, Seshadri R, Shulman ST. Performance of a rapid antigen-detection test and throat culture in community pediatric offices: implications for management of pharyngitis. Pediatrics. 2009;123:437–444. doi: 10.1542/peds.2008-0488. [PubMed] [CrossRef] [Google Scholar]
38. Spurling GKP, Del Mar CB, Dooley L, Foxlee R, Farley R. Delayed antibiotics for respiratory infections. Cochrane Database Syst Rev. 2013;4:CD004417. [PubMed]
39. Rubin MA, Bateman K, Alder S, Donnelly S, Stoddard GJ, Samore MH. A multifaceted intervention to improve antimicrobial prescribing for upper respiratory tract infections in a small rural community. Clin Infect Dis. 2005;40:546–553. doi: 10.1086/427500. [PubMed] [CrossRef] [Google Scholar]

40. Mölstad S, Erntell M, Hanberger H, Melander E, Norman C, Skoog G, et al. Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme. Lancet Infect Dis. 2008;8:125–132. doi: 10.1016/S1473-3099(08)70017-[PubMed] [CrossRef] [Google Scholar]