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MINI REVIEW

Antibiotic stewardship programmes had a low impact on prescribing for acute respiratory tract infections in children

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Abstract

Aim: This mini review summarises the available data on antibiotic stewardship programmes (ASP) for acute respiratory tract infections (ARTI) in paediatric outpatients, particularly the implementation and impact of programmes.

Methods: PubMed was searched from 1 January 2012 to 31 December 2021 for papers with abstracts that used the terms respiratory tract infection, antibiotic, child and guideline. We then saw how many of these included the individual terms impact, implementation or stewardship. After exclusions, we included 10 papers that were published in English on children treated as outpatients for ARTIs. All of these included data on implementing and assessing the impact of ASPs.

Results: The primary care data were mainly from the United States. The ASP programmes did not influence antibiotic prescription rates, but broad-spectrum antibiotics decreased by 43–48%. The emergency department data were mainly from France and the antibiotic prescription rate decreased by 31–35% and the rate for broad-spectrum antibiotics by 63–71%. A nationwide register-based study from France confirmed these results.

Conclusion: ASPs had a low impact on overall antibiotic prescription rates and a modest impact on prescribing broad-spectrum antibiotics. The implementation of ASP protocols needs further development, and more research is necessary on barriers to complying with ASPs.

KEYWORDS
antibiotic stewardship, guidelines, impact, implementation, respiratory tract infection

1 | INTRODUCTION

A Task Force set up by the European Academy of Paediatrics identified over-treatment of respiratory tract infections with antibiotics as one of the four main problems in child healthcare in Europe.[1] Most acute respiratory tract infections (ARTIs) in children are self-improving viral infections, which do not benefit from antibiotics. There are some exceptions. These include bacterial infections, such as pneumococcal pneumonia and streptococcal pharyngotonsillitis, and bacterial complications of upper respiratory tract infections that usually need antibiotic treatment, such as acute sinusitis and otitis media. The current guidelines recommend treating

Abbreviations: ARTIs, acute respiratory tract infections; ASP, antibiotic stewardship programmes.

paediatric community-acquired pneumonia with antibiotics, since bacterial and viral pneumonia cannot be reliably distinguished from each other.[2,3] There are some variations in the recommendations for acute otitis media. Most guidelines recommend a wait-and-see approach, with no antibiotics, and re-examining the child after 2–3 days if the symptoms continue.[4] Clinicians are advised to start antibiotics immediately if patients are less than 24 months of age. Prompt antibiotics are also recommended for children of all ages who have acute otitis media, which manifests with bulging ear drums in both ears or with purulent drainage.[5] Pharyngitis, especially nasopharyngitis in young children, is usually caused by viruses, but tonsillopharyngitis may be caused by group-A streptococci after 2–3 years of age. That is why most guidelines suggest that clinicians carry out a streptococcal antigen test and throat culture before making decisions about antibiotic treatment.[6] Acute sinusitis needs to be considered if upper respiratory tract symptoms present with continuing nasal mucous or purulent discharge and a biphasic course with relapsing fever.[7]

No new antibiotics have been launched to treat ARTIs in children in the last 20 years[8] and we are seeing increasing antibiotic resistance to bacterial pathogens.[1] This means that exposure to antibiotics must be reduced at the population level to enhance the stewardship of currently available antimicrobial drugs. Antibiotic stewardship programmes (ASP) have been carried out with varying results in both children and adults.

The aim of this mini review was to summarise the available data on ASP implementations in paediatric outpatients with ARTIs, particularly the implementation and impact of programmes.

I recently reviewed the management of community-acquired pneumonia and bronchiolitis in this journal,[9,10] including the use of antibiotics. Therefore, specific data relating to pneumonia and bronchiolitis were not included.

2 | METHODS

PubMed was searched for papers published in English from 1 January 2012 to 31 December 2021 using the terms respiratory tract infection, child, antibiotic and guideline, filtered by the presence of an abstract. This identified 338 papers. When the terms impact or implementation or stewardship were individually added, the number decreased to 56, 48 and 43, respectively. These were reduced to 19, 16 and 20, respectively, when papers on bronchiolitis, antivirals, chronic infections like tuberculosis, hospitalised patients and those not published in English were excluded. There were 5, 3 and 6 papers that included data on the impact of ASP on child outpatients or implementation protocols. One paper was found by all 3 searches and 2 others by 2 searches. Some studies included community-acquired pneumonia or acute otitis media in the ARTI group, but studies that specifically focused on pneumonia or otitis media were excluded. This meant that the mini review consisted of 10 papers on ARTIs in children.[11-20] The guideline-concordant treatments were defined as either refraining from antibiotics if clinicians presumed children had viral infections or prescribing narrow-spectrum instead of broad-spectrum antibiotics if they presumed that they were bacterial infections. In addition, papers revealed by the searches that covered factors beyond prescriptions, and references in the selected papers, were reviewed when appropriate (Table 1).

Key notes

- Studies that examined antibiotic stewardship programmes (ASP) for acute respiratory tract infections in paediatric outpatients were reviewed from 1 January 2012 to 31 December 2021.
- Primary care ASP programmes, mainly from the United States, did not influence antibiotic prescription rates, but broad-spectrum antibiotics decreased by 43–48%.
- The French emergency department data showed that the antibiotic prescription rate decreased by 31–35% and the rate for broad-spectrum antibiotics fell by 63–71%.

3 | RESULTS

3.1 | Primary care clinics

An American cluster-randomised trial on outpatient ASP intervention compared prescriptions issued by intervention and control practices using the same electronic health record system.[11] Prescribing rates for ARTIs were estimated in 2008–2010 before and in June 2010 through June 2011 during the intervention. There were nine intervention and nine control practices, covering 162 clinicians and 771,332 paediatric visits for ARTIs. The multifaceted intervention consisted of live educational sessions, followed by personalised quarterly audits and feedback on antibiotic prescriptions for presumably viral and bacterial ARTIs. The main outcomes were antibiotic prescriptions issued for viral respiratory infections and broad-spectrum antibiotics prescribed for presumably bacterial ARTIs in the 1-year period after the intervention. Unnecessary antibiotic prescribing was not common. The overall figures for the two outcomes were 8% and 6% at baseline and 8% and 5% after the intervention.[11] Broad-spectrum antibiotic prescribing decreased from 27% to 14% in the intervention group versus 28% to 23% in the control arm.[11] The relative decreases were 48% and 18%, respectively.

Another American ASP study looked at nine intervention practices with 27 physicians and 61 control practices.[12] They all used the same electronic health record system,[12] but an additional electronic clinical decision support template was provided for the intervention practices. The baseline data were collected in 2009, before the intervention started, and the 15-month follow-up data were collected in 2010–2011. The multifaceted intervention included disseminating best-practice guidelines in meetings, quarterly electronic audits and feedback and links to reviews by the Centers for Disease Control

TABLE 1 Impact of ASP programmes on antibiotic prescriptions for ARTIs in primary care, emergency department or population-based settings by country, study design and implementation and intervention activities

Author/study/year/country	Setting/numbers/definitions	Design	Implementation/intervention	Impacts
Primary care clinics				
Gerber et al.[11] (2013) USA	Nine intervention clinics, nine controls. 162 clinicians and 771,332 visits. Divided into viral ARTIs and bacterial ARTIs[a]	Cluster- randomised controlled study Before and after comparisons	Educational session, followed by personal quarterly audits and feedback for 12 months. Guidelines advised against antibiotics for viral ARTIs and against broad-spectrum antibiotics for bacterial ARTIs	Off-guideline prescribing was <10% before and after intervention. Broad-spectrum prescribing decreased from 27% to 14% in intervention group and from 28% to 23% in control group
Mainous et al.[12] (2013) USA	Nine intervention practices (mean 214 paediatric visits per clinic) and 61 control practices (mean 136 visits). Divided into viral ARTIs and bacterial ARTIs[a]	Non-randomised controlled study Before and after comparisons	Best-practice guidelines released in meetings. Quarterly electronic audits and feedback, Links to reviews by Centers for Disease Control and Prevention on antibiotic use	Off-guideline prescribing was 21% before and 28% after intervention. Broad-spectrum prescribing decreased from 46% to 26% in intervention group and increased from 49% to 50% in control group
Aoybamroong et al. (2019)[13] Thailand	Primary care clinic in teaching hospital 2553 children with viral ARTIs and 2935 with bacterial ARTIs[a]	Before and after comparisons	Guideline released via e-mail and application to staff, fellows and residents. Guideline posters in examination rooms	Appropriate prescriptions increased from 78% to 83% (to 95% in residents, 82% in fellows and 75% in staff members)
Westerhof et al. (2021)[14] USA	Family medicine clinic. 90/435 antibiotic prescriptions before/after intervention. Local guidelines for all ARTI diagnoses	Before and after comparisons Adults and children combined. Urinary tract infections were included	Education provided by trained ASP physicians and pharmacists. Pocket cards provided	Guideline-concordant prescribing increased from 53% to 61%. Change was 8% for avoiding all antibiotics and 13% for avoiding broad-spectrum antibiotics
Emergency departments				
Angoulvant et al. (2012)[15] France	One emergency department. 53,055 children with ARTIs. Antibiotics recommended for: otitis media (<2 years), sinusitis, tonsillitis (>3 years), pneumonia and bronchiolitis if fever	Before and after comparisons	Guideline released, with no intervention	Antibiotic prescribing decreased from 32% to 21%. Proportion of broad-spectrum antibiotics increased from 34% to 50%
Angoulvant et al. (2014)[16] France	Three emergency departments. 36,413 children with ARTIs	Before and after comparisons	Change in antibiotic recommendations, with no intervention. Amoxicillin-clavulanic acid and cephalosporins were limited to specific situations	Amoxicillin prescribing increased from 30% to 85%, while amoxicillin-clavulanic acid and cephalosporin prescribing decreased to 10% and 2.5%, respectively
Ouldali et al. (2017)[17] France	Seven paediatric emergency departments. 242,534 children with ARTIs	Before and after comparisons	National updated guidelines released, with no intervention	Antibiotic prescribing decreased from 5% to 3.5%. Proportion of broad-spectrum antibiotics decreased from 67% to 9%. Appropriateness was not assessed

TABLE 1 (Continued)

Author/study/year/country	Setting/numbers/definitions	Design	Implementation/intervention	Impacts
Sánchez et al. (2021)[18] Ecuador	One emergency department: 114 before, 114 one years after and 216 seven years after. Indications for antibiotics strictly defined by specific ARTI diagnosis	Before and after comparisons. Children and adults combined	Local guidelines disseminated, educational campaign, constant feedback and continuous training	Prescription rate 43% before and 18% one year and 18% seven years after. Appropriateness, increased from 22% to 67% and to 50%, respectively
Population-based register data				
Toubol-Lundgren et al. (2017)[19] South France	345 children aged <3 years attending day care centres. National health insurance data on 35,018–36,343 children aged <3 years	Before and after comparisons of patients. Time-series analysis of prescriptions in corresponding population	National guidelines released, with no intervention	No change in antibiotic prescription rate: 30% before and 31%) after. Proportions of prescriptions and reimbursements for cephalosporins fell from 40% to 18%
Trinh et al. (2020)[20] France	123 million antibiotics for ARTIs, dispensed with prescriptions by doctors and without prescriptions by pharmacists	Nationwide time-series analysis	National guidelines released, with no intervention	General practitioners prescribed antibiotics for 26% and paediatricians for 21% of cases. Overall dispensing rate fell by 33% and broad-spectrum antibiotic rate by 20–26%, depending on age

[a]Pneumonia, sinusitis, acute otitis media and streptococcal pharyngitis.

and Prevention on the overall antibiotics used for ARTIs and on the proportion of broad-spectrum antibiotics prescriptions. The mean numbers of children with ARTIs were 214 for the intervention practices and 136 for the control practices. The ASP intervention did not influence the frequency of inappropriate prescribing of antibiotics, but broad-spectrum antibiotics prescribed by the intervention group went down from 46% of cases before the intervention to 26% of cases during the follow-up period, which was a relative decrease of 43%.[12] The weighted mean decrease was 19.7%. Instead, prescribing of broad-spectrum antibiotics increased in mean 0.9% in the control practices.[12]

A study from Thailand, published in 2019, reported the results of an ASP intervention for ARTIs in an outpatient clinic of an academic teaching hospital.[13] The intervention defined appropriate and inappropriate antibiotic use and delivered antibiotic guidelines to faculty staff members, fellows and residents via e-mail and a mobile phone app. Posters on the guidelines were also placed in examination rooms. The medical records of 2553 paediatric patients were reviewed. The ASP intervention increased the rate of appropriate antibiotics from 78% to 83% and the figure was higher (95%) in residents than fellows (82%) and faculty staff members (75%).[13] The relative increase was only 6%, but the levels before and after the ASP intervention were regarded as rather good, probably because the study site was a teaching clinic.

An American, non-randomised controlled study, with a small but well-examined sample of antibiotic prescriptions, confirmed the earlier results of large register studies.[14] The use of antibiotics, according to the guidelines, was evaluated before and after an active multifaceted ASP intervention took place in a family medicine clinic affiliated with a community teaching hospital in 2017–2018. The ASP consisted of live education, provided by specially trained ASP physicians and pharmacists, and pocket cards with local guidelines for physicians. Audits and feedback were delivered every fortnight by the clinic's pharmacist and 90 antibiotic prescriptions issued to children and adults before the ASP intervention and 435 issued during the intervention were reviewed. Avoiding antibiotics was the most common treatment, with the exceptions of otitis media, acute sinusitis, bacterial pharyngitis and pneumonia. In these cases, narrow-spectrum antibiotics were recommended. The percentage of antibiotics issued for ARTIs in line with the guidelines rose from 53% at baseline to 61% during the intervention.[14] This modest 15% relative increase included avoiding antibiotics when the guidelines did not recommend them and selecting appropriate antibiotics when indicated.

3.2 | Emergency departments

One French study retrospectively analysed data that was prospectively collected in a paediatric emergency department for 4 years from November 2005, when the prescribing guidelines were implemented.[15] During the study period, 53,055 children were diagnosed with ARTIs and the team collected data on their age, specific

diagnosis and any antibiotics that were prescribed. Antibiotic prescriptions at discharge fell from 32% in 2005 to 21% in 2009,[15] which was a relative decrease of 34%. Despite this beneficial reduction in overall prescriptions, broad-spectrum amoxicillin-clavulanic acid accounted for 50% of antibiotic prescriptions, compared to 34% for amoxicillin.[15] In November 2011, French guidelines on antibiotic prescriptions for ARTI were revised when a consensus for changed antibiotic categories was reached between scientific societies. After that, broad-spectrum antibiotics, such as amoxicillin-clavulanic acid and cephalosporins, were only recommended for rare and specific situations.[16] The impact of the revised recommendations was studied by looking at 36,413 antibiotic prescriptions for ARTIs issued by seven paediatric emergency departments from November 2009 to October 2012. The use of amoxicillin nearly tripled from 30% to 85%, while amoxicillin-clavulanic acid prescriptions decreased from 42% to 10%,[16] which was a relative decrease of 76%. The figures for not prescribing any antibiotics decreased marginally, from 79% to 73%.[16]

Another French study that examined the impact of the November 2011 guidelines was a multi-centre interrupted time series analysis that covered periods before and after the guidelines.[17] This comprised prospectively collected electronic data from seven paediatric emergency departments in 2009–2015. The intervention consisted of constructing local clinical practice guidelines and organising educational sessions and unit-level feedback. A total of 242,534 children with ARTIs were included in the before and after comparisons. The intervention was associated with a significant decline in antibiotic prescriptions, from 5% to 3.5%,[17] which was a relative reduction of 31% and 13,000 fewer antibiotic prescriptions. Broad-spectrum antibiotic prescriptions decreased from 67% to 9%,[17] which was a relative reduction of 63%, and amoxicillin became the most often prescribed antibiotic (83%).

A quasi-experimental, before and after study from Ecuador reported both the short-term and long-term effects of implementing local clinical practice guidelines to decrease the rate of antibiotic prescriptions for upper respiratory tract infections.[18] The cohort were 444 children and adults who attended the emergency department of a teaching hospital: 114 (53 children) were examined just before the guidelines were implemented in 2010, another 114 (45 children) about a year later in 2011 and 216 (90 children) in 2018. The mean ages of the groups were 23, 25 and 33 years, respectively. The implementation strategy consisted of disseminating the guidelines, an educational campaign for physicians and the public and constant feedback and continuous training for the physicians over a 5-year period. The prescription rate for antibiotics was 43% before the guidelines were implemented and 18% a year later,[18] which was a relative decrease of 70%. The figure was still 18% after 7 years. Two independent experts in family and emergency medicine reviewed how appropriate the prescriptions were. These tripled from 22% to 67% at baseline and a year later and were 50% at 7 years.[18] The results highlighted the value of using multifaceted interventions to implement an ASP and the value of providing continuous training after implementation.

3.3 | Population-based register data

A paper from Southern France reported the findings of a study on ambulatory antibiotic prescriptions issued by paediatricians and general practitioners for children under 3 years of age with ARTIs. The authors studied 345 children attending day care centres before (2008–2012) and after (2013) the release of national guidelines for antibiotic prescriptions.[19] The antibiotic prescription rates did not really change, as they were 30% before and 31% after. The data were compared with the general population of 30,000 children below 3 years of age. This showed that total antibiotic prescriptions remained similar, but prescriptions and reimbursements for broad-spectrum cephalosporins more than halved, from 40% before the guidelines to 18% after the guidelines.[19]

A nationwide interrupted time-series analysis was performed using data on 123 million antibiotics dispensed to French children in 2009–2017.[20] These comprised those dispensed with and without prescriptions by pharmacies, which is permissible in that country. The study focused on overall dispensing rates and rates for amoxicillin and broad-spectrum antibiotics dispensed to children under 5 years of age and 5 years or older. The national guidelines for ARTIs were published in 2005 and updated in 2011. Over the 9-year study period, the annual rate for dispensing antibiotics with and without a prescription decreased by 33% in both age groups.[20] At the same time, broad-spectrum antibiotics decreased by 26% and 20%, respectively.[20] General practitioners prescribed antibiotics more often than paediatricians, 26% versus 21%.[20] The data did not allow the authors to analyse the appropriateness of the prescriptions.

3.4 | Factors behind antibiotic use and prescriptions

Greece is a country with high levels of antibiotic use, substantial over-the-counter sales and high antibiotic resistance to bacterial pathogens. A questionnaire completed by 5312 parents living in all parts of the country evaluated their knowledge, attitudes and family customs with regards to antibiotic use.[21] A number of factors were associated with inadequate knowledge, inappropriate attitudes and incorrect practices. These were being a father, being a single parent, low education, immigrant status, low income and no previous experience of childhood ARTIs. These problems were a question of socioeconomics, not medicine. An ASP campaign was performed in Larnaca, Greek Cyprus and Limasson without any intervention acted as a control area.[22] The intervention consisted of workshops for paediatricians, and educational lectures for parents, and pamphlets, newsletters and radio advertisements for the general public. The use of antibiotics decreased in the intervention area, without any changes in the control area. The decrease was driven by fewer cephalosporins and macrolides, but there were no substantial changes in amoxicillin or amoxicillin-clavulanic acid. During a French study series on ASP implementation, the hospital pharmacist from one emergency department delivered face-to-face education on antibiotics to

parents before their child was discharged. The controls were not provided with this advice. This resulted in higher awareness on the benefits and harms of antibiotics in the intervention group when they took part in phone interviews 14 days later.[23]

Physicians' specialist areas have been associated with adherence to guidelines and paediatricians tend to be more compliant than other physicians, such as family doctors or general practitioners working in primary care. One French study found that primary care doctors prescribed antibiotics and broad-spectrum antibiotics more often than paediatricians for children with ARTIs. This practice was also more common in physicians over the age of 50 than younger colleagues.[20] Meanwhile, a qualitative questionnaire study from Ireland found that primary care doctors gave three reasons for failing to follow the ARTI guidelines.[24] They felt that the guidelines did not comprehensively cover real-life situations, especially during out-of-office hours and they felt pressured by patients and parents or guardians and their own perceptions of what their expectations were. These observations highlight the importance of establishing the practical and psychological reasons for low adherence among physicians and parents and taking these into account when planning activities related to implementing guidelines.

4 | DISCUSSION

The primary care data on antibiotic prescriptions came mainly from the United States and the ASPs were not able to change antibiotic prescription rates.[11,12] A rather low prescription rate of unnecessary antibiotics at baseline was one of the reasons for this observation. We did find that broad-spectrum antibiotics decreased by 43% to 48% and units taking part in ASPs interventions were more likely to achieve reductions than control units.[11,12] This important result suggests that successful interventions should include both educational and follow-up elements, such as dissemination of information followed by regular audits and repeated personalised feedback.

Two studies found a minor increase of 5%–8% in more appropriate prescribing, including avoiding unnecessary antibiotics and broad-spectrum antibiotics, and these were relative increases of 6%–15%[13,14] The interventions included distributing information using various methods, but no monitoring elements, such as audits or feedback. Interestingly, a study that focused on a teaching outpatient clinic in Thailand found that appropriate prescribing improved most in residents, next in fellows and least in staff members.[13]

The emergency department data came mainly from France. Three studies found that the relative reduction in antibiotic prescription rate was a decrease of 31%–35% and the relative reduction in prescribing broad-spectrum antibiotics was 63%–71%.[15-17]The beneficial changes were rather good, despite the fact that the only activity was releasing the guidelines, and this was partly due to the high baseline prescription rates. Surprisingly, the 2005 guidelines led to an increase in the use of broad-spectrum antibiotics, which was corrected by changing the categories for antibiotics in 2011.[16] A large register-based study from France, that comprised 130 million paediatric antibiotics dispensed between 2009 and 2017 confirmed these results.[20]

The benefits of appropriate prescribing lasted for years in a study from Ecuador.[18]The ASP implementation contained elements for physicians, parents and the public, and the training for physicians continued for 5 years. Education campaigns for parents and the general public are essential elements in countries such as Greece, Cyprus and France where antibiotics can be purchased, although not recommended, without prescriptions.[21-24]

The implementation of ASPs needs further development. Electronic health record systems allow online monitoring of clinical and prescription data by specific units and physicians, as seen in 2 studies in this mini review.[11,12] However, the effects were minor. Electronic health record systems can also automatically generate different reports for clinicians. They can contain algorithms that provide diagnostic support advice on therapies[12,25] and even mandatory restrictions on inappropriate prescriptions. Healthcare organisations can also use systems to provide educational information and links to web sites containing, for example, quick reference guides, evidence-based guidelines, saved lectures and actual reviews.[12,13] Recently, a 4-year active intervention managed to almost eradicate cough medicine prescribed for children with ARTIs by using online monitoring of prescriptions, targeted feedback, repeated educational releases and personalised emails and phonecalls.[26]

Finally, physicians may not be receptive to the messages that ASPs and other guidelines are trying to address. They may be driven by their attitudes, their reluctance to change old habits, pressure from parents and their fears about complicated disease progression.[24]

We need to know more about why physicians do or do not follow guidelines. Physicians and parents need to be more aware of the long-term consequences of antibiotics for their child and the wider local population. However, increasing awareness alone does not seem to result in rapid increases in adhering to ASPs. The final goals of the ASPs are long-term changes that last for years, such as decreasing difficult-to-treat pathogens in patients and antibiotic resistance in the wider local community.

5 | CONCLUSION

ASPs had a low impact on overall antibiotic prescribing rates, partly because prescriptions of unnecessary antibiotics were low at baseline. However, they did have a modest impact on prescriptions for broad-spectrum antibiotics. The protocols for implementing ASPs need further development and interventions should include both educational and follow-up elements, such as disseminating information to physicians and parents, unit-level audits and personalised feedback.

CONFLICT OF INTERESTS

None declared.

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