

# Electronically delivered interventions to reduce antibiotic prescribing for respiratory infections in primary care: cluster RCT using electronic health records and cohort study

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**Declared competing interests of authors:** Martin C Gulliford is a member of the Health Services and Delivery Research Board. A Toby Prevost is an employee of Imperial College London and is a member of the Public Health Research (PHR) Funding Board. Alastair D Hay is a member of the Health Technology Assessment (HTA) Clinical Trials Board. Paul Little is a member of the HTA Pandemic Influenza Board, the National Institute for Health Research Journals Library Board and the Programme Grants for Applied Research Expression of Interests – HTA Projects remit. Lucy Yardley is a member of the HTA Antimicrobial Resistance Themed Call Board, the HTA Efficient Study Designs Board and the PHR Funding Board. Michael Moore is a member of the government's Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection.

Published March 2019

DOI: 10.3310/hta23110

## Scientific summary

### **Reduce antibiotic prescribing for respiratory infections in primary care**

Health Technology Assessment 2019; Vol. 23: No. 11

DOI: 10.3310/hta23110

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# Scientific summary

## Background

This research was conducted in response to the National Institute for Health Research (NIHR)'s call for proposals on antimicrobial drug resistance (AMR). The research specifically aimed to address the problem of inappropriate and unnecessary prescribing of antibiotics to patients with self-limiting respiratory tract infections (RTIs) in primary care.

## Objectives

The research addressed three objectives:

1. to develop a complex multicomponent intervention to improve antimicrobial stewardship with respect to RTI management in primary care and to deliver this electronically into general practice systems
2. to conduct an efficient cluster randomised controlled trial (RCT) to evaluate whether or not this multicomponent intervention may be used to reduce antibiotic prescribing for self-limiting RTIs
3. to conduct a population-based cohort study in general practices not exposed to trial interventions to determine whether or not the incidence of pneumonia, peritonsillar abscess, mastoiditis, empyema, meningitis, intracranial abscess or Lemierre syndrome is higher at general practices that prescribe fewer antibiotics for self-limiting RTIs.

## Methods

### *Intervention development*

Individual semistructured interviews were conducted with general practitioners (GPs) and nurse prescribers (NPs) in several areas of England. Participants were shown prototype versions of the antimicrobial stewardship interventions on a tablet computer and asked to imagine that they were interacting with these during a patient consultation. Participants were also asked about any factors that, in their view, could hinder or promote their engagement with the study tools. Data were incorporated into a thematic analysis.

### *Cluster randomised trial*

#### Design

A parallel-group, cluster RCT.

#### Setting

The trial was conducted in 79 UK general practices that contribute to the UK's Clinical Practice Research Datalink (CPRD).

#### Participants

All registered patients were included.

#### Intervention

A complex intervention comprising a webinar to introduce and provide training in the use of the trial interventions, monthly feedback of general practice-specific data for respiratory consultations and antibiotic prescriptions in comparison with the preceding 12 months and decision support tools (DSTs) comprising patient information sheets and advice on the indications for antibiotic prescription.

## Main outcome measures

The primary outcome was the rate of antibiotic prescriptions for self-limiting RTIs over the 12-month intervention period. Secondary outcomes included rates of RTI consultations, proportion of RTI consultations with antibiotics prescribed and the incidence of 11 different safety outcomes.

## Analysis

Analysis was by Poisson regression of participant-level data, including general practice as a random effect, adjusting for age group, gender, comorbidity, region, study quarter, period of randomisation and baseline antibiotic prescribing. A process evaluation was conducted using an online questionnaire, as well as collection and analysis of data on intervention utilisation. Costs of health-care utilisation were also evaluated.

## Cohort study

A separate population-based cohort study was conducted in 610 UK-based general practices from the CPRD that were not exposed to the trial interventions. Data were analysed for registered patients with 45.5 million person-years' follow-up, from 2005 to 2014. Exposures included standardised proportions of RTI consultations with antibiotics prescribed for each general practice and the rate of antibiotic prescription for RTI per 1000 registered patients. The main outcome measures included the incidence of pneumonia, peritonsillar abscess, mastoiditis, empyema, meningitis, intracranial abscess or Lemierre syndrome, adjusting for age group, gender, region, deprivation quintile and RTI consultation rate, with a random effect for general practice.

## Results

### Intervention development

To refine the tools, individual interviews were conducted with GPs and NPs; 31 participants took part in the interviews for intervention development (28 GPs and three NPs). Repeated interviews were held with four participants. A majority of GPs and nurses preferred patient information leaflets, which were specific to a given respiratory condition, and suggested a number of ways of refining these leaflets, including condition-specific approaches to managing symptoms. Most participants considered that their own prescribing patterns were appropriate and the problem of overprescribing did not apply to them. However, participants reported that they were not aware of their actual antibiotic-prescribing rates for RTIs. Participants did not favour the inclusion of indicative target antibiotic-prescribing rates that were deemed unachievable. Many participants considered that the use of intervention tools should be promoted by making GPs aware of the benefits of taking part in the study, including reduced RTI consultations in the future and suitability of feedback reports to be used in audits and appraisals.

### Cluster randomised trial

There were 41 intervention arm practices (323,155 patient-years) and 38 control arm practices (259,520 patient-years). There were 98.7 antibiotic prescriptions for RTIs per 1000 patient-years in the intervention arm (31,907 antibiotic prescriptions) and 107.6 per 1000 in the control arm [27,923 antibiotic prescriptions; adjusted antibiotic-prescribing rate ratio (RR) 0.88, 95% confidence interval (CI) 0.78 to 0.99;  $p = 0.040$ ]. Estimates of intervention effect varied across age groups. Although there was no evidence of effect in children aged < 15 years (RR 0.96, 95% CI 0.82 to 1.12) or adults aged  $\geq 85$  years (RR 0.97, 95% CI 0.79 to 1.18), antibiotic prescribing was reduced in adults aged 15–84 years (RR 0.84, 95% CI 0.75 to 0.95). Assuming causation, one antibiotic prescription was avoided for every 62 (95% CI 40 to 200 antibiotic prescriptions) registered adult patients aged 15–84 years per year. Each quartile increase in utilisation of DSTs was associated with a 4% (95% CI 1% to 7%) reduction in antibiotic prescribing at 15–84 years. Analysis of the trial data showed no evidence that use of this intervention could be associated with any increase in a range of 12 different infective complications. Over the period of the trial, there was no evidence that the costs of health-care utilisation for patients consulting with a RTI were altered through this intervention.

### Cohort study

From 2005 to 2014, the proportion of RTI consultations with antibiotics prescribed declined from 53.9% to 50.5% in men, and from 54.5% to 51.5% in women. From 2005 to 2014, new episodes of meningitis, mastoiditis and peritonsillar abscess declined by 5.3%, 4.6% and 1.0% per year, respectively; however, new episodes of pneumonia increased by 0.4% per year. Age- and gender-standardised incidence rates for pneumonia and peritonsillar abscess were higher for practices in the lowest quartile of antibiotic prescribing than in the highest quartile. Adjusted relative risk increases for a 10% reduction in antibiotic prescribing were 12.8% (95% CI 7.8% to 17.5%;  $p < 0.001$ ) for pneumonia and 9.9% (95% CI 7.8% to 14.0%;  $p < 0.001$ ) for peritonsillar abscess. If a general practice with an average list size of 7000 patients reduces the proportion of RTI consultations with antibiotics prescribed by 10%, then it may observe 1.1 (95% CI 0.6 to 1.5) more cases of pneumonia per year and 0.9 (95% CI 0.5 to 1.3) more cases of peritonsillar abscess per decade. There was no evidence that mastoiditis, empyema, meningitis, intracranial abscess or Lemierre syndrome were more frequent at low-prescribing practices.

### Conclusions

Feedback from prescribers is essential for designing successful interventions for primary care, but implementation into practices may be limited if practitioners perceive that the intervention does not have personal relevance, is not feasible in the context of work load or is viewed as an additional source of external pressure or control.

This study found evidence that, overall, general practice antibiotic prescribing for RTIs was reduced by these electronically delivered interventions. Antibiotic prescribing was reduced for adults aged 15–84 years, but not for children or senior elderly. These findings suggest that future strategies for antimicrobial stewardship should employ stratified interventions that are tailored to specific age groups.

Although analysis of trial data revealed no safety concerns, a non-randomised study in non-trial practices found that general practices with lower antibiotic prescribing for RTIs may expect a slight increase in the incidence of treatable pneumonia and peritonsillar abscess. No increase in mastoiditis, empyema, bacterial meningitis, intracranial abscess or Lemierre syndrome is likely. Even a substantial reduction in antibiotic prescribing was predicted to be associated with only a small increase in the overall number of cases observed, but caution may be required in subgroups of patients at higher risk of pneumonia.

### Recommendations

The research illustrates the value of using electronic health record data to provide practitioners with detailed feedback on antibiotic prescribing for particular prescribing indications. Future research should develop and test age-stratified interventions, specifically focusing on antibiotic prescribing for more vulnerable age groups. Research should further investigate the safety of no prescribing strategies using individual-level patient data and a more comprehensive range of potential safety outcomes.

### Trial registration

This trial is registered as ISRCTN95232781.

### Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.



ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.513

*Health Technology Assessment* is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

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## This report

The research reported in this issue of the journal was funded by the HTA programme as project number 13/88/10. The contractual start date was in January 2015. The draft report began editorial review in January 2018 and was accepted for publication in June 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

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