Age-related decline in antibiotic prescribing for uncomplicated respiratory tract infections in primary care in England following the introduction of a national financial incentive (the Quality Premium) for health commissioners to reduce use of antibiotics in the community: an interrupted time series analysis

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Short running title: Antibiotic stewardship impacts RTI prescribing

Abstract

Objectives: To assess the impact of the 2015/16 NHS England Quality Premium (which provided a financial incentive for Clinical Commissioning Groups to reduce antibiotic prescribing in primary care) on antibiotic prescribing by General Practitioners (GPs) for respiratory tract infections (RTIs).

Method: Interrupted time series analysis using monthly patient-level consultation and prescribing data obtained from the Clinical Practice Research Datalink (CPRD), between April 2011 and March 2017. The study population comprised patients consulting a GP who were diagnosed with an RTI. We assessed the rate of antibiotic prescribing in patients (both aggregate and stratified by age) with a recorded diagnosis of uncomplicated RTI, before and after the implementation of the Quality Premium.

Results: Prescribing rates decreased over the six year study period, with evident seasonality. Notably, there was a 3% drop in the rate of antibiotic prescribing (equating to 14.65 prescriptions per 1,000 RTI consultations) (p<0.05) in April 2015, coinciding with the introduction of the Quality Premium. This reduction was sustained, such that after two years there was a 3% decrease in prescribing relative to that expected had the pre-intervention trend continued. There was also a concurrent 2% relative reduction in the rate of broad-spectrum antibiotic prescribing. Antibiotic prescribing for RTIs diagnosed in children showed the greatest decline with a 6% relative change two years after the intervention. Of the RTI indications studied, the greatest reductions in antibiotic prescribing were seen for patients with sore throats.

Conclusions: Community prescribing of antibiotics for RTIs significantly decreased following the introduction of the Quality Premium, with the greatest reduction seen in younger patients.

Introduction

There is widespread recognition that antibiotic use is a major driver for the emergence and spread of bacterial antibiotic resistance. This has highlighted the importance of antibiotic stewardship, which seeks to reduce unnecessary use of antibiotics in order to conserve the effectiveness of those currently available.[1] Particular emphasis is placed on primary care, which is the healthcare setting in which the highest level of antibiotic prescribing occurs.[2, 3,4] The majority of patients consulting in primary care present with respiratory tract infections (RTIs), which are also the most common indications for antibiotic prescribing in general practice.[5] RTIs (including otitis media, the common cold, sore throats, cough, acute bronchitis and sinusitis) are predominantly uncomplicated self-limiting infections. Treatment of these infections with antibiotics is often inappropriate as they are unlikely to be of clinical benefit while subjecting patients to adverse side effects such as toxicity and carriage of antibiotic-resistant bacteria.[3, 5, 6]

There are wide variations in community antibiotic prescribing rates both within the UK and when comparing the UK to other European countries.[2, 7] Community consumption of antibiotics in the UK (2016: 19.6 defined daily doses [DDD] per 1,000 inhabitants per day), although lower than the European average (21.9 DDD per 1,000 inhabitants per day), is still much higher than prescription rates seen in some European countries (e.g. the Netherlands: 10.4, Sweden: 12.0, Germany: 14.1 DDD per 1,000 inhabitants per day), suggesting that further reductions can be made.[7]

A range of antibiotic stewardship, educational and policy interventions have been implemented in England, aimed at improving the quality of antibiotic prescribing.[1, 8] One such initiative, introduced in April 2015 and published each financial year since, was the inclusion of an antibiotic prescribing element to the national Quality Premium (QP), which provides financial remuneration to Clinical Commissioning Groups (CCGs) responsible for the planning and commissioning of healthcare services in their region. The antibiotic prescribing component of the 2015/16 QP required CCGs to achieve a reduction of 1% in total antibiotic prescribing in primary care and a 10% decrease in the proportion of broad-spectrum antibiotics prescribed, specifically co-amoxiclav, cephalosporins and quinolones.

This study examined the impact of the QP on antibiotic prescribing for RTIs in primary care in England, using an interrupted time series design, which is often used in the evaluation of ‘natural experiments’.[9] The study focused on trends in antibiotic prescribing in patients with a recorded diagnosis of uncomplicated acute RTI after consulting their GP. This group of infections was selected as they are the most common indication for which antibiotics are inappropriately prescribed in primary care, and offer the most scope for improvements in the quality of prescribing. Patients were stratified by age to assess whether changes in prescribing were associated with particular age groups.

Methods

Ethical approval:

The protocol for this research was approved by the Independent Scientific Advisory Committee (ISAC) for Medicines and Healthcare products Regulatory Agency (MHRA) database research (protocol number 16_129R).

Data source and study population

The Clinical Practice Research Datalink (CPRD) is a large, validated electronic database containing routinely collected longitudinal patient-level primary care medical records. CPRD covers approximately 7% of the UK population,[10] with the data being representative of patient demographic characteristics (age, sex, ethnicity).[11, 12] Data were extracted from the CPRD by identifying all patients with a diagnosis of RTI recorded using Read codes, a hierarchical classification system that includes codes for clinical signs, symptoms and diagnoses.[11] Acute uncomplicated RTIs were classified as acute otitis media (AOM), rhinosinusitis, sore throats, upper RTIs, lower RTIs (not including pneumonia related codes), viral RTIs, and total respiratory infections (total of all diagnostic codes excluding duplicated codes). We included symptoms and viral infections and were inclusive with the selection of codes in order to increase sensitivity. Diagnostic codes were excluded if they were indicative of a more complicated infection, such as pneumonia, where antibiotic prescribing would be recommended.

The cohort of patients with an RTI was analysed to see whether their consultations resulted in antibiotic prescriptions. A prescription was linked to a patient's consultation if both occurred on the same day. The antibiotic therapy codes were identified and categorised using the British National Formulary sub-chapter 5.1, excluding anti-tuberculosis and anti-leprotic drugs.[13]

We included patients with permanent registration status (i.e. excluded temporary residents, visitors), for whom data had been recorded by GPs who met CPRD “up-to-standard” criteria. This ensured that the included data had been validated to meet reliable quality levels for completeness and recording. Data for individual patients were collected throughout the study period (April 2011 to March 2017), or until the date of transfer of a patient to another general practice, date of death or the date at which the practice had its last collection.

We estimated monthly antibiotic prescription rates (measured as antibiotic items) per 1000 RTI consultations for all practices. The RTI consultation denominator was stratified by age where age specific rates were being assessed. We compared rates by age group, infection group and antibiotic type (total antibiotic and broad-spectrum antibiotics). Aligned with the QP, broad-spectrum penicillins (including co-amoxiclav), cephalosporins and quinolones were the BNF antibiotic classes used to define broad-spectrum antibiotics. To assess potential differences in antibiotic prescribing by age, the data were split into three age groups: children (under 16 year olds), adults (16 to 64 year olds) and the elderly (65 years and older).

Statistical analyses:

Interrupted time series analysis is a strong quasi-experimental research design commonly used for evaluation of longitudinal effects of interventions, and is particularly appropriate for interventions that target population-level health outcomes.[9, 14] The analyses used a segmented regression of interrupted time series data to examine the impact of the QP 12 months and 24 months after its introduction in England. A monthly time series of the rate of antibiotic prescribing from April 2011 to March 2015 was used to establish the underlying trend (slope) prior to the introduction of the QP. The observed post-intervention trend line was then compared with the continuation of the pre-intervention trend that would have been expected in the absence of an intervention (the counterfactual), in terms of the change in the trend post-intervention, and the change in the level at the intercept (when the QP was introduced, 1st April 2015).[14] The model estimates were then used to quantify the absolute change and relative change at 12 months and 24 months. To model possible long-term seasonal patterns, the data were "time stratified" by month,[15] which permitted adjustment for confounding by seasonality. To account for autocorrelated data, Autoregressive Moving average (ARMA) models were fitted.[16] The order of the moving average and the autoregressive model parameters were determined using multiple methods including scatter plots of the deviance residuals versus time, the Durbin Watson test, and the autocorrelation and partial autocorrelation functions.[14, 15, 17] To assess the fit of the model parameters the maximum likelihood ratio test and quantile-quantile plots were used.[17] Data were tested for heteroscedasticity prior to modelling using residual plots (standardised residuals vs fitted values) along with Breush Pagan tests. The data for the models was homoscedastic.

STATA version 14 (STATA Corp, College Station, TX, USA) was used to perform the data management. The modelling and statistical tests were implemented in R Studio (http://www.r-project.org).

Sensitivity analysis:

The QP is an incentivised initiative targeted at the CCG-level and not the GP practice-level. Therefore the time to disseminate information or develop local agreements would not necessarily happen instantaneously. To account for this delay, a separate interrupted time series regression model was developed with a 3-month phase-in period. This sensitivity analysis assesses the extent to which the results were influenced by a lag in the implementation following the intervention.

Results

GP consultations for RTIs

Between April 2011 and March 2017, a total of 2,198,602 patients (mean age: 37.15 [SD: 25.7], age range=0-113 years; females: n=1,228,585, 55.9%) who were registered at 431 GP practices across England had 6,480,800 consultations for RTIs. Consultation rates for RTIs of registered patients over the six year study period decreased by 28% from 2011/12 (342.80 per 1,000 registered patients) to 2016/17 (247.20). The concurrent rate of registered patients being prescribed antibiotics for RTIs also decreased over these years (36% decrease, from 173.32 to 110.12 per 1,000 registered patients) (Table 1). Of the age groups studied, children consulted more often than the other age groups for RTIs (418.11 consultations per 1,000 registered patient in 2011/2012 compared with 187.48 and 277.08 for adults and the elderly respectively) (Figure S1, available as Supplementary data at JAC Online). Adults were prescribed fewer antibiotics (89.2 prescriptions per 1,000 registered patients in 2016/17) compared to children and the elderly (146.9 and 145.1 prescriptions per 1,000 registered patients, respectively) (Figure S1).

As the QP was aimed at changing prescribing behaviour, we continued the analysis by calculating the antibiotic prescription rate per 1,000 RTI consultations. Total antibiotic prescribing (prescription items per 1,000 consultations) for all RTIs showed a decreasing trend across the study period (Table 1, Figure 1) and seasonal fluctuation (Figure 1), with higher rates during the winter months (December) and lower in summer (August).

Reductions in antibiotic prescribing

Figure 1 shows the decrease in the antibiotic prescribing rate (prescription items per 1,000 RTI consultations) over the study period. Although the antibiotic prescribing rate was already decreasing by 0.83 prescription items per 1,000 RTI consultations per month prior to the introduction of the QP ($p<0.0001$), there was a 3% drop in the rate, corresponding to a reduction of 14.65 prescriptions per 1,000 RTI consultations ($p<0.05$) which coincided with the implementation of the QP in April 2015. This reduction continued post-QP with no significant change in the slope of the trend (Table 2). Twelve months and twenty-four months after the QP, the average monthly antibiotic prescribing rate was 14.6 per 1,000 RTI consultations less than would have been expected had the QP not been introduced. This represents a 3% decrease relative to that expected had the existing trend continued (Table 2).

When the rates were censored around a 3-month implementation period, the change in level was greater, and showed a decrease of 21.39 antibiotic items per 1,000 consultations ($p<0.0001$). Due to reduction in the gradient of the slope post-QP, the drop in level was not sustained and there was no difference in the relative change after two years compared to the model without a lag period (Figure 1B, Table 2).

The most commonly prescribed antibiotic group was broad-spectrum penicillins. The prescribing rate for broad-spectrum antibiotics decreased by 8.53 per 1,000 consultations per month ($p<0.05$). Whether this further reduction was sustained below that projected without the QP is questionable as there was a positive change in the post-QP trend; this reduction in the gradient of the post-QP slope was not statistically significant (Figure 2A, Table 2). Prescription of broad-spectrum antibiotics as a proportion of all antibiotic prescriptions did not vary considerably between the years, a finding that was consistently seen in all age groups (Figure 2B, Table 1).

Changes in antibiotic prescribing by age

The prescription rate per 1,000 consultations was highest in the elderly and lowest in children, who also consult the most often (elderly: 523.69 per 1,000 consultations, adults: 475.66, and children: 351.32 in 2016/17) (Figure S1, Figure 3).

The age-stratified interrupted time series analysis illustrates that the impact of the QP differed across the three age groups, with the greatest reduction in antibiotic prescribing for RTIs occurring in children (Table 2). Two years after implementation of the QP, there was a 6% reduction in the rate of antibiotic prescribing for children relative to that expected had the pre-QP trend continued. At implementation of the QP, the rate of antibiotic prescribing fell across all the age groups, with the largest seen in the adult category (decrease of 16 per 1,000 consultation, compared with 12.71 in children and 12.32 in the elderly) (Figure 3, Table 2). The interrupted time series graphs illustrate that only the prescription rate in children seemed to be widening from the counterfactual prescription rate trend as time progressed, due to the change in the children's post-QP trend which further declined by 0.47 per 1,000 consultations (children's post-QP trend was declining by 1.09 compared with 0.62 pre-QP, $p>0.05$).

Reductions in different RTI infection groups

The most commonly reported codes for a consultation were for upper RTIs, with 54% of consultations referring to such an infection. Of the total antibiotic prescriptions, 48% were prescribed for upper RTIs. Antibiotic prescribing for upper RTI consultations in adults and the elderly were higher than in children (Figure S2). However prescribing in children showed the greatest decrease in absolute and relative change (Figures S2 and S3), with the time series for the elderly showing a shift post-QP to an increase in antibiotic prescribing compared to the pre-QP trend. Adults and elderly had greater antibiotic prescription rates in all infection groups apart from AOM, which was highest in children.

Consultations for lower RTIs and rhinosinusitis resulted in the greatest rate of antibiotic prescribing, as shown by the highest estimate of the intercepts in Table 2. Sore throats and lower RTI consultations had the greatest decline in the level of antibiotic prescribing post-QP compared to the other infection groups (Table 2, Figure 4), with a 4% and 3% decline, respectively, in antibiotic prescriptions per 1,000 consultations relative to the counterfactual expected rate at the same point in time. The majority of the reductions in the sore throat and the lower RTI groups were influenced by the decreases in the level and trend post-QP seen in children (Figures S2 and S3).

Rhinosinusitis-related consultations showed an overarching decrease in antibiotic prescribing over time. The greatest reductions in absolute change was seen in children across all infection groups, apart from rhinosinusitis (Figure S3), where there was an increased change in level (16.61 per 1,000 consultations) and trend (1.47 per 1,000 consultations ($p<0.05$)).

Discussion

We observed a decreasing trend in antibiotic prescribing for RTIs in primary care, with seasonal peaks in the winter period and troughs in the summer. There was a significant drop in the level of this trend by 14.65 antibiotic items per 1,000 consultations in April 2015 ($p<0.05$), coinciding with the introduction of the QP in April 2015. A year after the implementation of the QP there was a 3% relative reduction below the level of antibiotic prescribing for RTI consultations expected in the absence of this intervention. Our findings suggest that this decline was sustained after 2 years. Similarly there was a level drop in the rate of broad-spectrum antibiotic prescribing, although no differences were seen in the proportions of broad-spectrum antibiotics prescribed.

The rate of antibiotic prescribing across the study period was highest in adults for the majority of RTIs, and lowest in children, apart from AOM, an infection most commonly seen in the young. This may be because adults attend with more pronounced or more numerous symptoms, and are better able to communicate subjective symptoms.[18] However, overall antibiotic prescribing for RTIs in children exhibited the greatest decline, with a 6% relative change in this age group two years post-QP. These reductions in prescribing for children were predominantly for upper RTI, sore throat and lower RTI related consultations (6%, 9% and 8% relative change 24 months post-QP, respectively). RTIs are more common in children, particularly those younger than four years, as they are immunologically naive and have an increased tendency to develop infections.[18] This along with parental anxiety regarding their child's infection may be responsible for the higher rates of consultations in this age group,[19] with research suggesting that two-thirds of young children visit their GP with an acute RTI at least once a year.[19] Doctors' concern around potential complications where a bacterial infection is not treated, difficulty in establishing a clinical diagnosis and perceived parental expectations may have contributed to high prescribing rates for RTIs in children.[18] Along with growing GP and patient awareness of antibiotic stewardship, the introduction of the pneumococcal conjugate vaccine in recent years may have decreased the perceived risk of bacterial infections in children.[20] It would therefore be expected that the greatest reductions in antibiotic prescribing, as has been seen in this study, would be made in children for self-limiting indications such as upper RTIs and sore throats. Assessment of the underlying lower RTI Read codes revealed that there have been reductions in prescribing for bronchial cough, acute bronchitis and bronchiolitis, and acute tracheitis consultations. Decrease in prescribing for acute tracheitis is of potential concern, as antibiotics may be advisable in certain instances; these findings would benefit further investigation.

The interrupted time series analysis that took account of a three month phase-in following the introduction of the QP suggested that there were greater reductions in the level change post-QP when a lag in the intervention was included. The QP was targeted at CCGs and therefore the time to disseminate information and develop local agreements would vary and would not necessarily happen instantaneously. An assumption made when using an interrupted time series analysis is that the pre-intervention trend would have continued unchanged in the absence of the intervention of interest and that there are no competing interventions. In addition to the QP, other initiatives, guidance and reports have highlighted the importance of reducing inappropriate antibiotic prescribing.[8] It could therefore be problematic when attempting to discriminate between whether the changes seen were truly an effect of the QP, or a cumulative impact of multiple initiatives. The QP is an NHS England-led national initiative, which provided a financial incentive for reductions in antibiotic prescribing in primary care, an approach which several studies have indicated as being effective in bringing about change in prescribing.[21-23] There are however studies which report improvements occurring prior to the schemes and no discernible effects.[25, 27-30] In England, the positive influence of financial incentives on clinical outcomes has been previously shown with the Quality and Outcomes Framework in 2004,[23, 24] although positive effects were not universal[25] and there were associated concerns about unintended consequences.[26, 27] Our results do show that although a decreasing trend was evident prior to the QP, there was a statistically significant further decrease in antibiotic prescribing, when compared to the expected counterfactual trend had the QP not been introduced. There are various mechanisms by which an intervention implemented at CCG-level may filter and impact on GP practice-level antibiotic prescribing behaviour. It has been suggested that medicine management teams may play an active role in mediating this transfer,[31] further research providing evidence for the route of QP translation into primary care would be beneficial.

Previous studies have shown declining trends in both consultation rates and antibiotic prescribing for acute RTIs,[32-34] and have suggested that reductions in antibiotic prescribing arose mainly because the rate of infections had been declining.[33] This reduction in consultations is either due to a true decrease in the incidence of RTIs or to the growth in public awareness around health issues, antibiotic consumption and self-management.[32] We used the count of RTI consultations as the denominator for the rate calculations, permitting us to attenuate for changes in consultations and therefore identifying changes to prescribing behaviours in primary care.

A limitation of the data used is that collection is not primarily for research purposes and as with all routine data, there is an inherent risk of miscoding and misclassification bias due to differences in the accuracy and completeness of clinical codes used by GPs and/or over time. To reduce selection bias, we were inclusive with the selection of codes, including symptom, diagnosis codes and viral respiratory infections. Having studied a large number of patients and including practices with good quality data, the sample is representative of the population in England and generalisable to other countries with similar healthcare settings.[11, 12]

A further limitation to be noted is that we were unable to assess whether prescriptions were dispensed or whether a delayed antibiotic prescription was given.

In summary, we have shown that there have been significant reductions in prescribing of antibiotics for RTIs following the implementation of the 2015-16 QP, with the greatest reductions seen in children. Many patients were still prescribed antibiotics for upper RTIs such as sinusitis, AOM and sore throats, which guidance suggests are likely to be self-limiting infections where antibiotics offer little clinical benefit. Further reductions in primary care antibiotic prescribing should therefore still be achievable. However, it will be important to monitor whether reductions in antibiotic prescribing are associated with any increases in morbidity, such work is currently on-going.

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Transparency declarations

None to declare.

Disclaimer

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health and Social Care or PHE.

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Table 1: Study population and summary of calculated rates by financial year, April 2011 to March 2017

Parameter		2011/12	2012/13	2013/14	2014/15	2015/16	2016/17
CPRD GP registered patients		4,235,620	4,100,117	3,895,895	3,439,041	2,832,256	1,949,629
Patients who consulted with an RTI included in study		871,406	906,658	750,018	662,462	454,962	309,724
RTI consultations		1,451,984	1,522,399	1,231,712	1,080,171	712,590	481,944
Number of antibiotic items prescribed for RTI		734,137	763,329	602,620	517,236	322,185	214,695
RTI consultation rate, per 1,000 registered patients		342.80	371.31	316.16	314.09	251.60	247.20
Rate of antibiotic prescribing for RTIs, per 1,000 registered patients		173.32	186.17	154.68	150.40	113.76	110.12
Rate of antibiotic prescribing, per 1,000 RTI consultations		505.61	501.40	489.25	478.85	452.13	445.48
Broad-spectrum antibiotic prescribing rate, per 1,000 RTI consultations		312.93	307.49	295.05	290.29	268.78	267.44
Broad-spectrum antibiotics as a proportion of the total antibiotics prescribed for RTI		69.5%	69.3%	69.2%	69.8%	69.2%	69.9%
Rate of antibiotic prescribing per 1,000 RTI consultations, with different recorded diagnoses	Acute Otitis Media	67.56	63.98	64.86	62.17	61.30	60.96
	Rhinosinusitis	719.30	705.28	687.31	676.99	648.10	641.49
	Sore throat	435.79	434.56	415.28	403.85	374.51	363.78
	Upper RTI	454.22	448.98	442.71	429.79	407.84	404.86
	Lower RTI	801.20	803.85	791.61	795.11	768.84	770.48
	Viral respiratory infection	122.95	126.47	105.18	101.23	82.93	84.81

Figure 1: Interrupted time series analyses of A) Total antibiotic prescription rate for RTI consultations in England, April 2011 to March 2017. B) Total antibiotic prescription rate with a 3 month phase-in period.

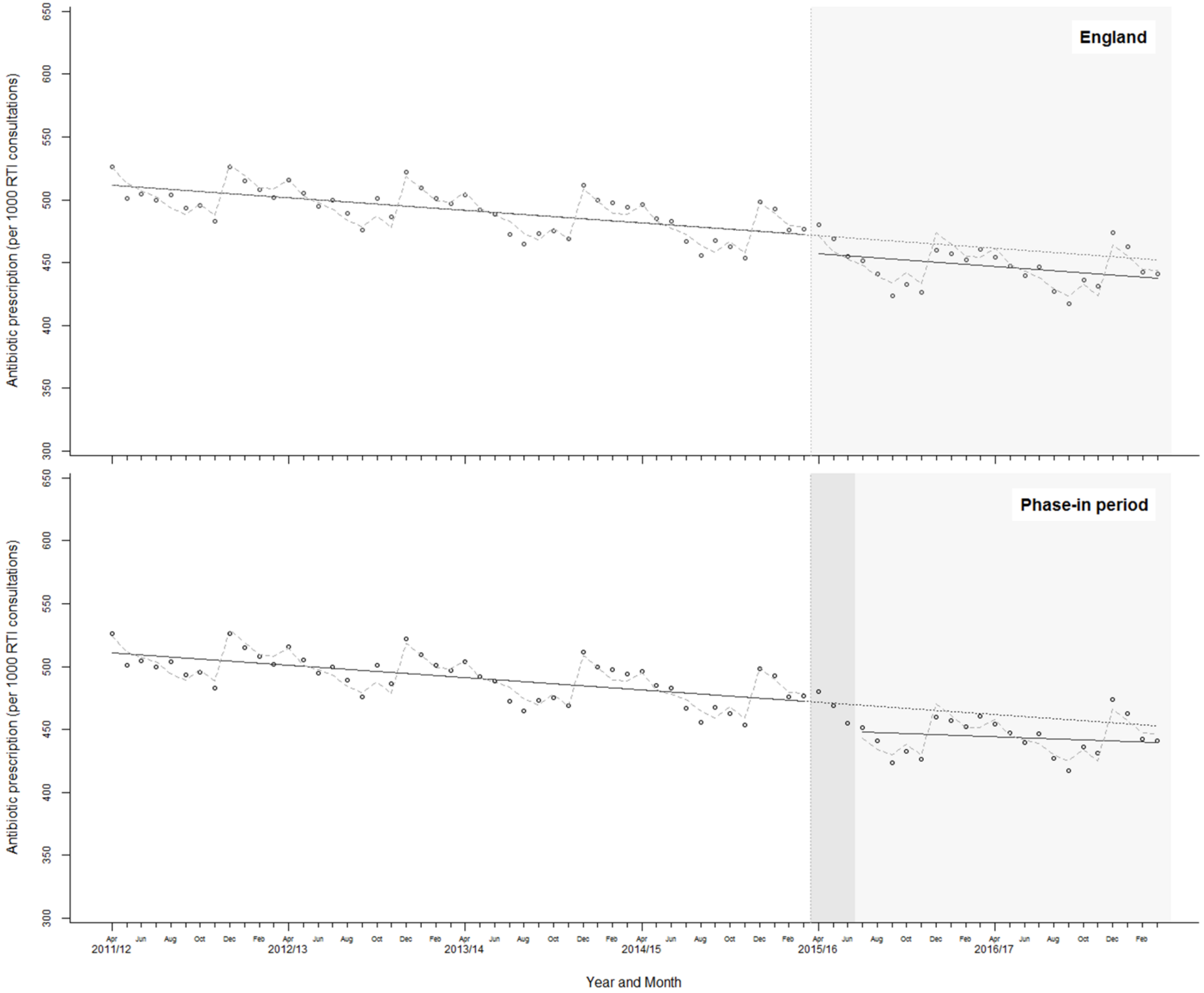

Table 2: Findings from the interrupted time series analyses on the change in trend and level of antibiotic prescribing for RTIs and the relative and absolute changes post-QP

Prescribing measure, 2011/12 - 2016/17 (item/per 1000 RTI consultations)		Estimate of intercept (*p*-value)	Pre-QP trend (*p*-value)	Change in level (*p*-value)	Change in post-QP trend (*p*-value)	Absolute change post 12 months	Relative change post 12 months (%)	Absolute change post 24 months	Relative change post 24 months (%)
England antibiotic prescribing		526.73 (<0.0001)	-0.83 (<0.0001)	-14.65 (0.0022)	0.0018 (0.9950)	-14.62	-3	-14.60	-3
Broad-spectrum antibiotic prescribing		321.18 (<0.0001)	-0.76 (<0.0001)	-8.53 (0.0022)	0.29 (0.0727)	-5.62	-2	-1.37	-0.5
Subgroup analyses:									
Age group	Children	418.85 (<0.0001)	-0.62 (0.0002)	-12.71 (0.0553)	-0.47 (0.3091)	-18.31	-5	-23.91	-6
	Adult	560.83 (<0.0001)	-0.91 (<0.0001)	-16.00 (0.0007)	0.17 (0.5315)	-18.03	-4	-20.05	-4
	Elderly	598.70 (<0.0001)	-1.02 (<0.0001)	-12.32 (0.002)	1.05 (<0.0001)	0.23	0	12.77	2
RTI group	Acute Otitis Media	65.80 (<0.0001)	-0.11 (0.0126)	-0.36 (0.8603)	-0.02 (0.8827)	0.58	1	0.81	1

Rhinosinusitis	729.26	-0.62	-12.71	-0.47	-6.36	-1	-5.91	-1
	(<0.0001)	(0.0002)	(0.0553)	(0.3091)				
Sore throat	462.08	-1.04	-13.75	-0.07	-14.54	-4	-15.33	-4
	(<0.0001)	(<0.0001)	(0.0869)	(0.9028)				
Upper RTI	474.19	-0.76	-13.21	0.28	-9.88	-2	-6.55	-2
	(<0.0001)	(<0.0001)	(0.0192)	(0.4297)				
Lower RTI	811.38	-0.23	-24.11	0.28	-20.74	-3	-17.38	-2
	(<0.0001)	(0.0461)	(0.0002)	(0.4352)				
Viral respiratory infection	139.93	-0.70	-8.36	0.39	-3.72	-4	0.92	1
	(<0.0001)	(<0.0001)	(0.2217)	(0.3565)				
Sensitivity analysis:								
3 month phase-in period, England antibiotic prescribing	525.08	-0.82	-21.39	0.44	-19.86	-4.2	-14.53	-3.15
	(<0.0001)	(<0.0001)	(<0.0001)	(0.1186)				

Figure 2: A) Interrupted time series analysis of broad-spectrum antibiotic prescription rate for RTI consultations in England, April 2011 to March 2017. B) Proportion of broad-spectrum antibiotics prescribed, by age group

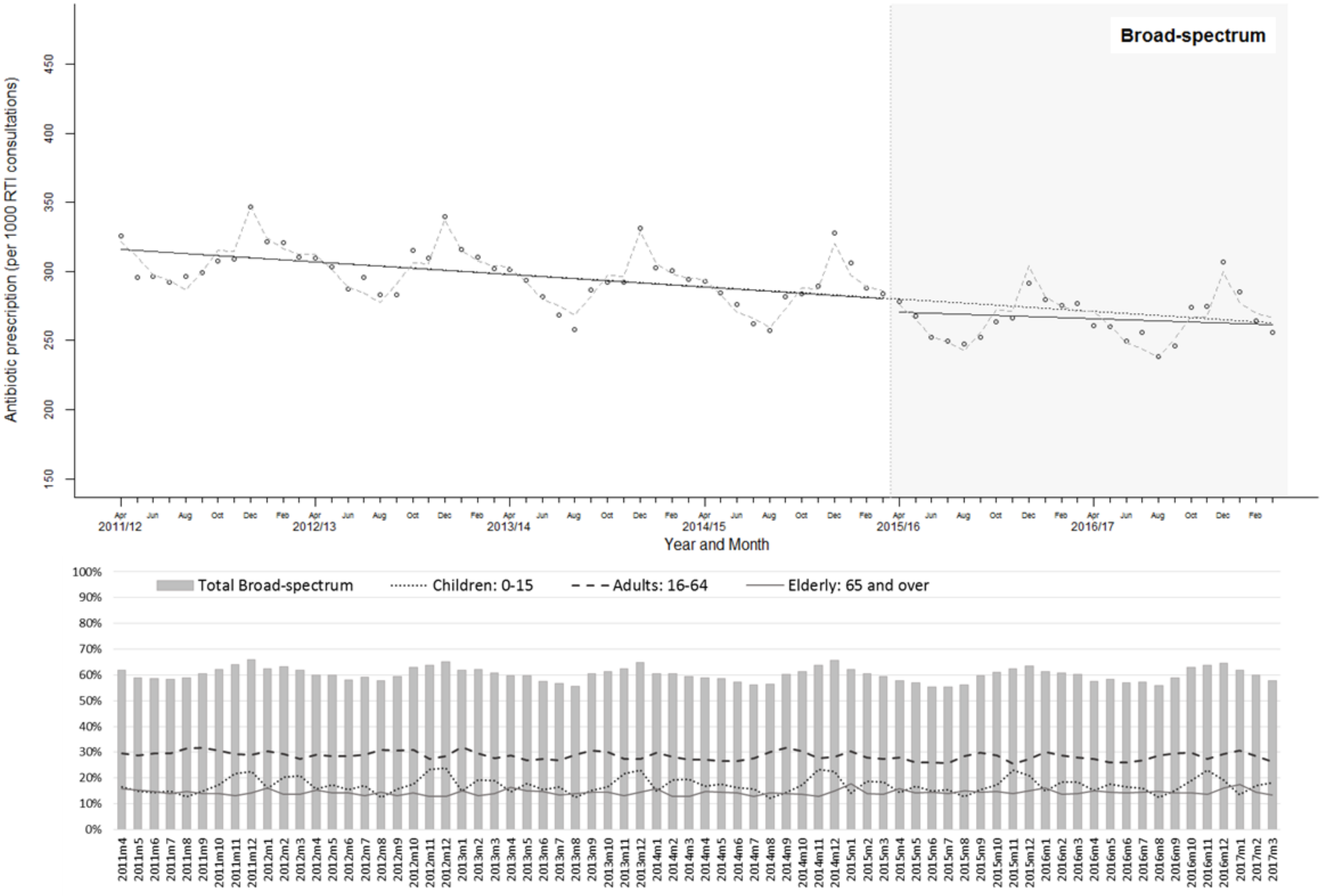

Figure 3: Interrupted time series analyses of Antibiotic prescription rate for RTI consultations in England, April 2011 to March 2017, for A) children, B) adults, C) the elderly

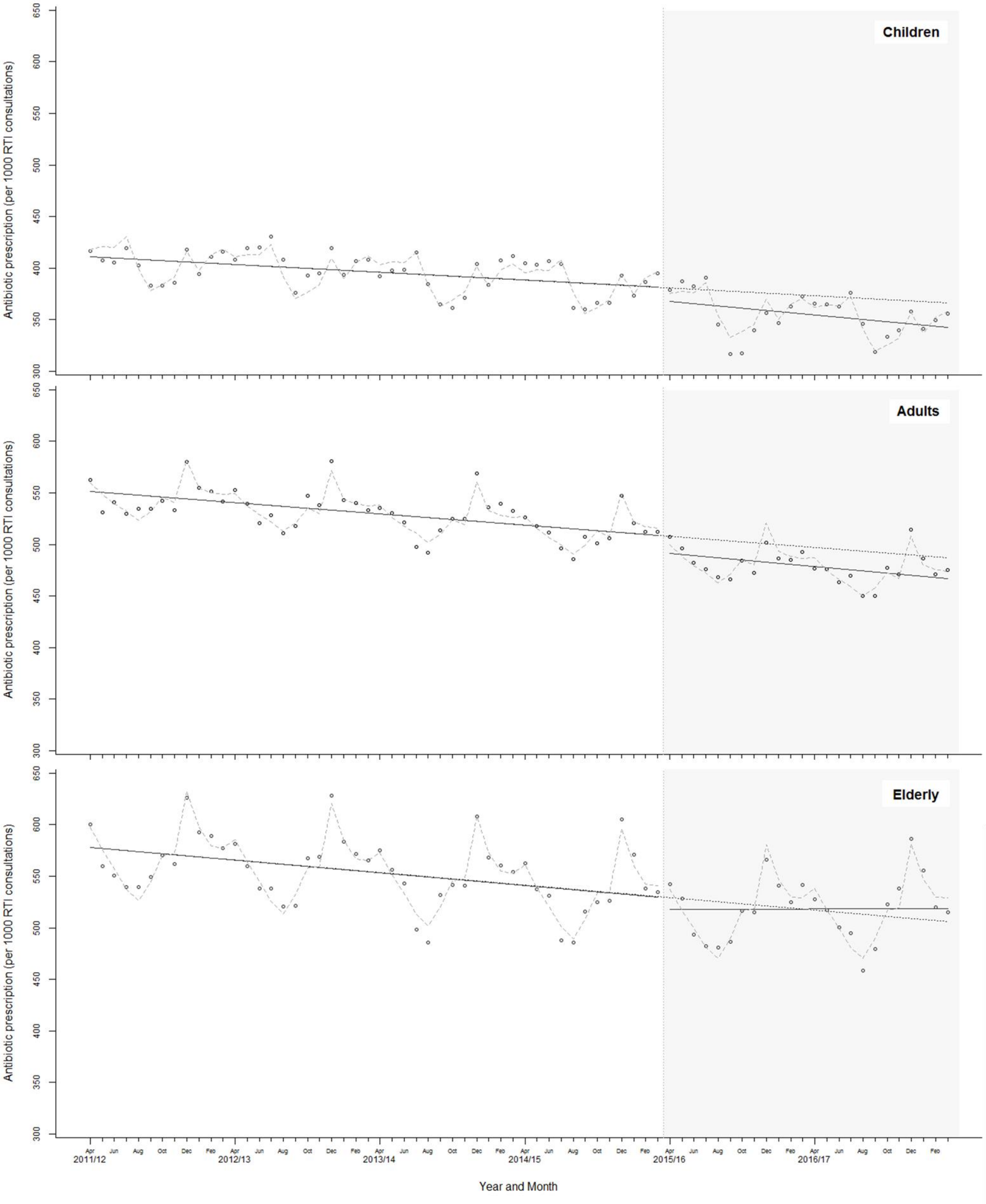

Figure 4: Antibiotic prescription rate for RTI consultations stratified by infection group, April 2011 to March 2017