

# Impact of Chief Medical Officer Activity on Prescribing of Antibiotics in England - An Interrupted Time Series Analysis

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**Short title:** Impact of CMO Activity on Antibiotics in England

## **Abstract**

### **Background**

Antimicrobial resistance is a growing problem, with the need for “strong action” highlighted by the UK Chief Medical Officer in 2013, along with a 5-year antimicrobial resistance strategy.

### **Objectives**

Five years on, we set out to determine if there was a measurable impact from the 5 year antimicrobial resistance strategy on overall antibiotic prescribing in NHS primary care in England.

### **Methods**

We calculated the volume of antibiotic prescription items using annual prescription cost analysis data from 1998-2016, and monthly prescribing data from October 2010 to June 2018. Antibiotic prescribing rate was calculated using an age and sex adjusted denominator (STAR-PU). We conducted interrupted time series analysis to measure any change in prescribing rate after the intervention.

### **Results**

After several years with a stable rate of antibiotic prescribing, there was a downward change in gradient after 2013: -46.4 items per 1000 STAR-PU per year; (95% confidence interval: -61.4 to -31.3). The prescribing rate dropped from 1,378 per 1000 STAR-PU per year in 2013, to 1,184 in 2017, representing a 14.1% reduction. The reduction is similar in monthly data (16.4%).

Assuming causality, when compared to predicted prescribing if the rate of prescribing had continued at the pre-2013 trend, we estimate that 9.7m antibiotic prescriptions were prevented over the past year by the 5 year antimicrobial resistance strategy.

### **Conclusions**

Though we cannot firmly attribute causality for the reduction in prescribing to the 5 year antimicrobial resistance strategy, the magnitude and timing of the change are noteworthy; the substantial change followed a long period of relatively static antibiotic prescribing.

## **Introduction**

Antimicrobial resistance has been described as “one of the most significant threats to patients’ safety worldwide”.<sup>1</sup> Primary care prescribing accounts for the majority of healthcare antibiotics (86.3%),<sup>2</sup> with between 8.8% and 23.1% of these prescriptions estimated to be inappropriate.<sup>3</sup> Higher antibiotic consumption has been shown to be associated with increased incidence of resistant infections.<sup>4</sup>

In 2013 the Chief Medical Officer for England (CMO) highlighted the need for “strong action” in 2013,<sup>5</sup> along with a 5-year Antimicrobial Resistance Strategy.<sup>6</sup> These include optimising prescribing practice by reducing unnecessary prescribing; and ‘better access to and use of surveillance data’. In line with this, we run an openly accessible and publicly funded service (OpenPrescribing.net) that facilitates detailed exploration of NHS England prescribing data by practice and by month, with four measures of antibiotic prescribing written to reflect national guidelines<sup>7</sup> including: the number of antibiotic items prescribed per STAR-PU (Specific Therapeutic group Age-sex Related Prescribing Units, population adjusted for likelihood of antibiotic prescribing by age group and gender); the proportion of antibiotic prescriptions that are broad-spectrum; and two measures on urinary tract infection (UTI) prescribing.

Five years on from the initiation of the antimicrobial resistance strategy, we set out to determine if there was a measurable impact from the antimicrobial resistance strategy on overall antibiotic prescribing in NHS primary care in England, using Interrupted Time Series Analysis (ITSA).

## Methods

### *Data Sources and Preparation*

We analysed routinely collected annual Prescription Cost Analysis data, aggregated nationally from 1998 to 2017,<sup>8</sup> and monthly primary care prescribing data, published by NHS Digital, from October 2010 to June 2018.<sup>9</sup> We used this combination of databases, as Prescription Cost Analysis data provides long term data back to 1998, but is aggregated annually, while the NHS Digital data provides monthly data, but for a shorter period.

### *Annual national-level data*

The annual Prescription Cost Analysis datasets contain one row for each treatment and dose, for all items dispensed in community settings in England, describing the number of prescriptions dispensed and the total cost. Data were processed as previously described.<sup>10</sup> Briefly: data for each year between 1998 and 2017 were compiled, corrected for changes in drug names, spellings and classifications over time.

### *Monthly data*

The monthly prescribing datasets from NHS England contain one row for each treatment and dose dispensed, in each prescribing organisation in NHS primary care in England, describing the number of prescriptions issued.

### *Analysis*

For both datasets, antibiotic prescribing rate was calculated using a pre-existing standardised population denominator adjusted for age and sex structure according to propensity to use antibiotics ("Specific Therapeutic group Age-sex Related Prescribing Unit" (STAR-PU)).<sup>11</sup> This method also adjusts for changes over time in the population of antibiotic users. The data also contained most non-GP community prescribing (e.g. out-of-hours services). We conducted interrupted time series analysis to determine whether there was a measurable change in national antibiotic prescribing rate after the antimicrobial resistance strategy. For the monthly data, we adjusted for seasonality by including each calendar month as an independent variable in the model. We set the 'intervention' date as June 2013. We used the Stata 'itsa' module, which produces Newey-West standard errors for coefficients estimated by ordinary least-squares regression.<sup>12</sup> Gradients of the resulting regression lines were reported, as annual changes in items per 1000 STAR-PU per year. For the monthly data, to more easily visualise any change, seasonal variation was smoothed using LOWESS regression.<sup>13</sup>

### *Number of Prescriptions Prevented*

We modelled the “number of prescriptions prevented” as follows: we predicted the expected rate of prescriptions for each month in the period July 2017 to June 2018 using the pre-2013 trend; we then applied this rate to the populations for July 2017 to June 2018 to generate an expected rate of prescriptions during this period; we then subtracted the observed number of prescriptions for the same time-period.

#### *Data and Code*

Data were extracted using SQL in Google BigQuery and Python. ITSA was carried out using Stata 13. Full details and code for data management and analysis can be found in Figure<sup>14</sup>.

## Results

### *Absolute number of antibiotic prescriptions*

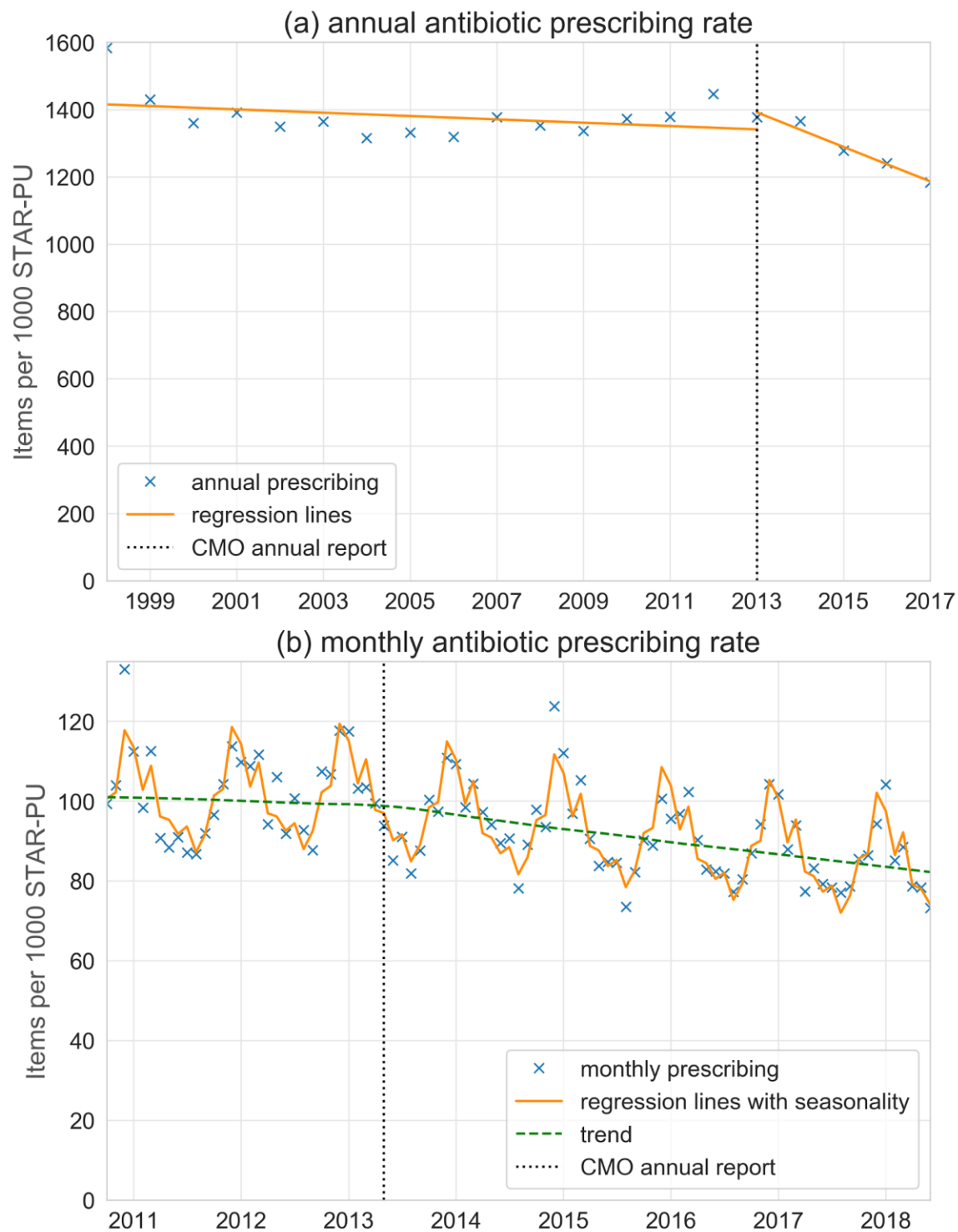
The absolute number of annual antibiotics prescriptions ranged from 36.5m (in 2004) to a maximum of 43.3m (in 2012). There was then a decrease of 14.4% in the number of antibiotic prescriptions between 2012 and 2017, to 37.1m. This was against a background of increasing population size.

### *Interrupted Time Series Analysis*

Prescribing rates, along with ITSA regression results are presented in Figure 1. In long-term annual data we found that, despite some undulation, antibiotic prescribing rates between 1998 and 2012 were stable (annual change: -5.0 items per 1000 STAR-PU per year; 95% CI: -17.0 to 7.1). Following the 2013 intervention there was a downward change in gradient: -46.4; (CI: -61.4 to -31.3). Overall the annual antibiotic prescribing rate (Figure 1a) dropped by 14.1%, from 1378 per 1000 STAR-PU per year in 2013, to 1184 in 2018.

A similar picture is seen in the monthly data: before the intervention, antibiotic prescribing was stable (annual change: 9.9 items per 1000 STAR-PU per year; CI: -22.0 to 41.7). After the intervention there was, again, a downward change in gradient (-48.5; CI: -81.0 to -15.9). Overall the smoothed monthly antibiotic prescribing rate (Figure 1b) dropped from 99.0 per 1000 STAR-PU per month in April 2013, to 82.7 in April 2018: a 16.4% reduction.

Figure 1: Total prescribing rate of antibiotics per STAR-PU over time, for annual rates (a) and monthly rates (b). Regression curves are derived from the interrupted time series analysis, and the trend line in (b) is calculated using locally weighted scatterplot smoothing (LOWESS).



### *Number of Prescriptions Prevented*

The expected rate of prescriptions for each month in the period July 2017 to June 2018 was calculated using the pre-2013 trend. This rate was applied to the populations for July 2017 to June 2018, yielding an expected number of prescriptions of 48.4m. The observed number of prescriptions for this period was 38.7. The modelled number of prescriptions prevented was therefore 9.7m, meaning an estimated 20.0% fewer prescriptions than if the pre-2013 trend had continued.



## Discussion

### *Summary*

Using annual and monthly data we found reductions of 14% and 16% respectively in the rate of antibiotic prescribing during the 5 years since publication of the 5 year antimicrobial resistance strategy. Results were reassuringly similar when comparing the two datasets from different sources.

### *Interpretation*

Although we cannot firmly attribute causality between the reduction in prescribing and the intervention, the magnitude and timing of the change are noteworthy. The change followed a long period of relatively static antibiotic prescribing up to 2013, after which a substantial reduction in prescribing has taken place. We estimate that, had the rate of prescribing continued on its pre June 2013 trend, an additional 9.7m antibiotic prescriptions would have been dispensed.

It is therefore plausible that the intervention, alongside many other efforts, has led to a reduction in prescribing of antibiotics. Alternative explanations might include a reduction in the need for antibiotics, for example from fewer patients presenting with infections; however we are not aware of any evidence for a substantial change in demand.

### *Strengths and Limitations*

By using the STAR-PU population denominator, we were able to adjust for changes in population size, age and gender balance over time. The ITSA method used here otherwise assumes that trends are linear and unaffected by any stimuli other than the intervention under investigation.<sup>15</sup> Interrupted time series analysis has been used extensively to monitor the impact of population-level policy interventions,<sup>16–19</sup> including those related to antibiotic resistance.<sup>20</sup>

A key strength of our analysis is that it covers the complete data for all prescription items dispensed in England, not a sample. A theoretical weakness of our analysis is that our dataset does not include detailed data on diagnosis and indication for each individual patient's prescription; however, there is no national dataset of patient-level data; and available datasets such as CPRD are a subset of the population, with data on diagnosis or indication for individual patients and prescriptions commonly absent. We were unable to measure prescribing in secondary care; however the majority of antibiotics are prescribed in the community.<sup>2</sup> It is possible that there may have been other factors influencing antibiotic prescribing, such as other

antibiotic prescribing initiatives and changes in demand. However we are aware of no large initiatives, nor substantial secular changes in prevalence of conditions that would provide an alternative explanation for the large and sustained changes observed in prescription rates at population level.

### *Conclusions*

National strategic public health interventions are an important and potentially effective way to modify clinical practice. The CMO report and Antimicrobial Resistance Strategy appears to have had a substantial impact on prescribing of antibiotics at population level in England.

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