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Social norm feedback reduces primary care antibiotic prescribing in a regression discontinuity study

Running title: Social norm feedback to high antibiotic prescribers

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Abstract

Background

Reducing antibiotic prescribing is a priority for health authorities responsible for preventing antimicrobial resistance. Northern Ireland has high rates of antimicrobial use. We implemented a social norm feedback intervention and evaluated its impact.

Objectives

To estimate the size and duration of the effect of a social norm feedback letter to general practitioners (GPs) who worked in the 20% of practices with the highest antimicrobial prescribing.

Methods

The letter was sent in October 2017 to 221 GPs in 67 practices. To assess the effect of the intervention, we used a sharp non-parametric regression discontinuity (RD) design, with prescribing rates in the four calendar quarters following the intervention as the outcome variables.

Results

In the quarter following the intervention (October to December 2017) there was a change of -25.7 (95% CI -42.5 to -8.8, *P* = 0.0028) antibiotic items per 1,000 Specific Therapeutic group Age-sex Related Prescribing Units (STAR-PU). At one year, the coefficient was -58.7 (95% CI -116.7 to -0.7, *P* = 0.047) antibiotic items per 1,000 STAR-PU. The greatest change occurred soon after the intervention. Approximately 18,900 fewer antibiotic items were prescribed than if the intervention had not been made (1% of Northern Ireland's annual primary care antibiotic prescribing).

Conclusions

A social norm feedback intervention reduced antibiotic prescribing in the intervention practices. The diminishing effect over time suggests the need for more frequent feedback. The RD method allowed measurement of the effectiveness of an intervention that was delivered as part of normal business, without a randomised trial.

Introduction

Unnecessary antibiotic consumption increases the risk of antimicrobial-resistant infections, *Clostridium difficile* infection and adverse drug reactions.[1,2] A global effort is underway to reduce antibiotic use.[3] Northern Ireland has high antibiotic consumption compared to the rest of the United Kingdom (UK).[4,5] Around 85% of antibiotics used in the publicly-funded Health and Social Care service (HSC) are prescribed in primary care.[4] Following the recent Review of Antimicrobial Resistance, the UK Government aims to reduce inappropriate antibiotic use by 50% by 2020.[6,7] The Northern Ireland Department of Health committed to this goal and HSC introduced measures to reduce antibiotic use.[7] These included promoting the TARGET toolkit for primary care[8,9] and the Start Smart then Focus guidance for secondary care,[10] providing ward-level antibiotic prescribing feedback through a dashboard, funding general practices to identify an antibiotic champion, piloting near-patient C-reactive protein testing, introducing the e-Bug education programme and targets for the reduction of antibiotic use.[5] Since 2017 all general practices in Northern Ireland also had access to a practice-based pharmacist, whose role included antibiotic stewardship. Evaluating the effect of any single intervention is challenging in the context of such activities and secular and seasonal changes.

Behavioural science can be an important tool to address inappropriate antibiotic prescribing.[11] It has successfully influenced decision-making, often in low-cost, relatively simple environmental changes (‘nudges’) that facilitate desirable behaviours without forbidding choices.[12] Providing descriptive social norm feedback is an example of a nudge and has been shown to change behaviour in a variety of settings including

college drinking,[13] food choice,[14] hotel linen re-use[15] and littering.[16] Recently, it has been shown to reduce inappropriate antibiotic prescribing in primary care.[17,18]

In a 2014 trial, a letter signed by the Chief Medical Officer (CMO) for England was sent to general practitioners (GPs) who worked in practices in the top 20% for prescribing antibiotics in England.[18] The letter stated that the practice's antibiotic prescribing was higher than 80% of practices in its area. It was designed so that a simple and striking message was supported by information about steps that could be followed to address prescribing.[18,19] The letter was associated with a 3.3% relative reduction in antibiotic prescribing in the intervention practices. Patient-focused campaign materials tested in the same trial had no effect.[18] A similar intervention tested in a randomised trial in Australia targeted the highest 30% of individual prescribers of antibiotics and demonstrated a 9-12% reduction in antibiotic prescribing in the 6 months following the feedback letter.[20] A randomised trial carried out in the United States showed that peer comparison feedback delivered by email significantly reduced inappropriate antibiotic prescribing.[17] In Northern Ireland, routine information about practice-level antibiotic consumption with peer comparison was already available to practices through a routine quarterly report consisting of tables and charts. In light of recent successful interventions elsewhere that provided this feedback more directly to individual prescribers in formats informed by behavioural science, we adopted the same social norm feedback approach used in England for use in Northern Ireland and evaluated the effect size and duration using regression discontinuity (RD) design, which has comparable robustness to a randomised trial, and is suited to interventions delivered on the basis of a threshold value.[21–24]

Methods

Ethics

This intervention was part of normal service, and this study was a service evaluation that did not require research ethics approval according to UK Health Research Authority guidance.

Intervention assignment and outcome measurement

The intervention assignment was made at general practice level on the basis of practices being in the highest prescribing 20% by standardised total antibiotic prescribing rate between 1 July 2016 and 30 June 2017. The total amount of antibiotics (medicines from the British National Formulary Chapter 5, Section 1) prescribed (measured in items issued) was obtained from the Electronic Prescribing Database (EPD) as part of normal HSC business intelligence. The EPD records all dispensed medications paid for by the HSC service in primary care. The prescribing was standardised to give a rate per 1,000 Specific Therapeutic group Age-sex Related Prescribing Units (STAR-PUs).[25] STAR-PU is an age and gender-weighted population that allows comparison between general practice populations. The weights were derived by the Northern Ireland Department of Health for the age and gender composition of the Northern Ireland population and are therefore not directly comparable to those used in England. The STAR-PU for each practice was provided by the Department of Health for April 2018 (the mid-point of the follow-up period).

The outcome measures were the standardised total antibiotic prescribing rates after intervention (1 Oct 2017 to 31 Sept 2018) for the main outcomes of the study and

between intervention assignment and the intervention (1 July to 30 September 2017) for a sensitivity analysis.

Intervention Procedure

We used the English social norm feedback ‘nudge’ letter with minimal changes. The letter was signed by Northern Ireland’s CMO, Dr Michael McBride, and sent on behalf of the Northern Ireland Department of Health to every GP in the top 20% antibiotic prescribing practices between 1 July 2016 to 30 June 2017. The Health and Social Care Board (the commissioner for general medical services) identified the named individual GPs who worked in the intervention practices so that they could be written to directly. There was no pre-announcement of the intervention. The letters were posted to each GP on 9 October 2017. The measures of antibiotic prescribing used in this study were for whole practices, not individual prescribers, though the feedback was addressed to the individual GPs in each practice.

Study participants

At the time of the intervention, there were 338 general practices in Northern Ireland. The letter was sent to 221 GPs who worked in the 67 practices with the 20% highest standardised antibiotic prescribing rates between 1 July 2016 to 30 June 2017. We did not attempt to control for the movement of intervention or control GPs between practices during the follow-up period related to mergers, closures and normal staff recruitment.

Statistical methods

Regression discontinuity analyses

We used a RDdesign to assess the effect of the intervention. RD studies estimate the treatment effects in non-experimental settings where the intervention is chosen on the basis of a threshold of an assignment variable.[21,22] RD requires mild assumptions and causal inference is more credible than in other natural experiment methods.[22,26] We used this method to take advantage of the threshold that determined whether practices received the intervention. For practices near to the threshold, whether or not they received an intervention was "as good as randomised."[22]

Analyses were conducted in *R* version 3.5.1.[27] For analysis, the assignment variable was centred to make the threshold equal to 0 antibiotic items per STAR-PU by subtracting 1,173 antibiotic items per 1,000 STAR-PU, which was equivalent to the top 20% antibiotic prescriber threshold. We plotted a smoothed histogram and used the McCrary test[28] in *rddtools* version 0.4.0 to check for density discontinuities in the assignment variable that would suggest practices could manipulate their rank precisely.[29] We drew scatter plots with fitted Loess regression lines either side of the threshold to visualise the relationships between the assignment and outcome variables.[30]

We used the sharp RD method as the assignment variable was perfectly associated with intervention status. We used the Imbens and Kalyanaraman (IK) 2012 method for bandwidth selection in *rddtools*.[31] We used a non-parametric local linear regression design with a triangular kernel. Significance was accepted at $P < 0.05$. The pre-intervention total antibiotic dispensing rate was the assignment variable, and the post-intervention rates were the outcome variables. We conducted analyses for each quarter

of follow-up data separately, and for the time range from the intervention (at the start of October, 2017) to the end of each quarter for the following year.

Sensitivity analyses

We performed a 'placebo' analysis of alternative thresholds, and we plotted the local area treatment effect (LATE) against bandwidth to investigate the effects of bandwidth selection on the effect estimate.

To ensure that the coincidental merging of some practices around the time of the intervention did not influence the results, we repeated the RD analyses with the exclusion of seven practices that had merged with another practice during the pre- or post-intervention period (Sensitivity Analysis A). The practices that closed during the study (and which therefore were missing follow-up data) were excluded from all analyses. We conducted a further sensitivity analysis (Sensitivity Analysis B) excluding one practice whose antibiotic prescribing decreased markedly in the follow-up period.

As a further sensitivity test (Sensitivity Analysis C), we performed the RD analysis using the antibiotic prescribing rate in the quarter July 2017 to September 2017 (before the intervention) as the outcome variable. The aim of this analysis was to identify whether the results might be susceptible to any confounding, such as by other routine measures to improve antimicrobial stewardship.

Estimates of change in prescribing and costs

We interpreted the RD estimate as a weighted average treatment effect, as described in Lee and Lemieux.[22] The STAR-PU weights based on the registered population for each general practice (i.e. the weighted registered population) at 1 April 2018 were provided

by the Department of Health, Northern Ireland. The number of antibiotic prescriptions avoided was estimated by multiplying the effect estimate from the RD analyses (total antibiotic items per 1,000 STAR-PU) by sum of the STAR-PU weighting for the intervention practices and dividing by 1,000.

To estimate the approximate cost of each antibiotic item avoided, we investigated the change in antibiotic consumption in the year before and after the intervention for the 65 intervention practices using data from the OpenDataNI website.[32] We calculated the average actual cost per item, at the October 2017 to September 2018 prices, of antibiotics which showed a reduction in consumption and applied this average cost to the reduction due to the intervention. This approximation relies on the assumption that the cost of antibiotics not prescribed as a result of the intervention had a similar mean cost to those that were generally less frequently prescribed in the post-intervention period than in the pre-intervention period.

When estimating the change in number of prescriptions and cost in sensitivity analyses, in order to allow comparison with the main analysis, the effect rate estimate was multiplied by the sum of the denominator for all 65 intervention practices. This therefore assumes that the excluded practices experienced the average treatment effect.

Results

Data were available from 331 practices for the full follow-up period (65 practices that received the letter and 266 practices that received no intervention). Attrition was due to the merging and closure of practices. Approximately 18% of the Northern Ireland registered population was registered at intervention practices, and these practices prescribed approximately 24% of antibiotic items dispensed (Table 1).

The assignment variable showed no evidence of discontinuous density (Figure S1; p=0.46).[28] This indicates that there was no precise manipulation of the assignment variable that could make the RD design inappropriate. Inspection of a scatter plot of the assignment variable and the outcome variable (Figure 1) and the RD binned average plot (Figure 2) in October to December 2017, immediately following the intervention, reveals a step change with the intervention. Less pronounced steps are visible in the subsequent calendar quarters individually and in the full time-period of follow-up (Figure S2 and Figure S3).

In the first quarter following the intervention (October to December 2017), there was a change of -25.7 (95% CI -42.5 to -8.8, *P* = 0.0028) antibiotic items per 1,000 STAR-PU (Table 2). Plots of the LATE against bandwidth with 95% CI shows that the bandwidth selected by the IK method was conservative (Figure S4). A sensitivity analysis using 'placebo' thresholds with the IK-selected bandwidth showed no evidence of alternative thresholds existing (Figure S5).

With each subsequent quarter, the coefficient increased by a diminishing amount, to -58.7 (95% CI -116.7 to -0.7, *P* = 0.047) antibiotic items per 1,000 STAR-PU after one year. In the final three quarters of follow-up, none of the individual calendar quarters

showed a significant change in antibiotic prescribing rate from the pre-intervention period, though in incremental time periods, the overall change in the antibiotic prescribing rate was detected (Table 2). In sensitivity analyses A (excluding practices that experienced mergers) and B (excluding one practice that showed marked improvement following the letter), the pattern of results were similar (Table S1 and Table S2). Sensitivity Analysis B showed that without one practice that improved markedly following the intervention, the cumulative effect was detectable only up to 6 months of follow-up.

An analysis using the same assignment variable time period but the pre-intervention antibiotic prescribing rate in July 2017 to September 2017 as the outcome (Sensitivity Analysis C) showed no effect associated with the threshold (effect estimate 0.0, 95% CI -13.0 to 13.0, *P* = 1; Figure S6 and Table S3). This supports the interpretation that the change following the intervention was due to the intervention itself and not due to any other programme of prescribing support for practices. RD bandwidths and numbers of observations included are reported in Table S4.

Interpreting the RD estimate as the weighted average treatment effect,[22] at the end of one year's follow-up, approximately 18,938 fewer antibiotic items had been prescribed due to the intervention.

During the year of follow-up, there was an overall reduction in antibiotic prescribing of 21,849 items compared to the previous year in the intervention practices (Table S5), though some antibiotics were prescribed more frequently due to changes in guidance and practice (for example, pivmecillinam). Antibiotics that had a reduced rate of prescription (i.e. excluding those antibiotics with increased rates of use) had a mean

cost of £3.09 per item. If the 18,938 antibiotic items avoided due to the intervention followed the same pattern of reduction as in the general reduction, the cost avoided of the antibiotics *not prescribed* was approximately £58,500.

Discussion

Reducing inappropriate antibiotic prescribing is a complex challenge that requires understanding of the factors underlying prescribing behaviours and the design of interventions for behaviour change that are easy, attractive, social and timely.[19] We found that a social norm feedback intervention, previously successful in England,[18] also worked in Northern Ireland.

A 59 item per 1,000 STAR-PU reduction over one year is approximately a 5% reduction in standardized prescribing rates for practices close to the cut-off threshold. The reduction in antibiotic prescribing by approximately 19,000 antibiotic items represents approximately a 4.6% reduction in antibiotic prescribing by the intervention practices and a 1% reduction in Northern Ireland's primary care antibiotic prescribing. This is a considerable contribution to reducing antibiotic use. Approximately £58,500 less was spent by the health service on antibiotics due to the intervention in the year of follow-up. The effect that we observed was comparable to that reported by Hallsworth *et al.*.[18] The largest reductions were in amoxicillin, ciprofloxacin, clarithromycin, co-amoxiclav, trimethoprim and erythromycin. Ciprofloxacin and co-amoxiclav are among the '4C' antibiotics that increase the risk of *Clostridium difficile* infection.[33] Resistance to co-amoxiclav in Gram-negative bloodstream infections has increased markedly in recent years, so this reduction in consumption is welcome.[20]

The effect of the intervention appeared to wane over the course of the year, which is an important finding. The diminishing effect could be supposed to relate to the more opportunities to prescribe appropriately that the annual influenza season presents, but the main intervention effect was seen before influenza was circulating.[34] It seems likely

that the feedback became less pressing to prescribers over time. This finding could be used to test variations on the ‘dosing schedule’ in future interventions. We will be interested to observe whether future ‘doses’ maintain their effectiveness.

A feedback intervention offers several advantages over traditional, more complex, face-to-face interventions. The cost of the intervention was very low, amounting to the cost of preparing and posting letters, as well as a modest amount of person-time from our teams in planning, delivering and evaluating the effects of the intervention. Second, a feedback letter does not make further demands on GPs’ time. Finally, a letter can easily be repeated and adapted to future contexts.

The measurable success of this intervention is welcome, as it is often difficult to be certain that any one policy intervention has had an effect, given the lack of randomisation, and in a context of seasonal variation, regression to the mean and numerous potentially confounding initiatives. We have shown that the RD design can be effectively used for healthcare policy interventions that are delivered based on meeting a threshold.[23] This robust method gives easily interpretable effect estimates. RD could be used for the monitoring and evaluation of existing interventions where it would not be appropriate to repeat randomised trials, but where other use of other observational methods would be complicated by confounding and bias.

One drawback of the RD design is that it has less power than a randomized trial.[35] Another issue with the conduct of RD studies is the large number of different choices that can be applied when selecting bandwidth or kernel, which could impact on the effect size and significance.[27] We chose to use the widely used standard RD methods of non-parametric regression, IK-bandwidth and triangular kernel, and we conducted

sensitivity analyses to demonstrate that our choices were reasonable. In the RD literature, there is debate about generalising the RD estimate “away from the threshold”. According to Lee and Lemieux, in the presence of heterogeneous treatment effects, the discontinuity gap can be interpreted as a weighted average across *all* observations, with observations closest to the threshold being weighted most heavily.[22] We have used this assumption to estimate the overall effect of the intervention.

GPs are not the only healthcare professionals who prescribe antibiotics in primary care, and it is a limitation of this study that we were unable to target prescribing nurses, pharmacists and optometrists because details of these prescribers employed by each practice was not available to us. We do not have information about whether the intervention reduced inappropriate antibiotic prescribing, or whether any harm resulted from the intervention. There is an urgent need for much more detailed information about the indication for antibiotics prescribed, which can only be met on a population level by codified diagnostic information with prescribing data.

This intervention is an example of a low-cost, simple behavioural ‘nudge’ that policy-makers can use to effectively meet their goals without introducing new policies or rules. The use of the RD design allowed us to confirm and estimate the treatment effect in a robust study in the course of normal service delivery, and it could be applied to other public health policy interventions that are delivered based on a threshold.

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This study was carried out as part of our routine work.

Transparency declarations

We declare that we have no conflicts of interest

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Tables

Table 1. Registered patients and STAR-PU by intervention status

	Practices (n)	Practices in final analyses (n)	Registered patients at practices in final analyses 1 April 2018 (n)	STAR-PU at practices in final analyses 1 April 2018 (n)	Estimated antibiotic items dispensed by practices in final analyses 1 July 2016 to 30 June 2017 (%)	Estimated antibiotic items dispensed by practices in final analyses 1 Oct 2017 to 30 Sept 2018 (%)
Nudge letter	67	65	357,810	322,627	423,811 (23.5)	389,785 (22.9)
No intervention	271	266	1,610,472	1,451,480	1,376,167 (76.5)	1,309,658 (77.1)
Total	337	331	1,968,282	1,774,107	1,799,979	1,699,443

Table 2. Regression discontinuity analyses showing effect estimate at quarterly intervals, Oct 2017 to Sept 2018

	Individual quarters				From Oct 2017 to end of quarter			
Quarter	Coefficient (95% CI)	P	Estimated Change in Antibiotic Prescriptions	Estimated Dispensing Cost Difference	Coefficient (95% CI)	P	Estimated Change in Antibiotic Prescriptions	Estimated Dispensing Cost Difference
Oct-Dec 2017	-25.7 (-42.5 to -8.8)	0.0028	-8,275	-£25,571.17	-25.7 (-42.5 to -8.8)	0.0028	-8,275	-£25,571.17
Jan-Mar 2018	-14.7 (-36.1 to 6.7)	0.18	-4,734	-£14,628.72	-40.2 (-76.8 to -3.6)	0.031	-12,957	-£40,037.08
Apr-Jun 2018	-12.9 (-28.8 to 3.0)	0.11	-4,163	-£12,864.44	-54.2 (-101.5 to -6.8)	0.025	-17,475	-£53,997.40
Jul-Sep 2018	-3.7 (-16.2 to 8.8)	0.56	-1,196	-£3,695.59	-58.7 (-116.7 to -0.7)	0.047	-18,938	-£58,519.96

Figures

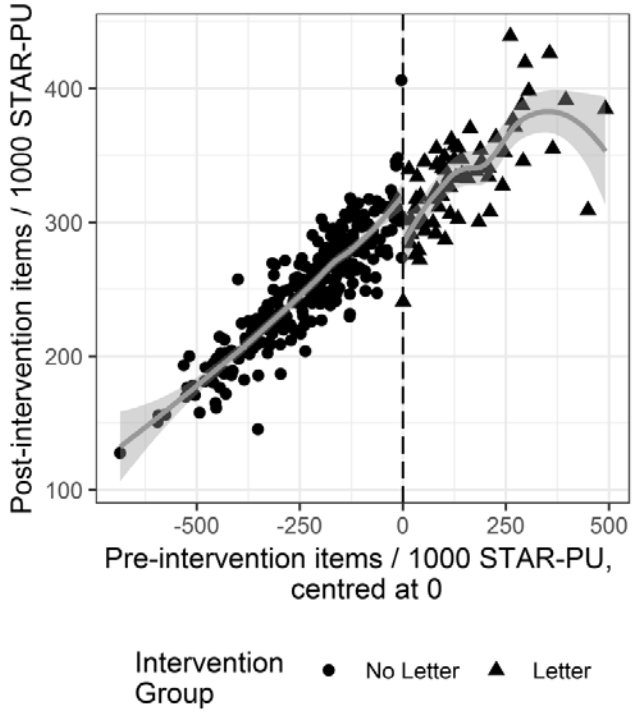

Figure 1. Scatter plot of pre-intervention total antibiotic prescribing and post-intervention antibiotic prescribing, October to December 2017

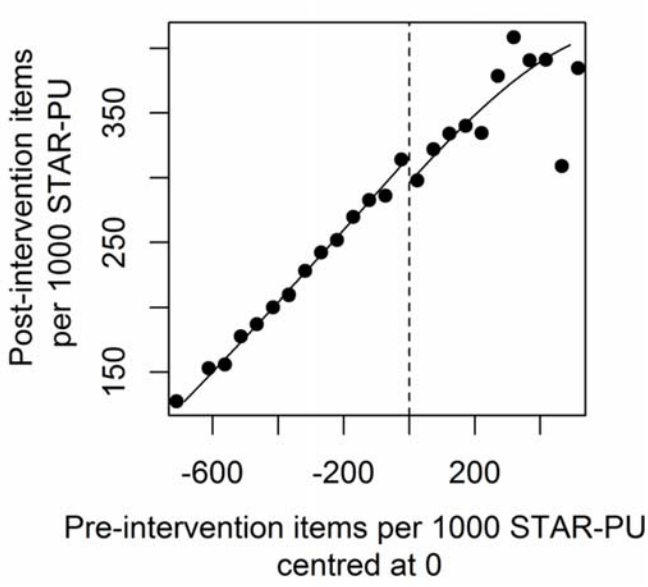

Figure 2. RD plot showing local averages of binned pre-intervention and post-intervention total antibiotics items per 1,000 STAR-PU, the intervention threshold and separate fitted regression lines, October to December 2017

Supplementary Materials

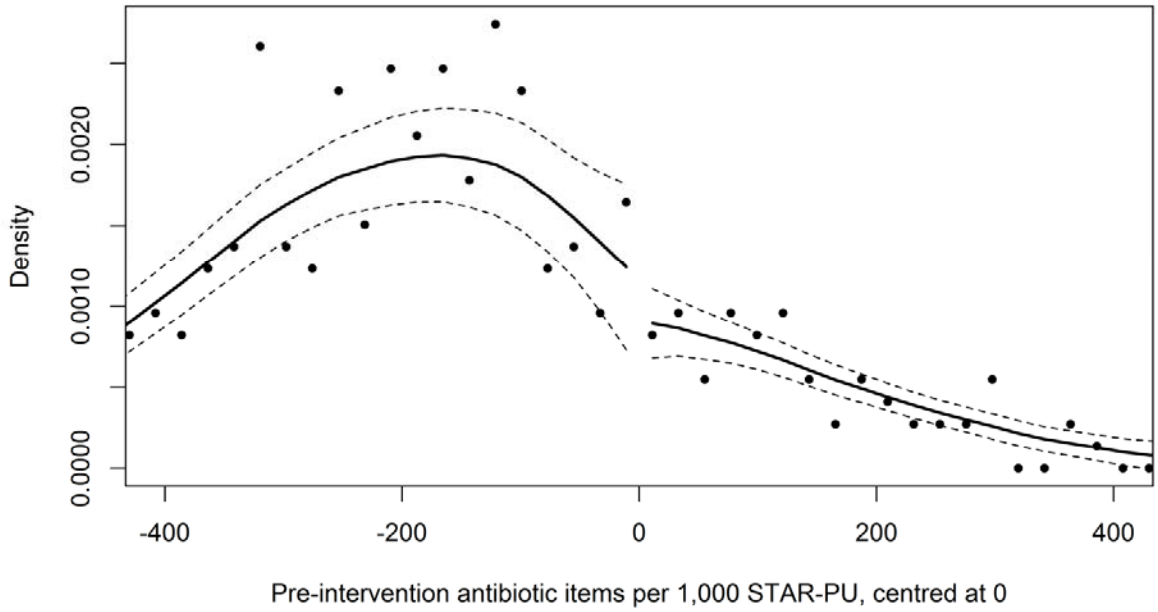

Figure S1. Smoothed histogram using binned local averages with local regression to inspect for discontinuous density.

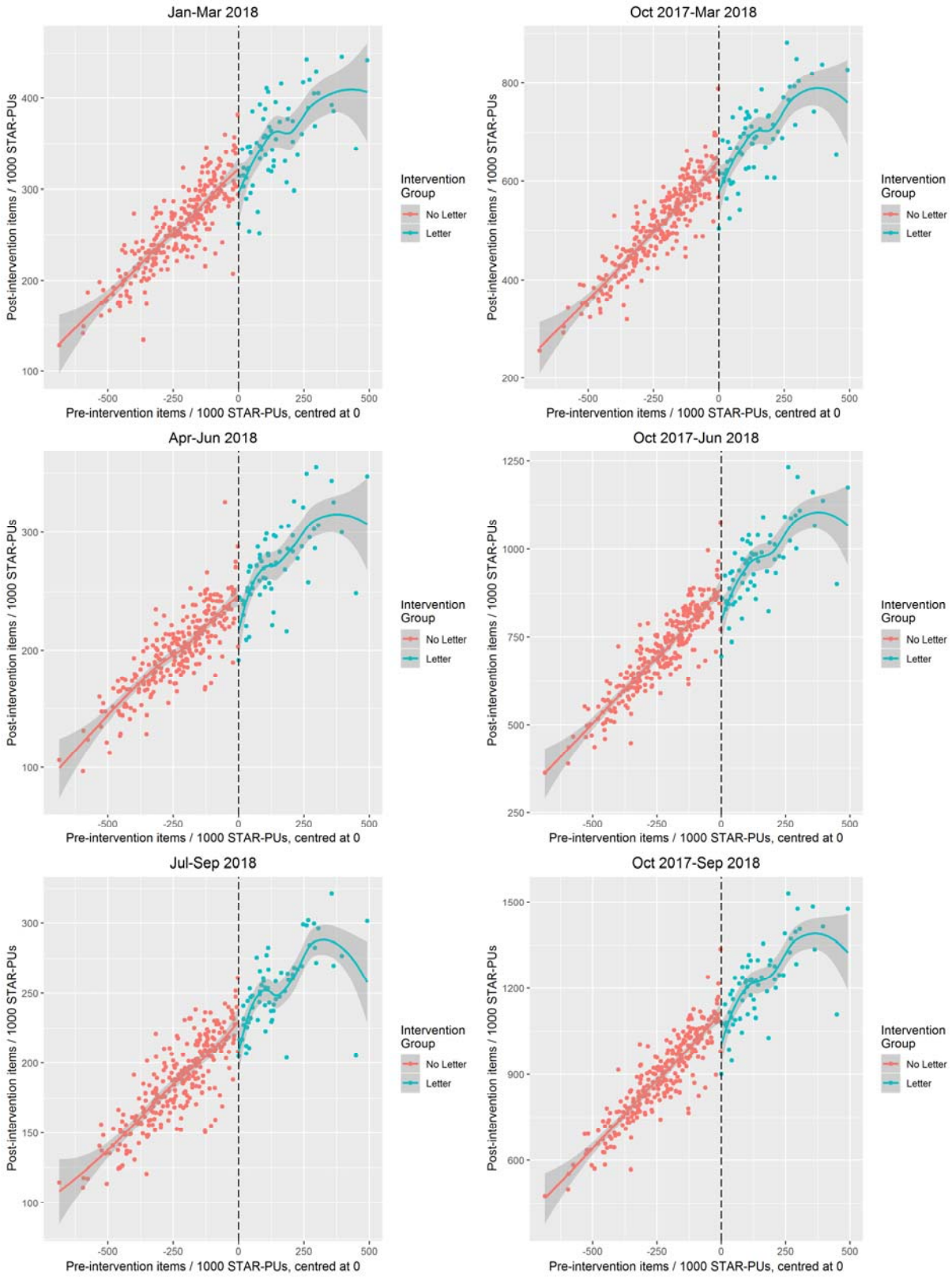

Figure S2. Scatter plots for quarters 2-4 individually and incrementally.

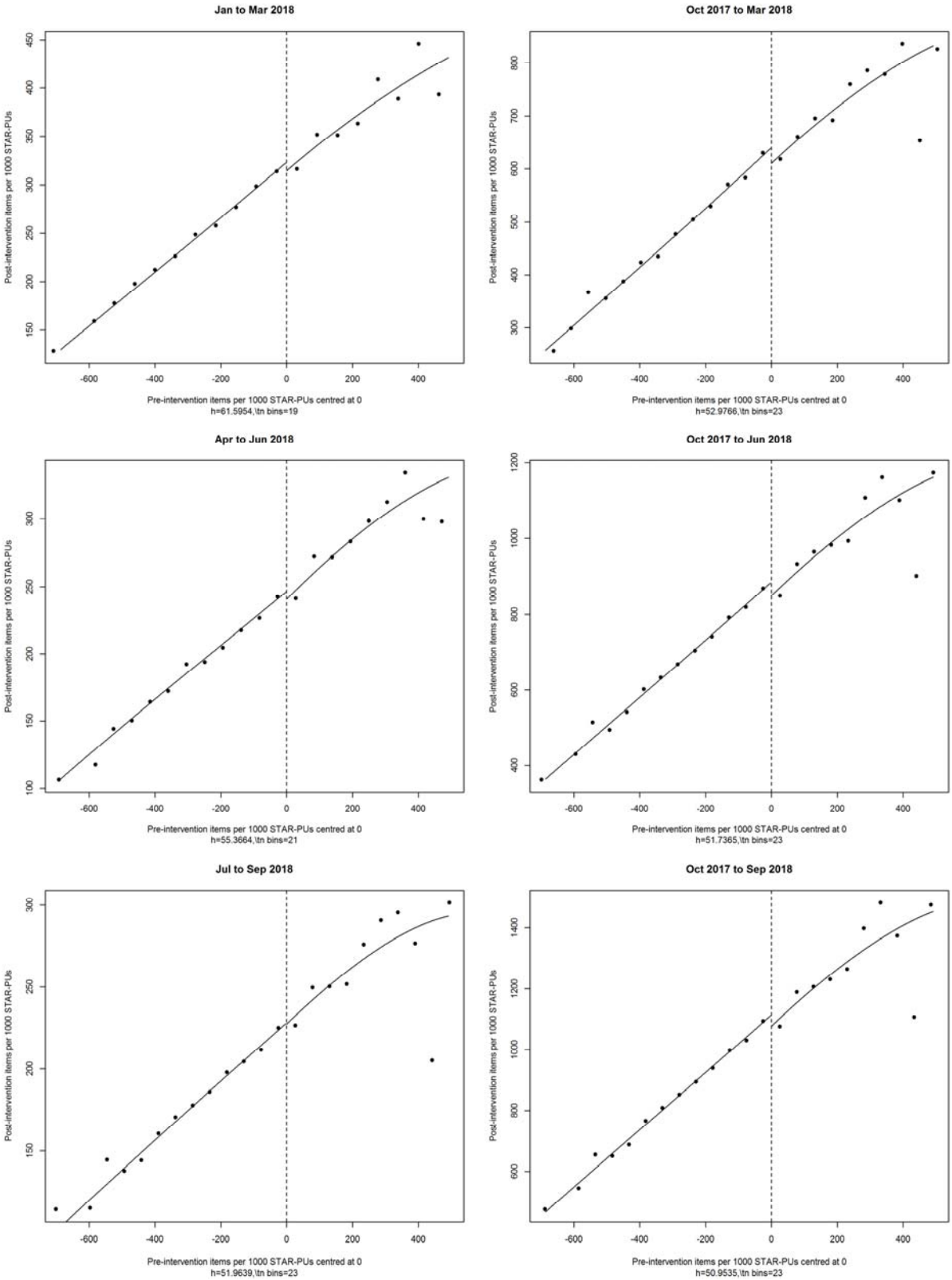

Figure S3. RD plots with binned sample means for quarters 2-4 individually and

incrementally.

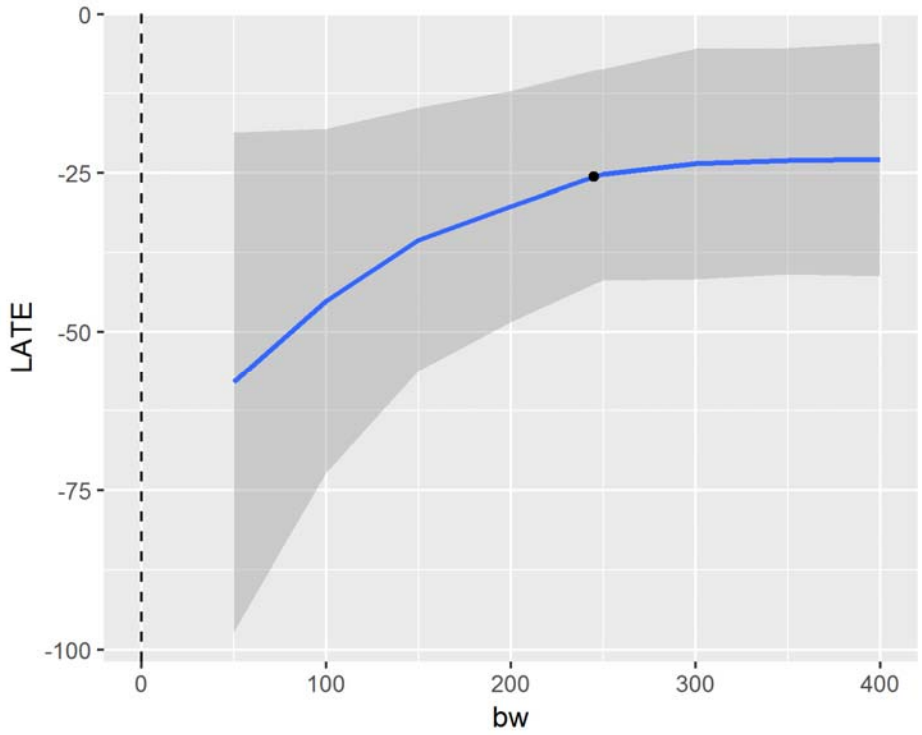

Figure S4. Plot showing coefficient and confidence limits for ‘placebo’ cut-points, using IK (2012)-selected bandwidth, for October-December 2017 follow-up period,

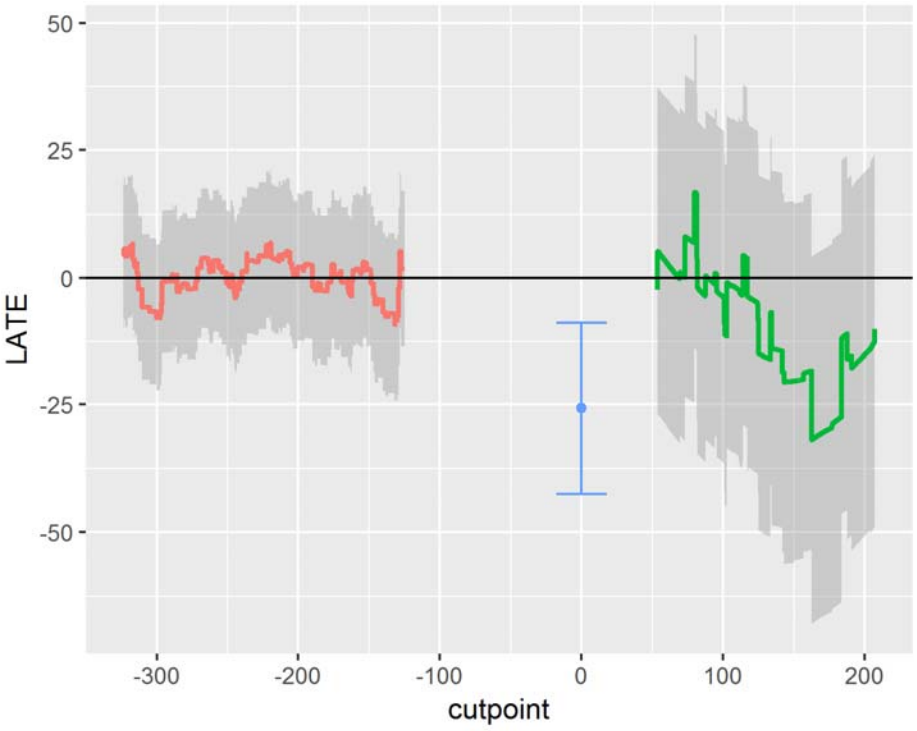

Figure S5. Plot showing coefficient and confidence limits for different bandwidth selections for October-December 2017 follow-up period

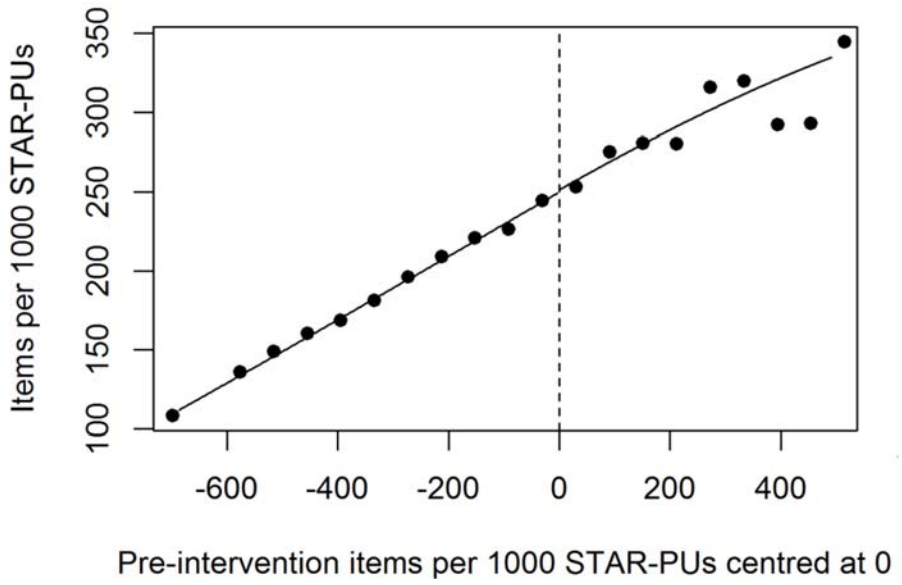

Figure S6. Sensitivity Analysis C. RD plot showing local averages of binned pre-intervention total antibiotics items per 1,000 STAR-PU, the intervention threshold and separate fitted regression lines, with a pre-intervention outcome period July to September 2017

Table S1. Sensitivity Analysis A: Excluding practices with mergers during study period

	Single quarter only				From 1 Oct 2017 to end of quarter			
Quarter	Coefficient (95% CI)	P	Estimated Change in Antibiotic Prescriptions	Estimated Dispensing Cost Difference	Coefficient (95% CI)	P	Estimated Change in Antibiotic Prescriptions	Estimated Dispensing Cost Difference
Oct-Dec 2017	-19.5 (-35.8 to -3.2)	0.019	-6295	-£19,451.07	-19.5 (-35.8 to -3.2)	0.019	-6295	-£19,451.07
Jan-Mar 2018	-16.5 (-37.5 to 4.5)	0.12	-5322	-£16,444.64	-36.8 (-72.3 to -1.3)	0.042	-11872	-£36,683.28
Apr-Jun 2018	-14.2 (-30.4 to 2.0)	0.08	-4584	-£14,166.10	-52.6 (-100.7 to -4.5)	0.032	-16970	-£52,436.56
Jul-Sep 2018	-5.5 (-18.4 to 7.4)	0.40	-1781	-£5,503.84	-59.0 (-118.0 to -0.1)	0.050	-19049	-£58,860.83

Table S2. Sensitivity Analysis B: Excluding one outlier

	Single quarter only				From 1 Oct 2017 to end of quarter			
Quarter	Coefficient (95% CI)	P	Estimated Change in Antibiotic Prescriptions	Estimated Dispensing Cost Difference	Coefficient (95% CI)	P	Estimated Change in Antibiotic Prescriptions	Estimated Dispensing Cost Difference
Oct-Dec 2017	-23.7 (-41.4 to -6.1)	0.0085	-7651	-£23,641.07	-23.7 (-41.4 to -6.1)	0.0085	-7651	-£23,641.07
Jan-Mar 2018	-12.6 (-33.5 to 8.2)	0.23	-4073	-£12,585.69	-37.4 (-74.3 to -0.5)	0.047	-12064	-£37,277.53
Apr-Jun 2018	-9.8 (-25.4 to 5.8)	0.22	-3161	-£9,768.84	-47.7 (-97.3 to 1.9)	0.06	-15390	-£47,556.45
Jul-Sep 2018	-3.0 (-16.0 to 10.0)	0.65	-982	-£3,035.28	-50.8 (-111.1 to 9.5)	0.10	-16395	-£50,661.94

Table S3. Sensitivity Analysis C: RD Analysis using data from pre-intervention time period 1 July to 30 September 2017 as the outcome variable.

Quarter	Coefficient (95% CI)	P
Jul-Sep 2017	0.0 (-13.0 to 13.0)	1.0

Table S4. RD Analysis parameters, selected by Imbens and Kalyanaraman (2012) method

Analysis	Time Period	Bandwidth	Observations left	Observations right
Main	Oct-Dec 2017	245.0	153	52
	Jan-Mar 2018	308.0	186	60
	Apr-Jun 2018	276.8	171	56
	Jul-Sep 2018	259.8	163	53
	Oct 2017-Mar 2018	264.9	167	54
	Oct 2017-Jun 2018	258.7	163	53
	Oct 2017-Sep 2018	254.8	161	53
Sensitivity A	Oct-Dec 2017	233.0	141	51
	Jan-Mar 2018	257.6	159	53
	Apr-Jun 2018	228.9	139	50
	Jul-Sep 2018	220.5	135	50
	Oct 2017-Mar 2018	239.6	144	51
	Oct 2017-Jun 2018	228.0	137	51
	Oct 2017-Sep 2018	222.7	136	50
Sensitivity B	Oct-Dec 2017	290.4	179	57
	Jan-Mar 2018	402.6	233	63
	Apr-Jun 2018	357.6	217	61
	Jul-Sep 2018	359.7	218	61
	Oct 2017-Mar 2018	327.0	202	60
	Oct 2017-Jun 2018	332.0	205	60
	Oct 2017-Sep 2018	332.4	205	60
Pre-intervention test	Jul-Sep 2017	303.2	184	60

Table S5. Antibiotic items and associated costs in 65 intervention practices

Antibiotic name	Number of items 1 Oct 2016 to 30 Sep 2017	Number of items 1 Oct 2017 to 30 Sep 2018	Actual cost of items 1 Oct 2017 to 30 Sep 2018	Change in items	Cost per item 1 Oct 2017 to 30 Sep 2018	Change in cost where reduced
Not Available	5	9	885.70	4	98.41	NA
Amoxicillin	108658	98023	96766.11	-10635	0.99	-10498.63
Ampicillin	158	90	4057.77	-68	45.09	-3065.87
Azithromycin	7652	7267	47802.39	-385	6.58	-2532.53
Benzylpenicillin	112	170	1481.52	58	8.71	NA
Cefaclor	441	326	3144.70	-115	9.65	-1109.33
Cefadroxil	1	4	85.37	3	21.34	NA
Cefalexin	15731	15425	23024.62	-306	1.49	-456.76
Cefixime	4	6	59.63	2	9.94	NA
Cefradine	636	573	1889.98	-63	3.30	-207.80
Ceftazidime	2	3	193.48	1	64.49	NA
Ceftriaxone	61	37	1960.57	-24	52.99	-1271.72
Cefuroxime	75	59	1715.44	-16	29.08	-465.20
Chloramphenicol	NA	10	1121.09	NA	112.11	NA
Ciprofloxacin	8270	7174	23830.62	-1096	3.32	-3640.70
Clarithromycin	26509	23428	55675.08	-3081	2.38	-7321.79
Clindamycin	607	675	12698.02	68	18.81	NA
Co-amoxiclav	18560	16574	35300.61	-1986	2.13	-4229.94
Co-fluampicil	82	77	314.61	-5	4.09	-20.43
Co-trimoxazole	1525	1654	6323.67	129	3.82	NA
Colistin	636	649	80717.38	13	124.37	NA
Cycloserine	1	1	4.01	0	4.01	NA

Dapsone	339	384	30109.75	45	78.41	NA
Demeclocycline	23	67	37345.92	44	557.40	NA
Doxycycline	33499	33011	54448.86	-488	1.65	-804.91
Ertapenem	2	4	600.24	2	150.06	NA
Erythromycin	5052	3817	13227.09	-1235	3.47	-4279.66
Erythromycin ethyl succinate	3258	2448	17140.60	-810	7.00	-5671.52
Erythromycin stearate	436	456	6530.46	20	14.32	NA
Ethambutol	169	201	7727.13	32	38.44	NA
Flucloxacillin	26403	25689	108534.86	-714	4.22	-3016.62
Fosfomycin	14	133	814.32	119	6.12	NA
Fusidic acid	9	9	362.48	0	40.28	NA
Gentamicin	5	3	181.60	-2	60.53	-121.07
Isoniazid	60	50	2944.54	-10	58.89	-588.91
Levofloxacin	255	318	8708.41	63	27.38	NA
Linezolid	2	2	869.09	0	434.54	NA
Lymecycline	7473	7280	54122.88	-193	7.43	-1434.85
Meropenem	NA	1	453.82	NA	453.82	NA
Methenamine	66	87	1352.58	21	15.55	NA
Metronidazole	5689	5505	26558.08	-184	4.82	-887.68
Minocycline	1246	1006	17582.83	-240	17.48	-4194.71
Moxifloxacin	26	45	2132.71	19	47.39	NA
Neomycin	11	NA	NA	NA	NA	NA
Nitrofurantoin	18449	17557	224497.62	-892	12.79	-11405.81
Ofloxacin	294	228	7353.81	-66	32.25	-2128.74
Oxytetracycline	1831	1775	3442.24	-56	1.94	-108.60
Phenoxymethylpenicillin	21547	21007	98245.13	-540	4.68	-2525.46
Piperacillin + Tazobactam	9	3	955.71	-6	318.57	-1911.42

Pivmecillinam	3111	5419	37166.87	2308	6.86	NA
Pyrazinamide	NA	5	447.38	NA	89.48	NA
Rifabutin	1	1	60.25	0	60.25	NA
Rifampicin	232	301	15269.64	69	50.73	NA
Rifampicin + Isoniazid	97	83	2158.10	-14	26.00	-364.02
Rifampicin + Isoniazid + Pyrazinamide	17	6	249.05	-11	41.51	-456.60
Rifaximin	588	686	176555.03	98	257.37	NA
Sodium fusidate	94	69	2070.08	-25	30.00	-750.03
Sulfadiazine	1	3	340.76	2	113.59	NA
Teicoplanin	4	NA	NA	NA	NA	NA
Tetracycline	274	255	920.81	-19	3.61	-68.61
Tinidazole	9	13	140.86	4	10.84	NA
Tobramycin	NA	1	23.32	NA	23.32	NA
Trimethoprim	31564	29875	28464.05	-1689	0.95	-1609.23
Vancomycin	12	13	2262.40	1	174.03	NA

NA, not applicable