

# Prescriptive variability of drugs by general practitioners

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## 1 **Abstract**

2 Prescription drug spending is growing faster than any other sector of healthcare.  
3 However, very little is known about patterns of prescribing and cost of prescribing  
4 between general practices. In this study, we examined variation in prescription rates  
5 and prescription costs through time for 55 GP surgeries in Northern Ireland Western  
6 Health and Social Care Trust. Temporal changes in variability of prescribing rates and  
7 costs were assessed using the Mann–Kendall test. Outlier practices contributing to  
8 between practice variation in prescribing rates were identified with the interquartile  
9 range outlier detection method. The relationship between rates and cost of prescribing  
10 was explored with Spearman's statistics. The differences in variability and mean  
11 number of prescribing rates associated with the practice setting and socioeconomic  
12 deprivation were tested using t-test and *F*-test, respectively. The largest between-  
13 practice difference in prescribing rates was observed for Apr-Jun 2015, with the  
14 number of prescriptions ranging from 3.34 to 8.36 per patient. We showed that  
15 practices with outlier prescribing rates greatly contributed to between-practice  
16 variability. The largest difference in prescribing costs was reported for Apr-Jun 2014,  
17 with the prescription cost per patient ranging from £26.4 to £64.5. In addition, the  
18 temporal changes in variability of prescribing rates and costs were shown to undergo  
19 an upward trend. We demonstrated that practice setting and socio-economic  
20 deprivation accounted for some of the between-practice variation in prescribing. Rural  
21 practices had higher between practice variability than urban practices at all time points.  
22 Practices situated in more deprived areas had higher prescribing rates but lower  
23 variability than those located in less deprived areas. Further analysis is recommended  
24 to assess if variation in prescribing can be explained by demographic characteristics  
25 of patient population and practice features. Identification of other factors contributing

26 to prescribing variability can help us better address potential inappropriateness of  
27 prescribing.

## 28 **Introduction**

29 In recent years, NHS spending on drugs has substantially risen, from £13.0 billion in  
30 2010/11 to £16.8 billion in 2015/16 [1]. Most of the expenditure on prescribed  
31 medicines is incurred in primary care and closely related to the steadily growing  
32 workload of general practitioners (GPs) [1]. In England, patient consultations with GPs  
33 increased by 16% in the period 2007-14 [2] whereas in Northern Ireland, the GPs  
34 workload grew by 22% over the same period [3]. In addition, there has been an  
35 approximately 60% increase in prescription items dispensed from 2005 to 2014 in  
36 Northern Ireland [3] and a corresponding 50.4% rise in the number of prescriptions  
37 dispensed in England [4].

38 The National Audit Office report found that substantial savings for the NHS could be  
39 achieved by improving the overall quality and cost-effectiveness of prescribing [5].  
40 Accordingly, a lot of interest has been focused on variation in prescribing practice as  
41 a potential source to save money [5,6]. Despite a wealth of literature on prescribing  
42 patterns [5,7,8,9], there is a lack of full understanding of factors that contribute to  
43 between-practice differences in prescribing. Among key influences upon prescribing  
44 variation, the demographic and socio-economic characteristics of patient population  
45 (e.g. age, ethnicity, deprivation) are most often acknowledged by researchers [10,11].  
46 GP practices with a greater proportion of people in older age groups were more likely  
47 to prescribe minor tranquilisers [10], sex hormones, anticoagulants and protamine,  
48 and treatments for glaucoma [12]. Significant differences in prescribing were also

49 associated with the level of deprivation [13]. Several studies have shown that extent  
50 of local deprivation influences antidepressant and lipid-lowering medication  
51 prescribing [14,15,16]. On the other hand, lower volume of prescribing was observed  
52 in practices with higher proportions of patients from ethnic minority populations [17].  
53 Practice features were also among factors contributing to the variation in prescribing  
54 behaviour. Examples of that include higher prescription rates issued by practices  
55 located in urban areas with a greater proportion of female GPs [18]. Lower prescribing  
56 was found for single-handed practices, practices in rural areas, with a higher average  
57 age of general practitioners, and with GPs born outside the UK [15,19,20].

58 Differences in characteristics of GP practices or a patient population do not always  
59 explain GPs prescribing behaviour. In many cases, the variability in prescribing rates  
60 is associated with inefficient or inappropriate prescribing [5,21]. It has been estimated  
61 that the prescription costs could be reduced by as much as £1bn if unwarranted  
62 variations in prescribing levels were eliminated and the drugs were prescribed with the  
63 same standard [21]. Better efficiency and appropriateness in prescribing practice could  
64 be achieved by addressing the over- or under-utilisation of drugs. It was shown that  
65 prescribed medications are often taken for long periods beyond the point when they  
66 are needed and around 30% of drugs are abandoned by patients [22,23,24,25]. Major  
67 NHS savings could also be generated by using treatments that are most cost-effective.  
68 Moon et al. [26] showed that a large number of GPs are still prescribing brand name  
69 medications, even though the cheaper, equally safe and effective alternatives are  
70 available.

71 The aim of this study was to investigate temporal changes in rates and costs of  
72 prescribing as well as between-practice variation in prescribing. In addition, we

73 examined if prescribing rates of GPs were related to the practice setting and  
74 socioeconomic deprivation.

## 75 **Methods**

### 76 **Data and pre-processing**

77 We analysed the number and actual cost of prescription items issued by 55 general  
78 practices within the Northern Ireland Western Health and Social Care Trust (WHSCT)  
79 during twelve consecutive periods of 3 months, starting from Apr 2013 to Mar 2016.  
80 The actual cost of prescriptions was defined as the estimated cost to the NHS  
81 calculated by subtracting the discount per item from the gross cost which is the basic  
82 price of a drug.

83 The GP prescribing data was obtained from the Business Services Organisation's  
84 (BSO) prescribing and dispensing information systems [27]. It includes prescribing for  
85 all GPs and other non-medical prescribers who are attached to GP practices i.e.  
86 nurses, pharmacists, optometrists, chiropodists, and radiographers. To allow temporal  
87 comparison of prescribing data, the number of drug prescriptions and their total cost  
88 calculated for each general practice was adjusted for the total number of patients in  
89 each practice and expressed as prescriptions/cost (£) per patient.

90 Given data from the Census Office of the Northern Ireland Statistics and Research  
91 Agency [28], a practice was designated as urban if its postal address was situated in  
92 a settlement of more than 10,000 residents. Under this definition, 31 practices were  
93 categorised as urban and 24 as rural.

94 In addition, practices were categorised based on the Northern Ireland Multiple  
95 Deprivation Measure (NIMDM) at the level of Super Output Area (SOA) [29]. The

96 NIMDM consists of seven domains i.e. Income; Employment; Health, Deprivation, and  
97 Disability; Education, Skills and Training; Proximity to Services; Living Environment;  
98 and Crime and Disorder. On this overall measure, the SOA with a NIMDM rank of 1 is  
99 considered the most deprived, and 890 the least deprived. Accordingly, a practice  
100 situated in SOA with the NIMDM rank larger than 445 was designated as 'located in a  
101 less deprived area' while a practice situated in SOA with a NIMDM rank smaller than  
102 445 was designated as 'located in a more deprived area'. Under this definition, we  
103 identified 11 practices 'located in less deprived areas' and 44 practices 'located in  
104 more deprived areas'.

### 105 **Statistical analysis**

106 The variation in the number and cost of prescriptions per patient was assessed by  
107 calculating the variance ( $\sigma^2$ ) for each of the 12 considered time points [30]. In addition,  
108 we analysed changes in mean ( $\mu$ ) and range of the rate and cost of prescriptions.

109 The outlier GP practices were identified for all time points using the interquartile range  
110 (IQR) method for outlier detection [31]. Accordingly, a practice with the prescribing rate  
111 that fell outside either 1.5 times the IQR below the first quartile or 1.5 times  
112 the IQR above the third quartile, was considered to be an 'outlier'. We however  
113 acknowledge that a statistical outlier in terms of prescribing rate is not necessarily an  
114 example of inappropriate practice.

115 The differences in the mean number of prescribing rates, for the rural and urban  
116 practices as well as practices located in areas of different levels of socioeconomic  
117 deprivation, were assessed using an unpaired t-test [31]. The equality of variances of  
118 prescribing rates for above-mentioned practice categories was evaluated using F-test  
119 [30]. The normality of prescribing data was confirmed with Shapiro-Wilks test [32].

120 To determine if temporal changes in variability of rates and costs of prescribing  
121 underwent a statistically significant upward or downward trend over the study period,  
122 we used the Mann–Kendall test which has been commonly employed to detect trends  
123 in series of data [33,34].

124 The relationship between rates and cost of prescribing was explored with Spearman's  
125 rank correlation (*rho*) [35]. We chose the Spearman correlation measure due to it  
126 insensitivity to individual contribution of outliers. The strength of correlation was  
127 defined as very weak for  $|rho| = 0.2$  to  $0.39$ , moderate for  $|rho| = 0.4$  to  $0.59$ , strong for  
128  $|rho| = 0.6$  to  $0.79$ , and very strong for  $|rho| = 0.8$  to  $1$  [35].

## 129 **Results**

130 The total number of patients registered at 55 general practices providing services  
131 throughout 2013–16 increased from 318,057 in 2013-14 to 326,429 in 2015-16. Over  
132 this time, the total actual prescription cost continued to rise from £58,669,971 in 2013-  
133 14 to £63,803,168 in 2015-16.

134 Fig 1 shows the magnitude and temporal changes in variability of the number of  
135 prescriptions per patient. We observed large differences in drug prescribing rates  
136 among individual practices. The largest between-practice difference in prescribing  
137 rates was observed for the quarter of Apr-Jun 2015, with the number of prescriptions  
138 ranging from 3.34 to 8.36 per patient. During this period, the prescription rate for the  
139 practice with the largest number of prescriptions per patient was ~ 60% higher than  
140 the average prescribing rate for all the practices ( $\mu = 5.20$ , 95%CI = [4.96,5.44]  
141 prescriptions per patient). The smallest between-practice difference in prescribing  
142 rates was observed in the period Apr-Jun 2013, with the number of prescriptions

143 ranging from 3.21 to 7.60 per patient. At that time, the practice with the highest  
144 prescribing rate issued ~ 49% more prescriptions per patient compared to the average  
145 prescribing rate of  $\mu = 5.11$ , 95%CI = [4.89, 5.33]. The high inter-practice variability in  
146 drug prescribing behaviour was caused by: 1.8% (Oct-Dec 2013), 3.6% (Apr-Jun  
147 2013, Oct 2014 -Mar 2016), 5.5% (Jan-Sep 2014), and 7.3% (Jul-Sep 2013) of GP  
148 practices with outlier prescribing rates. By eliminating the effect of these outliers (i.e.  
149 practices with higher or lower prescribing rates than the calculated outlier cut-off  
150 values), we were able to reduce the between-practice variability in prescribing rates  
151 from 21% ( $\sigma^2$  reduced from 0.71 to 0.59 in Oct-Dec 2013) up to 70% ( $\sigma^2$  reduced from  
152 0.67 to 0.39 in Jul-Sep 2013) (S1 Table). It is worth highlighting that despite varying  
153 number of outliers identified in each quarterly period, they were mostly the same  
154 practices: one practice (with substantially higher prescribing rate than outlier cut-off  
155 values) was identified as an 'outlier' throughout the studied period while two other  
156 practices (one with higher and the other with lower prescribing rate than outlier cut-off  
157 values) were labelled as 'outliers' at 11 and 4 considered time periods respectively.

158 **Fig 1.** Temporal variability in the standardized number of prescriptions. Each data  
159 point (dot): a single practice. Solid, horizontal line inside the box: median of data.  
160 Green diamond: mean. Lower and upper "hinges" of the boxplots: 1<sup>st</sup> and 3<sup>rd</sup> quartiles,  
161 respectively. Red, green, and blue lines: trend lines for maximum, average, and  
162 minimum values of prescription rates respectively. Lower and upper extremes of  
163 whiskers: interval boundaries of the non-outliers (black dots). Data outside interval  
164 (red dots): outliers.

165 Temporal variability in the actual cost of prescribed medications per patient is shown  
166 in Figure 2. The largest between-practice difference in prescribing costs was observed



167 for the quarter of Apr-Jun 2014, with the prescription cost per patient ranging from  
168 £26.4 to £64.5. During this time period, the highest actual cost of prescribed  
169 medications per patient for the individual practice was ~40% higher than the average  
170 prescribing cost of  $\mu = £46.1$ , 95%CI = [£45.2, £47.0]. In addition, the average cost  
171 of prescribing per person was observed to increase by 11.3%, 95%CI =  
172 [10.4%,12.2%] over the period of investigation; from £45, 95%CI = [£43.2, £46.8] in  
173 the first quarter (Apr-Jun 2013) to £48.6, 95%CI = [£46.7, £50.6] in the last quarter  
174 (Jan-Mar 2016) of the study.

175 **Fig 2.** Temporal variability in the actual cost of prescribed medications per patient.  
176 Each data point (dot): a single practice. Solid, horizontal line inside the box: median of  
177 data. Green diamond: mean. Lower and upper "hinges" of the boxplots: 1<sup>st</sup> and 3<sup>rd</sup>  
178 quartiles, respectively. Red, green, and blue lines: trend lines for maximum, average,  
179 and minimum values of prescription costs respectively.

180 The distribution of costs through time appeared to show a similar trend to the  
181 prescribing rates. The moderate to strong association between prescription rates and  
182 actual costs of prescribed medications was reflected in the value of the Spearman's  
183 coefficient (Fig 3 A). The *rho* was found to increase from 0.547 in Apr 2013 – Mar 2014  
184 to 0.609 in Apr 2015 – Mar 2016. We also looked at the relationship between  
185 prescribing rates and the actual cost per prescription. We found those two measures  
186 to be moderately correlated (Fig 3 B); the cost per prescription was shown to be lower  
187 for practices with higher rates of prescribing.

188 **Fig 3.** The relationship between standardized number of prescriptions and: A) the  
189 actual cost of prescribed medications per patient; B) the actual cost per prescription.

190 Our trend analysis showed that temporal changes in variability of prescribing rates and  
191 costs underwent an upward trend. Despite some temporal fluctuations in variance, the  
192 best fit line indicates that the value of  $\sigma^2$  for prescribing rates increased from £0.70 in  
193 Apr-Jun 2013 to £0.77 in Jan-Mar 2016 (Fig 4). At the same time, the between-practice  
194 variability in prescribing costs increased from  $\sigma^2 = £45.6$  in Apr-Jun 2013 to  $\sigma^2 = £53.4$   
195 in Jan-Mar 2016. The Mann–Kendall test confirmed a statistically significant upward  
196 trend in variability of GPs prescribing rates ( $p = 0.011$ ) over the study duration.

197 **Fig 4.** Temporal changes in variance calculated for: A) the number of prescriptions per  
198 patient; B) the actual prescription cost per patient for 55 investigated general practices.  
199 Black line represents the best-fit trend line for rates (A) and cost (B) of prescribing.

200 Rural practices had a lower average number of prescriptions per patient than urban  
201 practices at all time points (Table 1). Over the period of investigation, the mean number  
202 of prescriptions per patient for rural practices rose by ~3.3 % from 5.07, 95CI =  
203 [4.70,5.44] in Apr-Jun 2013 to 5.24, 95CI = [4.83,5.64] in Jan-Mar 2016 while urban  
204 practices reported a ~6.7% increase in average prescribing rate from 5.14, 95CI =  
205 [4.86,5.41] in Apr-Jun 2013 to 5.48, 95CI = [5.22,5.75] in Jan-Mar 2016. In all quarterly  
206 periods, the difference in the mean number of prescribed medications per patient  
207 between urban and rural practices was found statistically insignificant.

208 Rural practices had a higher between practice variability than urban practices at all  
209 time points (Table 1). The variance for practices designated as rural grew from  $\sigma^2 =$   
210 0.84 in Apr-Jun 2013 to  $\sigma^2 = 1.02$  in Jan-Mar 2016. This upward trend in variability  
211 was found statistically significant with  $p = 0.0032$ . Conversely, the variance for urban  
212 practices decreased from  $\sigma^2 = 0.62$  in Apr-Jun 2013 to  $\sigma^2 = 0.58$  in Jan-Mar 2016;

213 however, this change was statistically insignificant ( $p = 0.54$ ). At all studied time  
214 periods, F-test  $p$ -value showed no significant differences in variance in prescribing  
215 rates between rural and urban practices.

216 **Table 1.** Prescribing rates for rural and urban practices. T-test  $p$ -value refers to the  
217 significance level of differences in the mean number of prescribing rates between rural  
218 and urban practices for all considered time period. The  $p$ -value of F-test assesses the  
219 difference in variances in prescribing rates between rural and urban practices.

220 Practices situated in more deprived areas were found to have higher prescribing rates  
221 than those located in less deprived areas although this difference was not statistically  
222 significant in any of the considered quarterly periods (Table 2). The average number  
223 of prescriptions per patient in less deprived areas grew by ~7.5% from 5.0, 95CI =  
224 [4.38,5.61] in Apr-Jun 2013 to 5.37, 95CI = [4.76,5.98] in Jan-Mar 2016 while practices  
225 situated in more deprived areas reported a ~4.6% increase in mean prescribing rate  
226 from 5.14, 95CI = [4.92,5.38] in Apr-Jun 2013 to 5.38, 95CI = [5.13,5.62] in Jan-Mar  
227 2016. The variability in prescribing rates for practices in less deprived areas was  
228 substantially higher than for practices in more deprived areas and this difference in  
229 variances was shown to be statistically significant for 8 quarterly periods (Apr 2013-  
230 Mar 2015) (Table 2).

231 **Table 2.** Prescribing rates for practices located in areas of different levels of socio-  
232 economic deprivation. T-test  $p$ -value refers to the significance level of differences in  
233 mean number of prescribing rates between practices from less and more deprived  
234 areas. The  $p$ -value of F-test assesses the difference in variances in prescribing rates  
235 between practices from less and more deprived areas. Asterisk: Statistically significant  
236 difference ( $p < 0.05$ ) in variability in prescribing rates.

## 237 Discussion

238 Over the period of investigation, the average between-practice variation in rates of  
239 prescribing was  $\sigma^2 = 0.74$ , 95%CI = [0.71, 0.77]. The prescribing rates of individual  
240 practices ranged, on average, from 3.34, 95%CI = [3.26,3.42] to 8, 95%CI =  
241 [7.86,8.14] prescriptions per patient. At the same time, the average variance of  
242 prescribing costs was  $\sigma^2 = \text{£}47.6$ , 95%CI = [£44.4, £50.8] with actual cost of prescribed  
243 medications per patient ranging, on average, from £27.2, 95%CI = [£26.1, £28.3] to  
244 £67.9, 95%CI = [£66.5, £69.3]. While it may be challenging to define what represents  
245 an appropriate rate or cost of prescribing, it is certainly difficult to justify large  
246 differences in prescribing between individual practices providing care to broadly similar  
247 groups of patients within a single healthcare system.

248 It is worth highlighting that both rates and costs of prescribing observed in Northern  
249 Ireland Western Health and Social Care Trust were found to be higher than the rates  
250 and costs recorded in England. In 2015, an average of 18.6 items was dispensed in  
251 primary care for each patient registered with a GP practice in England [36] compared  
252 to 21.2 items per head issued in WHSCT. In England, the cost of prescribed items was  
253 roughly £157 per patient, £5 per patient higher than in 2014. In comparison, the  
254 average prescription cost per patient in WHSCT was £189.8, 95%CI = [182.9,196.7],  
255 ~£7.6 higher than in 2014. Despite higher average rates of prescribing per patient, the  
256 variation across England in the number of prescribed medications was higher than in  
257 WHSCT with the prescribing rates ranging from 9.5 to 33.3 items per head in 2015. At  
258 the same time, the number of items per patient issued in WHSCT ranged from 13.7 to  
259 31.7 [36].

260 Since no demographic data was published alongside the GP prescribing data for

261 WHSCT, we could not estimate the effect of demographics of patient population on  
262 variation in prescribing rates. Previous studies however showed that demographic  
263 characteristics of patient population did not fully explain prescribing behaviour of GPs  
264 [21]. Among the factors related to the varying prescription activity, age of patients was  
265 most often factored into analyses of variation [37], although age alone did not account  
266 for enough variation to develop an accurate model for predicting prescribing rates [38].  
267 It was shown that age and gender accounted for approximately 25% of variation  
268 [39,40] and additional demographic characteristics (e.g. mortality rates) up to 51%  
269 [41].

270 Our study shows differences in both prescribing rates and between practice variation  
271 in prescribing between rural and urban practices. The mean number of prescribed  
272 items was higher in urban practices than in rural practices. The reasons for this are  
273 unclear and were beyond the scope of the present study. However, possible  
274 explanations include differing patient populations in rural and urban areas, differences  
275 in practice organisation and workflow, as well as differences in characteristics of  
276 general practitioners such as training, background, and age. Our results appear  
277 consistent with previous studies. In Scotland, lower levels of prescribing of  
278 antidepressants were found for practices in rural areas while higher rates were  
279 observed for urban practices [18]. In addition, lower rates of prescribing of  
280 psychotropic drugs were reported by rural/small town practices in Denmark [19].

281 Our results indicate higher levels of prescribing for practices located in more deprived  
282 areas of Western Health and Social Care Trust and lower levels for practices from less  
283 deprived areas. Furthermore, the differences in variances of prescribing rates given  
284 different levels of local deprivation were found statistically significant for 8 quarterly

285 periods. So far, several studies have demonstrated that socio-economic deprivation  
286 can influence prescription rates for some medications, such as antidepressants and  
287 lipid-lowering drugs. In England, the difference in the number of prescriptions between  
288 the bottom 1% and top 1% areas by deprivation was 20% [42,43].

289 In addition, we found that the variability in prescribing rates underwent a statistically  
290 significant upward trend reflecting larger deviations of prescribing rates of individual  
291 practices from the mean prescribing rate. This can be related to the changes in socio-  
292 economic and demographic characteristics of patient populations but we also cannot  
293 exclude possibility that these growing deviations may reflect growing differences in  
294 quality of care leading to, in fact, avoidable increase in prescribing costs. However,  
295 higher variability does not necessarily imply lower quality practice. It therefore requires  
296 further inspection to determine if the patient populations associated with specific GP  
297 practices are different and have different needs.

298 A moderate (Apr 2013-Mar 2015) to strong (Apr 2015-Mar 2016) relationship was  
299 observed between prescription rates and actual costs of prescribing; a higher cost of  
300 prescribed medications per patient was associated with a higher number of issued  
301 items per patient. The differences in pharmaceutical costs observed for the practices  
302 with similar prescription rates might be related to the type of prescribed drugs e.g. the  
303 cost of one pack of Amiodarone (100mg tablets) is £2.21 whereas for a pack of  
304 Allopurinol (100mg tablets), we have to pay over £35. The differences in prescription  
305 costs in practices with similar prescribing rates may also be associated with the  
306 medication choice i.e. a generic vs. brand name drug. There is evidence that inefficient  
307 prescribing by GPs increases NHS costs by hundreds of millions of pounds every year  
308 [21]. Of course, there can be legitimate reasons why patients require brand name

309 drugs. However, our data do not allow us to examine the appropriateness of such  
310 decisions. We also found the number of items per patient to be negatively correlated  
311 with the cost per item i.e. the cost per prescription was shown to be higher for practices  
312 with lower rates of prescribing. It suggests that practices that prescribe more items per  
313 head appear to prescribe cheaper drugs.

314 We believe that the identification of outlier practices i.e. practices with higher or lower  
315 prescribing rates than the calculated outlier cut-off values may act as an important  
316 consideration when deciding which practices may benefit from interventions to alter  
317 prescribing behaviour of GPs [44]. That is, there might be greater merit in engaging  
318 with individual practices where prescribing rates appeared significantly higher or lower  
319 than average. The identification of such practices could reduce the time, effort, and  
320 cost of any intervention. However, we are aware that a statistical outlier in terms of  
321 prescribing rates is not equivalent to inappropriate practice and therefore, further  
322 analysis would be required to assess if higher/lower rates than outlier cut off values  
323 can be explained by characteristics of patient populations (e.g. age, ethnicity) or  
324 practice features (e.g. age, training of general practitioners).

325 The main limitation of our study results from its design. Our analysis was conducted  
326 to investigate the variability patterns and changes in prescribing rates and costs, but  
327 due to data unavailability, we were not able to examine how the differences in patient  
328 or provider factors may affect variation in prescribing. Business Services Organisation  
329 in Northern Ireland does not provide free and open access to data sets related to  
330 demographic characteristics of patient population and practice features at the level of  
331 the GP practice. We believe that when such data becomes available, further  
332 investigation of characteristics of practices and patient populations in Western Health

333 and Social Care Trust may shed more light on other factors contributing to variations  
334 in GPs prescribing. This can help us to better address potential inappropriateness and  
335 inefficiency of prescribing.

336 In conclusion, our study provided information on variability patterns and temporal  
337 changes in rates and cost of prescribing in Western Health and Social Care Trust. We  
338 showed that practice setting and socio-economic deprivation account for some of the  
339 between-practice variation in prescribing. We suggest that optimisation of prescribing  
340 could be enhanced by conducting appropriate clinical interventions when other factors  
341 contributing to prescribing variation are identified. These interventions could include  
342 educational initiatives and feedback during which GP practices would be informed  
343 about their own frequency of prescribing relative to the mean prescribing of other  
344 practices. The prescribing behaviour of GPs could also be altered by comparing their  
345 past performance to clearly defined professional standards/targets. The quality  
346 improvement initiatives including normative feedback proved to be effective in  
347 decreasing variability in prescribing in the past [45].

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## 353 **Contributorship**

354 MB performed the analysis and interpretation of the results, and wrote the manuscript.  
355 MJO edited the manuscript. KWL initiated the collaborative project, guided the data



356 analysis and interpretation of the results, and wrote the manuscript. SA monitored  
357 the data collection. All the authors have accepted responsibility for the entire content  
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### 363 **Competing interests**

364 The authors have declared that no competing interests exist.

365 **References**

- 366 1. Prescribing Costs in Hospitals and the Community: England 2015/16.  
367 Government Statistical Service. 2016. Available at:  
368 [http://www.content.digital.nhs.uk/catalogue/PUB22302/hosp-pres-eng-](http://www.content.digital.nhs.uk/catalogue/PUB22302/hosp-pres-eng-201516-report.pdf)  
369 [201516-report.pdf](http://www.content.digital.nhs.uk/catalogue/PUB22302/hosp-pres-eng-201516-report.pdf). Accessed: 3 May 2017.
- 370 2. Thompson M, Walter F. Increases in general practice workload in England. The  
371 Lancet 2016;387(10035):2270-2272.
- 372 3. Thompson J, Todd D. Primary Care Prescribing. Northern Ireland Assembly.  
373 2015. Available at:  
374 [https://www.degruyter.com/downloadpdf/j/cclm.2017.55.issue-5/cclm-2016-](https://www.degruyter.com/downloadpdf/j/cclm.2017.55.issue-5/cclm-2016-0740/cclm-2016-0740.pdf)  
375 [0740/cclm-2016-0740.pdf](https://www.degruyter.com/downloadpdf/j/cclm.2017.55.issue-5/cclm-2016-0740/cclm-2016-0740.pdf). Accessed: 4 May 2017.
- 376 4. Prescriptions Dispensed in the Community, Statistics for England - 2005-2015.  
377 Prescribing and Medicines Team Health and Social Care Information Centre.  
378 2016. Available at:  
379 [http://content.digital.nhs.uk/catalogue/PUB20664/pres-disp-com-eng-2005-15-](http://content.digital.nhs.uk/catalogue/PUB20664/pres-disp-com-eng-2005-15-rep.pdf)  
380 [rep.pdf](http://content.digital.nhs.uk/catalogue/PUB20664/pres-disp-com-eng-2005-15-rep.pdf). Accessed: 4 May 2017.
- 381 5. Duerden M, Millson D, Avery A, Smart S. The quality of GP prescribing. The  
382 King's Fund. 2011. Available at:  
383 [https://www.kingsfund.org.uk/sites/files/kf/field/field\\_document/quality-gp-](https://www.kingsfund.org.uk/sites/files/kf/field/field_document/quality-gp-prescribing-gp-inquiry-research-paper-mar11.pdf)  
384 [prescribing-gp-inquiry-research-paper-mar11.pdf](https://www.kingsfund.org.uk/sites/files/kf/field/field_document/quality-gp-prescribing-gp-inquiry-research-paper-mar11.pdf). Accessed: 6 May 2017.
- 385 6. Alderwick H, Robertson R, Appleby J, Dunn P, Maguire D. Better value in the  
386 NHS: The role of changes in clinical practice. The King's Fund. 2015.

- 387 7. Pharoah PD, Melzer D. Variation in prescribing of hypnotics, anxiolytics and  
388 antidepressants between 61 general practices. *Br J Gen Pract.*  
389 1995;45(400):595-9.
- 390 8. Covvey JR, Johnson BF, Elliott V, Malcolm W, Mullen AB. An association  
391 between socioeconomic deprivation and primary care antibiotic prescribing in  
392 Scotland. *Journal of Antimicrobial Chemotherapy.* 2014;69(3):835-41.
- 393 9. Ventola CL. The Antibiotic Resistance Crisis: Part 1: Causes and  
394 Threats. *Pharmacy and Therapeutics* 2015;40(4):277-283.
- 395 10. Wagner AC, Hann M, Ashcroft DM. Influence of population and general practice  
396 characteristics on prescribing of minor tranquilisers in primary care. *Pharmacy  
397 Practice* 2010;8(3):193-200.
- 398 11. Hann M, Cantrill J, Baker D. Gill P. Prescribing patterns in high-need Health  
399 Authority populations: how does an ethnically mixed composition affect volume  
400 and cost? *Journal of Clinical Pharmacy and Therapeutics* 2004;29:537-546.
- 401 12. Backer C. *Medicine statistics: GP prescribing by constituency, 2015.* House of  
402 Commons Library. 2016.
- 403 13. Mackenzie IF, Buckingham K, Wankowski JM, Wilcock M. Morbidity,  
404 deprivation, and antidepressant prescribing in general practice. *Br J Gen Pract.*  
405 1999;49(448):884-6.
- 406 14. Wu J, Zhu S, Yao GL, Mohammed MA, Marshall T. Patient factors influencing  
407 the prescribing of lipid lowering drugs for primary prevention of cardiovascular  
408 disease in UK general practice: a national retrospective cohort study. *PLoS  
409 One* 2013;8(7):e67611.
- 410 15. Hull SA, Aquino P, Cotter S. Explaining variation in antidepressant prescribing  
411 rates in east London: a cross sectional study. *Fam Pract* 2005;22(1):37-42.

- 412 16. Ashworth M, Lloyd D, Smith RS, Wagner A, Rowlands G. Social deprivation  
413 and statin prescribing: a cross-sectional analysis using data from the new UK  
414 general practitioner 'Quality and Outcomes Framework'. *J Public Health*  
415 2007;29(1):40-47.
- 416 17. Szczepura A. Access to health care for ethnic minority populations.  
417 *Postgraduate medical journal* 2005;81(953):141-7.
- 418 18. Morrison J, Anderson MJ, Sutton M, Munoz-Arroyo R, McDonald S, Maxwell M,  
419 et al. Factors influencing variation in prescribing of antidepressants by general  
420 practices in Scotland. *Br J Gen Pract* 2009;59(559): e25-e31.
- 421 19. Holm M, Olesen F. Factors affecting prescription of psychotropic drugs in  
422 general practice. *Scandinavian journal of primary health care* 1988;6(3):169-  
423 73.
- 424 20. Haastrup PF, Rasmussen S, Hansen JM, Christensen RD, Søndergaard J,  
425 Jarbøl DE. General practice variation when initiating long-term prescribing of  
426 proton pump inhibitors: a nationwide cohort study. *BMC family practice*  
427 2016;17(1):57.
- 428 21. Cahir C, Fahey T, Teeling M, Teljeur C, Feely J, Bennett K. Potentially  
429 inappropriate prescribing and cost outcomes for older people: a national  
430 population study. *Br J Clin Pharmacol* 2010;69:543-552.
- 431 22. Ofori-Asenso R, Agyeman AA. Irrational Use of Medicines—A Summary of Key  
432 Concepts. *Pharmacy*. 2016 Oct 28;4(4):35.
- 433 23. Paying the Price Prescription Charges and People with Long-Term Conditions.  
434 Prescription Charges Coalition. 2013. Available at:  
435 [http://www.prescriptionchargescoalition.org.uk/uploads/1/2/7/5/12754304/paying\\_the\\_price\\_report.pdf](http://www.prescriptionchargescoalition.org.uk/uploads/1/2/7/5/12754304/paying_the_price_report.pdf). Accessed: 20 April 2017.  
436

- 437 24. Lash S, Harding J. Abandoned Prescriptions: A Quantitative Assessment of  
438 Their Cause. *Journal of Managed Care Pharmacy* 1995;1(3):193-9.
- 439 25. Fischer SH, Field TS, Gagne SJ, Mazor KM, Preusse P, Reed G, et al. Patient  
440 completion of laboratory tests to monitor medication therapy: a mixed-methods  
441 study. *Journal of general internal medicine* 2013;28(4):513-21.
- 442 26. Moon JC, Flett AS, Godman BB, Grosso AM, Wierzbicki AS. Getting better  
443 value from the NHS drug budget. *BMJ (Online)* 2010;341.
- 444 27. Prescribing by GP Practice. Available at:  
445 <http://www.hscbusiness.hscni.net/services/2471.htm>. Accessed: 1 February  
446 2017.
- 447 28. Northern Ireland Statistics and Research Agency. Review of the Statistical  
448 Classification and Delineation of Settlements,  
449 [http://www.nisra.gov.uk/archive/geography/review-of-the-statistical-](http://www.nisra.gov.uk/archive/geography/review-of-the-statistical-classification-and-delineation-of-settlements-march-2015.pdf)  
450 [classification-and-delineation-of-settlements-march-2015.pdf](http://www.nisra.gov.uk/archive/geography/review-of-the-statistical-classification-and-delineation-of-settlements-march-2015.pdf) (2015, accessed  
451 8 Nov 2017).
- 452 29. Northern Ireland Multiple Deprivation Measure 2010. Northern Ireland  
453 Statistics and Research Agency. 2010. Available at:  
454 [http://www.prescriptionchargescoalition.org.uk/uploads/1/2/7/5/12754304/payi](http://www.prescriptionchargescoalition.org.uk/uploads/1/2/7/5/12754304/paying_the_price_report.pdf)  
455 [ng\\_the\\_price\\_report.pdf](http://www.prescriptionchargescoalition.org.uk/uploads/1/2/7/5/12754304/paying_the_price_report.pdf). Accessed: 8 Nov 2017.
- 456 30. Asimow LA, Maxwell MM. *Probability and statistics with applications: A problem*  
457 *solving text*. Actex Publications. 2010.
- 458 31. Peck R, Olsen C, Devore JL. *Introduction to statistics and data analysis*.  
459 Cengage Learning; 2015.
- 460 32. Sen A, Srivastava M. *Regression analysis: theory, methods, and applications*.  
461 Springer Science & Business Media; 2012.

- 462 33. McLeod AI, Hipel KW, Bodo BA. Trend analysis methodology for water quality  
463 time series. *Environmetrics* 2010;2:169-200.
- 464 34. Meals DW, Spooner J, Dressing SA, Harcum JB. Statistical analysis for  
465 monotonic trends, Tech Notes 6. Developed for U.S. Environmental Protection  
466 Agency by Tetra Tech, Inc. 2011. Available at:  
467 [www.bae.ncsu.edu/programs/extension/wqg/319monitoring/tech\\_notes.htm](http://www.bae.ncsu.edu/programs/extension/wqg/319monitoring/tech_notes.htm).  
468 Accessed: 10 May 2017.
- 469 35. Kvam PH, Vidakovic B. Nonparametric statistics with applications to science  
470 and engineering. John Wiley & Sons. 2007.
- 471 36. Baker K. Medicine statistics: GP prescribing by constituency, 2015. House of  
472 Commons Library, 2016.
- 473 37. Purves I, Edwards C. Comparison of prescribing unit with index including both  
474 age and sex in assessing general practice prescribing costs. *Br Med J*  
475 1993;306:496-8.
- 476 38. Sleator D. Towards accurate prescribing analysis in general practice:  
477 accounting for the effects of practice demography. *Br J Gen Pract*  
478 1993;43(368):102-6.
- 479 39. Favato G, Mariani P, Mills R, Capone A, Pelagatti M, Pieri V et al. ASSET  
480 (Age/Sex Standardised Estimates of Treatment): a research model to improve  
481 the governance of prescribing funds in Italy. *PLoS ONE* 2007;2(7): e592.
- 482 40. Majeed A, Head S. Controversies in primary care. Setting prescribing budgets  
483 in general practice. Capitation based prescribing budgets will not work. *BMJ*  
484 1998;316(7133):748 –50.

- 485 41. Forster D, Frost C. Use of regression analysis to explain the variation in  
486 prescribing rates and costs between family practitioner committees. *Br J Gen*  
487 *Pract* 1991;41(343):67-71.
- 488 42. Hann M, Cantrill J, Baker D, Gill P. Prescribing patterns in high-need Health  
489 Authority populations: how does an ethnically mixed composition affect volume  
490 and cost? *Journal of Clinical Pharmacy and Therapeutics* 2004;29:537-546.
- 491 43. Wise J. Antibiotic prescribing is higher in deprived areas of England. *BMJ:*  
492 *British Medical Journal (Online)* 2005;351.
- 493 44. Hallsworth M, Chadborn T, Sallis A, Sanders M, Berry D, Greaves F, et al.  
494 Provision of social norm feedback to high prescribers of antibiotics in general  
495 practice: a pragmatic national randomised controlled trial. *Lancet*  
496 2016;387:1743–52.
- 497 45. Burton JH, Hoppe JA, Echternach JM, Rodgers JM, Donato M. Quality  
498 improvement initiative to decrease variability of emergency physician opioid  
499 analgesic prescribing. *Western Journal of Emergency Medicine*. 2016  
500 May;17(3):258.

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504

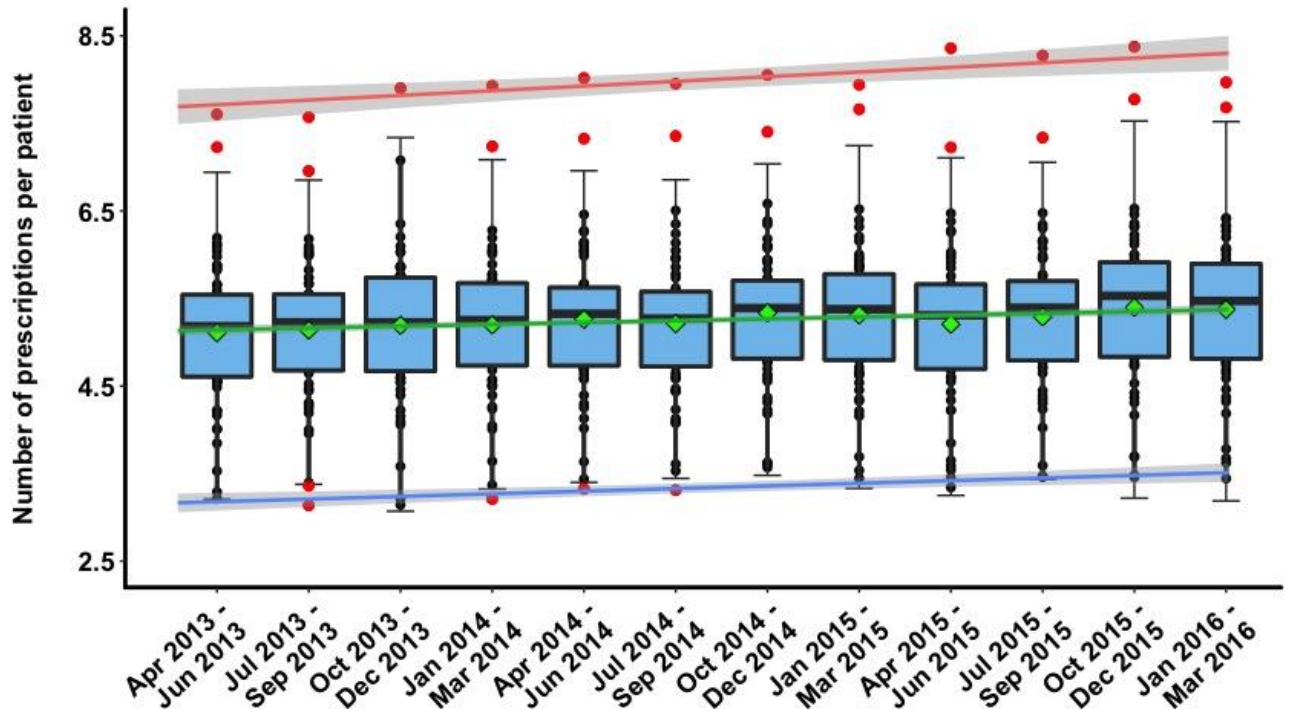
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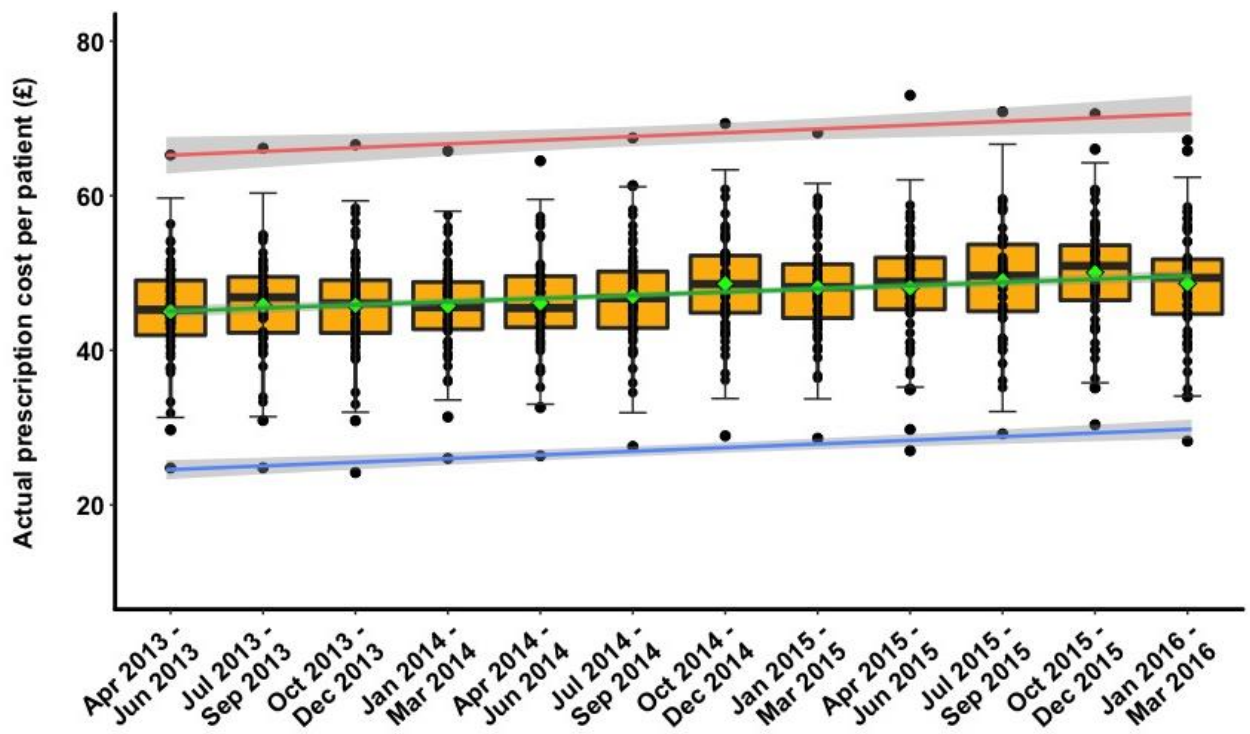
509 **Figure 1**



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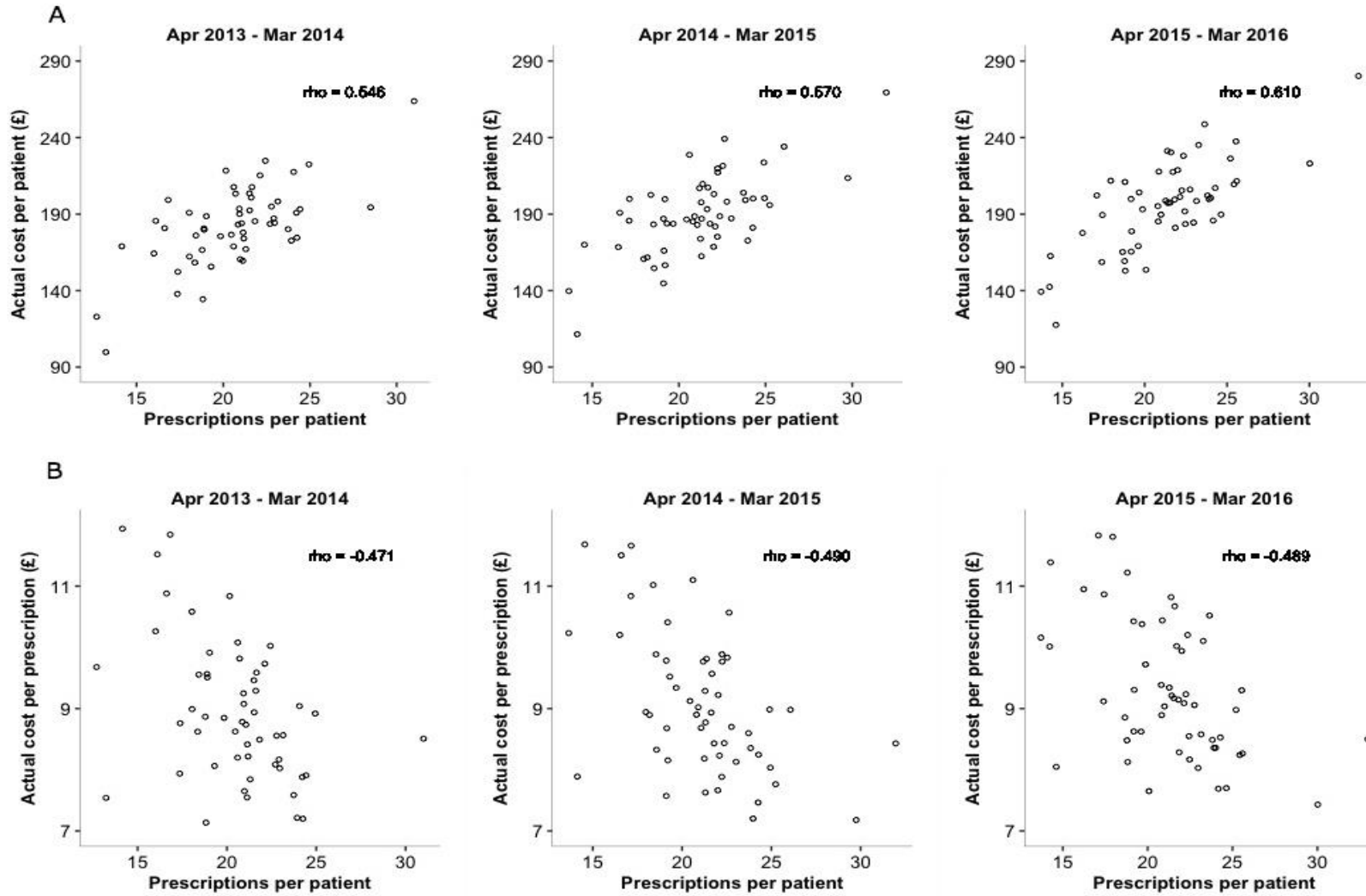
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512 **Figure 2**

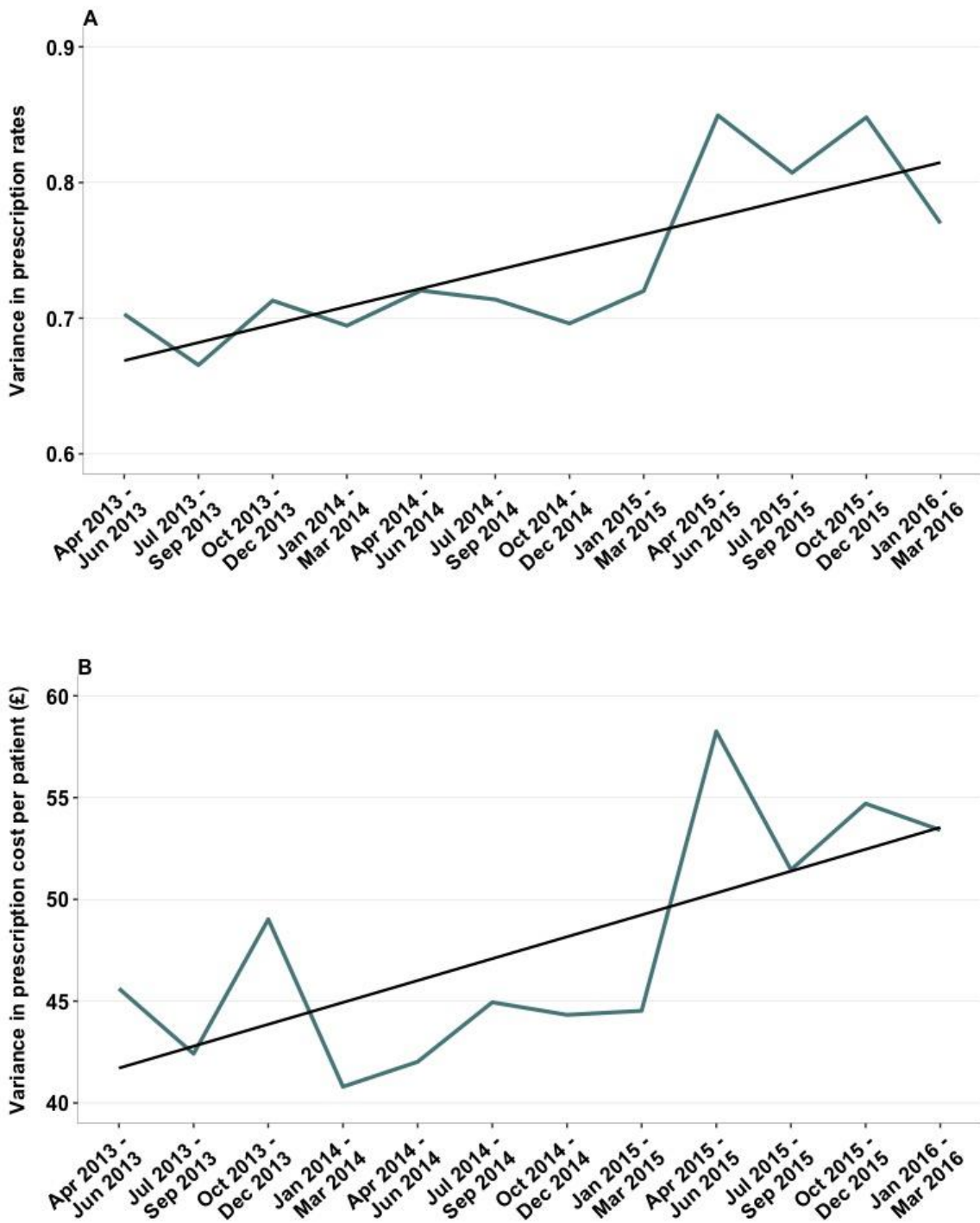


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516 Figure 4



517 **Table 1**

	Apr- Jun 2013	Jul- Sep 2013	Oct- Dec 2013	Jan- Mar 2014	Apr- Jun 2014	Jul- Sep 2014	Oct- Dec 2014	Jan- Mar 2015	Apr- Jun 2015	Jul- Sep 2015	Oct- Dec 2015	Jan- Mar 2016
<i>Rural</i>												
Mean	5.07	5.08	5.15	5.16	5.16	5.17	5.26	5.28	5.07	5.11	5.26	5.24
Variance	0.84	0.74	0.78	0.78	0.78	0.80	0.77	0.87	0.94	0.94	1.07	1.02
<i>Urban</i>												
Mean	5.14	5.19	5.23	5.23	5.34	5.24	5.39	5.33	5.31	5.43	5.50	5.48
Variance	0.62	0.62	0.68	0.65	0.68	0.67	0.65	0.62	0.79	0.69	0.68	0.58
<i>F-test p-value</i>	0.41	0.65	0.72	0.63	0.72	0.64	0.66	0.38	0.65	0.41	0.24	0.14
<i>T-test p-value</i>	0.77	0.64	0.72	0.78	0.44	0.77	0.58	0.83	0.35	0.21	0.36	0.32

519 **Table 2**

	Apr- Jun 2013	Jul- Sep 2013	Oct- Dec 2013	Jan- Mar 2014	Apr- Jun 2014	Jul- Sep 2014	Oct- Dec 2014	Jan- Mar 2015	Apr- Jun 2015	Jul- Sep 2015	Oct- Dec 2015	Jan- Mar 2016
<i>Less deprived areas</i>												
Mean	5.00	5.01	5.12	5.13	5.13	5.11	5.26	5.23	5.22	5.22	5.42	5.37
Variance	1.27	1.25	1.39	1.37	1.37	1.41	1.31	1.33	1.49	1.41	1.41	1.25
<i>More deprived areas</i>												
Mean	5.14	5.18	5.22	5.22	5.30	5.24	5.36	5.34	5.20	5.31	5.39	5.38
Variance	0.55	0.51	0.53	0.51	0.54	0.52	0.53	0.56	0.68	0.65	0.70	0.65
<i>F-test p-value</i>	0.046*	0.031*	0.022*	0.018*	0.027*	0.018*	0.032*	0.037*	0.065	0.066	0.096	0.117
<i>T-test p-value</i>	0.665	0.625	0.776	0.788	0.624	0.709	0.770	0.767	0.966	0.790	0.926	0.979

**S1 Table. The variance in prescribing rates for the data set with and without outlier practices.**

	Apr- Jun 2013	Jul- Sep 2013	Oct- Dec 2013	Jan- Mar 2014	Apr- Jun 2014	Jul- Sep 2014	Oct- Dec 2014	Jan- Mar 2015	Apr- Jun 2015	Jul- Sep 2015	Oct- Dec 2015	Jan- Mar 2016
<i>With outlier practices</i>												
$\sigma^2$ (£)	0.70	0.67	0.71	0.69	0.72	0.71	0.70	0.72	0.85	0.81	0.85	0.77
<i>Without outlier practices</i>												
$\sigma^2$ (£)	0.52	0.39	0.59	0.43	0.45	0.44	0.49	0.50	0.60	0.58	0.59	0.56