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ORIGINAL ARTICLE

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Rescheduling gabapentinoids had negligible effects on prescribing behaviour by general practitioners in England

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Abstract

Purpose: To determine whether the rescheduling of gabapentinoids in England as Schedule 3 Controlled Substances in April 2019, changed prescribing behaviour for gabapentinoids by general practitioners.

Methods: Data on the monthly number of prescription items and the monthly average dose per prescription item were analysed for the period April 2017 to April 2021 under three models: (i) a simple linear regression, (ii) a linear spline with a knot at April 2019, and (iii) a parallel slopes model with time before and after the rescheduling as a covariate. Best fit models were selected based on them having the lowest corrected Akaike's information criterion. Auto-regressive integrated moving average (ARIMA) models were also generated.

Results: For gabapentin, the best fit model for the number of prescription items was the simple linear model, and for the dose per prescription item it was the parallel slopes model. For pregabalin, the best fit model was the linear spline for the number of prescription items and the dose per prescription item. For all models, the interval estimates for the slopes were consistent with no change or no meaningful change in prescribing behaviour after April 2019. Forecasts from ARIMA models for gabapentin and pregabalin were consistent with no change in the number of prescription items per month. However, forecasts for the dose per prescription item for gabapentin or pregabalin did not fully capture the post-April 2019 trajectories.

Conclusion: The reclassification of gabapentinoids did not materially change the prescribing behaviour of these drugs by general practitioners in England.

KEYWORDS

anticonvulsants, controlled substances, drug misuse, gabapentin, neuropathic pain, pregabalin

Key Points

- The prescription of gabapentinoids, pregabalin and gabapentin, in the UK has increased substantially over the last decade.
- With this increase in prescription of gabapentinoids, there has been growing evidence of misuse of the medications.
- In response to the evidence of misuse, the gabapentinoids were rescheduled as Schedule 3 Controlled Substance in England in April 2019

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- This study shows that reclassification of gabapentinoids in April 2019 did not materially affect the trends in prescribing of gabapentinoids by general practitioners in England.
- The results suggest that the increased prescribing restrictions placed on Schedule 3 Controlled Substances do not alter prescribing behaviour.

Plain Language Summary

The prescription of gabapentinoids (drugs used to treat epilepsy and neuropathic pain), in the UK has increased substantially over the last decade. With this increase in prescription of gabapentinoids, there has been growing evidence of misuse of the medications. In response to the evidence of misuse, the gabapentinoids were rescheduled as Schedule 3 Controlled Substance in England in April 2019, which made the prescription of the medications more onerous. This study shows that making the prescription of gabapentinoids more onerous did not materially affect the trends in prescribing of the drug class by general practitioners, thus raising the question of whether prescribing barriers are an effective means of altering prescribing behaviour.

1 | INTRODUCTION

The National Health Services (NHS) England rescheduled gabapentin and pregabalin (gabapentinoids) as Schedule 3 Controlled Substances from 1 April 2019.[1] The rescheduling placed greater controls on the prescription of these agents, which are recommended as first-line treatments in the management of neuropathic pain,[2,3] and was brought on by accumulating evidence of the misuse of the drugs.[4]

Before the rescheduling, the number of prescriptions for gabapentin and pregabalin had increased markedly in the UK for roughly a decade.[5,6] For example, between 2007 and 2017, first-time prescriptions for gabapentin increased almost threefold from 230 to 679 per 100 000 persons per year, and first-time prescriptions of pregabalin saw a similar-fold increase from 128 to 379 per 100 000 persons per year.[5] The reclassification of gabapentinoids was expected to decrease the prescription of the drugs,[7] but an analysis of changes in prescribing brought on by the reclassification has not been made.

In this descriptive study, I report on the prescription of gabapentin and pregabalin by general practitioners in England for a 2-year period before (April 2017 to March 2019) and after (April 2019 to March 2021) the change in the scheduling of gabapentinoids. I describe the changes in the number of prescription items and the dose of drug per prescription item. To describe the changes, I compared several regression models with the aim of finding the most parsimonious model to describe the data.

2 | METHODS

2.1 | Obtaining and processing the data

The data originated from the NHS Business Service Authority, and consisted of deidentified monthly prescription records from individual general practitioner practices across NHS England Clinical Commissioning Groups. The data were released under a UK Open Government Licence. The data for a 4-year period (April 2017 to March 2021) was accessed through the OpenPrescribing.net portal, using the website's application programming interface (https://openprescribing.net/api/). Data were downloaded using British National Formulary codes as identifiers. These codes allow the identification of data for individual drugs according to the chemical molecule (gabapentin or pregabalin), type (non-proprietary or named brand), formulation (capsule or tablet), and dose (e.g., the code for non-proprietary gabapentin 100 mg capsules is 0408010G0AAAAAA) (see Supplement 1 for details). Each downloaded file contained the following columns: (i) actual cost (total estimated cost to the NHS of supplying a medicine per month), (ii) date, (iii) items (total number of times a medicine was prescribed per month), and (iv) quantity (total number of pills prescribed).

2.2 | Data processing

The total number of prescription items per month and the total quantity of pills prescribed per month was calculated for each for dose of drug (gabapentin: 100, 300, 400, 600, 800 mg; pregabalin: 25, 50, 75, 100, 150, 200, 225, 300 mg) by summing the monthly data for each dose of drug across the various formulations (capsule or tablet) and types (non-proprietary or named brand) for that drug. These data were then used to calculate the total monthly dose prescribed for each dose of a drug (e.g., in April 2019, the total dose of 100 mg gabapentin pills prescribed = total monthly quantity of 100 mg pills prescribed × 100 mg). The grand monthly total for the number of prescription items and the grand monthly total dose prescribed for a drug was calculated by summing across drug doses (e.g., grand total dose of gabapentin in April 2019 = total $\text{dose}_{(100\ \text{mg, April 2019})}$ + total $\text{dose}_{(300\ \text{mg, April 2019})}$ + … + total monthly $\text{dose}_{(800\ \text{mg, April 2019})}$). Once these monthly grand totals had been calculated, the average monthly dose of a drug per prescription was calculated (e.g., average monthly dose of gabapentin per prescription item = grand monthly total dose of gabapentin÷grand monthly total of the number of prescription items).

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2.3 | Statistical analysis

The analysis was undertaken in the R Statistical Environment (v4.2.0)[8] using the following packages: broom,[9] dplyr,[10] forecast,[11,12] ggplot2,[13] ggthemes,[14] kableExtra,[15] lspline,[16] moderndive,[17] MuMIn,[18] patchwork,[19] readr,[20] skimr,[21] tseries.[22]

Two outcome variables were assessed: (i) the total monthly number of prescription items for each drug, and (ii) the average monthly dispensed dose per prescription item. Regression models were built using linear regression. Three models were built for both outcome variables for each drug: (i) a simple linear model, (ii) a linear spline model with a single knot point at April 2019, and (iii) a parallel slopes model. For all models, month was included as the continuous independent variable. In order to generate the parallel slopes models, an additional categorical independent variable (whether the date was before or after April 2019) was included. All models were checked for autocorrelation of residuals.

A second-order Akaike's information criterion (AICc), a measure of model fit, was calculated for each of the three models generated for the outcome variables for each drug. The difference in AICc (ΔAICc) was calculated by subtracting the model with the smallest AIC (best approximating model) from the models with larger AICc values. ΔAICc values were used to calculate the likelihood for models relative to the best approximating model $\left(\text{Relative likelihood} = \exp\left(-\frac{1}{2}\Delta\text{AICc}\right)\right)$. The evidence ratio, which describes how many times more likely the best approximating model is relative to the other models, was calculated by taking the ratio of the relative likelihood of the best approximating model (relative likelihood = 1) to that of model i (relative likelihood <1) $\left(\text{Evidence ratio} = \frac{\text{Relative likelihood}_{(\text{best model})}}{\text{Relative likelihood}_{(\text{model } i)}}\right)$. Finally, model probabilities (Akaike weights), which give the probability that the model is the best approximating model, were calculated $\left(\text{Akaike weight for model } i = \frac{\text{Relative likelihood}_{(\text{model } i)}}{\sum_j \text{Relative likelihood}}\right)$.[23]

In addition to linear regression modelling, auto-regressive integrated moving average (ARIMA) models were generated for the data. ARIMA modelling has recently been suggested as an alternative method for assessing interrupted time-series analysis of healthcare interventions.[24] ARIMA models were built for both outcome measures for pregabalin and gabapentin using the data from before April 2019. Time-series stationarity was assessed using the augmented Dickey–Fuller test and seasonality was assessed be inspecting autocorrelation plots. These checks informed the selection of modelling parameters used in an automated search (*auto.arima* function in the "forecast" package in R) for the best fit ARIMA model (AIC was used to rank models). The residuals of the best fits models were then checked using the Ljung–Box test. The selected models were used to forecast the time-series for the 2-year period from April 2019 to May 2021. In addition to monthly point estimates, 90% prediction intervals were constructed. These intervals were then used to assess whether the actual course of the data over time was consistent with the predicted course of the time-series. That is, whether the actual data fell within the 90% prediction interval of the forecast.

ARIMA models are expressed using the ARIMA (p, d, q) notation, were p is the order of the auto-regressive component, d is the order of differencing, and q is the order of the moving average component.

3 | RESULTS

None of the linear regression models displayed autocorrelation of residuals.

3.1 | Gabapentin

Summaries of the number of prescription items per month, number of pills dispensed per month, total amount of drug dispensed per month, monthly drug dose per prescription item, and average daily dose for each dose of gabapentin and the total dose for gabapentin for the 2-year period before and after rescheduling can be found in Supplement 2. Briefly, for monthly totals, the mean number of prescription items per month increased slightly (1.1%) between the pre- and post-rescheduling periods [before: mean = 602 660 items per month (SD = 24 566), after: mean = 609 251 items per month (SD = 24 077)]. In comparison, the mean monthly dose prescribed per prescription item fell slightly (by about 2%) between the pre- and post-rescheduling periods [before: mean = 29 125 mg per item per month (SD = 135), after: mean = 28 568 mg per item per month (SD = 116)].

Figure 1A–C shows the regression lines and AICc values for the monthly number of prescription items for gabapentin. Figure 1D–F shows the regression lines and AICc values for the monthly dose of gabapentin per prescription item. The estimates for each regression model are shown in Table 1. Additional data on model fits are provided in Table 2.

For the monthly number of prescription items, the interval estimates (95% confidence intervals) for month for all models included zero, that is, no relationship between the time and monthly number of prescription items was a plausible outcome (Table 1). With regards to model fit (AICc, Table 2), the simple linear model provided the best fit (lowest AICc). When looking at the evidence ratios (Table 2), the simple linear model was more than twice as likely as the linear spline linear model and the parallel slopes model to be the best approximating model. The probability (Akaike weight, Table 2) that the simple linear model was the best approximating model was 0.57, compared with 0.22 for the linear spline model and 0.21 for the parallel slopes model. That is, there was moderately strong evidence for the simple linear model as the best approximating model.

For the monthly dose of gabapentin per prescription item, none of the interval estimates for the three models included zero, and in all cases the relationship between month and monthly dose of gabapentin per prescription item was negative (Table 1). That is, the mean dose of gabapentin decreased over time. However, the upper limit of all interval estimates for month indicated a small effect was a plausible outcome (Table 1). For the parallel slopes model, the mean monthly dose of gabapentin per prescription item before versus after April 2019 was

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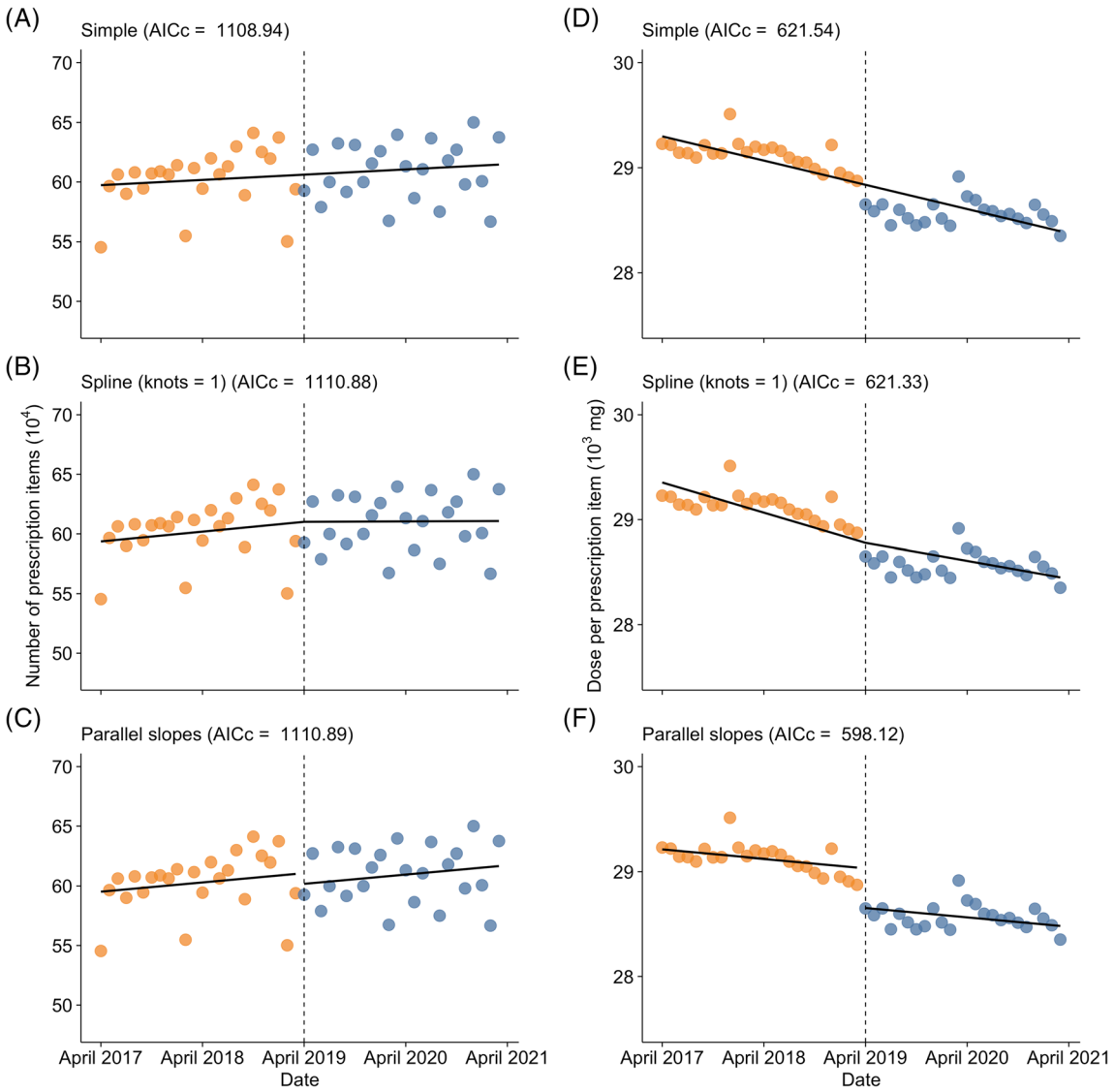


FIGURE 1 Regression models and AICc values for the monthly number of prescription items for gabapentin (A–C) and the monthly dose of gabapentin per prescription item (D–F). The dashed vertical lines show the time when the new regulation came into effect (April 2019). For each drug, the best model fit is indicated by the lowest AICc value.

(95% confidence interval) 244 to 513 mg, indicating a small decrease in dose prescribed from April 2019. With regards to model fit (AICc, Table 2), the parallel slopes model provided the best fit. For the evidence ratios (Table 2), the parallel slopes model was 1.2×10^5 times as likely as the simple linear model and about 1.1×10^5 times as likely as the linear spline model. The probability (Akaike weight, Table 2) that the parallel slopes model was the best approximating model was slightly under 1, compared with very low probabilities for the simple linear and linear spline models. That is, there was very strong evidence for the parallel slopes model as the best approximating model.

3.2 | Pregabalin

Summaries of the number of prescription items per month, number of pills dispensed per month, total amount of drug dispensed per month, monthly drug dose per prescription item, and average daily dose for each dose of pregabalin and the total dose for pregabalin for the 2-year period before and after rescheduling can be found in Supplement 3. Briefly, for the monthly totals, the mean number of prescription items per month increased dramatically by 14% between the pre- and post-rescheduling periods [before: mean = 561 305 items per month (SD = 39 096), after: mean = 640 091 items per month (SD = 31 872)]. In comparison, the mean monthly dose prescribed per prescription item fell by 1.5% between the pre- and post-rescheduling periods [before: mean = 6344 mg per item per month (SD = 64), after: mean = 6243 mg per item per month (SD = 31)].

Figure 2A–C shows the regression lines and AICc values for the monthly number of prescription items for pregabalin. Figure 2D–F shows the regression lines and AICc values for the monthly dose of pregabalin per prescription item. The estimates for each regression model are shown in Table 3. Data on model fits are provided in Table 4.

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TABLE 1 Regression coefficients for models of gabapentin[a]

Model	Variable	Point estimate	95% confidence interval
Monthly number of prescription items			
Simple	Intercept	596 945	582 780 to 611 109
	Month	368	−135 to 871
Spline	Intercept	592 925	574 027 to 611 823
	Month (up to May 2019)	686	−419 to 1791
	Month (From April 2019)	29	−1133 to 1190
Parallel slopes	Intercept	585 609	547 279 to 623 939
	Month	504	−367 to 1662
	Period (up to May 2019)	13 953	−19 148 to 37 057
Monthly dose per prescription item (mg)			
Parallel slopes	Intercept	28 839	28 656 to 29 023
	Month	−7.4	−12.3 to −2.6
	Period (up to May 2019)	378	244 to 513
Spline	Intercept	29 378	29 262 to 29 493
	Month (up to May 2019)	−24.0	−30.7 to −17.2
	Month (From April 2019)	−14.3	−21.3 to −7.2
Simple	Intercept	29 318	29 230 to 29 407
	Month	−19.3	−22.4 to −16.1

[a]Models are ordered according to best fit (see Table 2 for model fit details).

TABLE 2 Model fits for gabapentin[a]

Model	AICc	ΔAICc from best model	Relative likelihood	Evidence ratio	Akaike weight[b]
Monthly number of prescription items					
Simple	1108.94	0	1	1	0.57
Spline	1110.88	1.93	0.38	2.63	0.22
Parallel slopes	1110.89	1.95	0.38	2.65	0.21
Monthly dose per prescription item					
Parallel slopes	598.12	0	1	1	1
Spline	621.33	23.21	9.1×10^{-6}	1.1×10^{5}	9.1×10^{-6}
Simple	621.54	23.42	8.2×10^{-6}	1.2×10^{5}	8.2×10^{-6}

[a]Models are ordered in descending order of fit.
[b]May not add to 1 because of rounding.

For the monthly number of prescription items, none of the interval estimates for month, for any of the three models, included zero. In all cases the relationship between month and monthly dose of pregabalin per prescription item was positive (Table 3). That is, the mean number of pregabalin prescription items increased over time. With regards to model fit (AICc, Table 4), the linear spline model provided the best fit. For the evidence ratios (Table 4), the linear spline model was about 1.4 times as likely as the simple linear model and about 3.3 times as likely as the simple linear model to be the best approximating model. The probability (Akaike weight, Table 4) that the linear spline model was the best approximating model was 0.49, compared with 0.36 for the simple linear model and 0.15 for the parallel slopes model. That is, there was little evidence to choose between the linear spline and simple linear models as being the best approximating model.

For the monthly dose of pregabalin per prescription item, the interval estimates for neither the simple linear regression model nor the parallel slopes models included zero, and in both cases, the relationship between month and dose of pregabalin per prescription item was negative (Table 3). That is, the mean dose of pregabalin decreased over time, but this effect was small. However, when it came to the linear spline model, the relationship between the monthly dose of pregabalin per prescription item and the period from April 2017 to May2019 was negative (decreasing dose being prescribed over time), while the data from April 2019 was consistent with a shift in the relationship such that the slope was much shallower, with the data also being consistent with a slightly positive slope (95% confidence interval of the slope: −1.39 to 1.31 mg). With regards to model fit (AICc, Table 4), the linear spline model provided the best fit. The second-best model was the simple linear model, followed by the parallel

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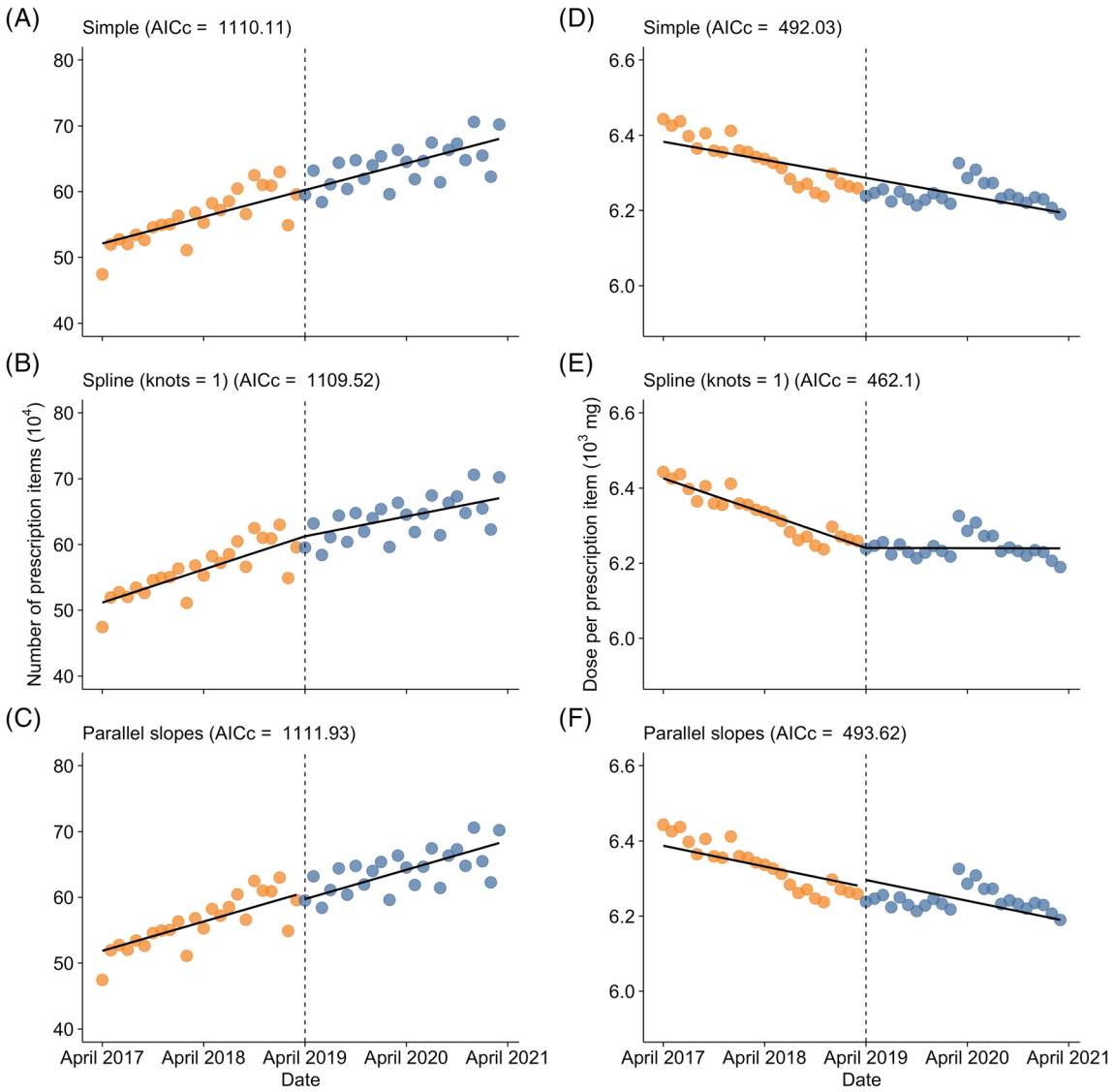


FIGURE 2 Regression models and AICc values for the monthly number of prescription items for pregabalin (A–C) and the monthly dose of pregabalin per prescription item (D–F). The dashed vertical lines show the time when the new regulation came into effect (April 2019). The best model fit is indicated by the lowest AICc value.

slopes model. When looking at the evidence ratios (Table 4), the linear spline model was about 3×10^6 times as likely as the simple linear model and about 7×10^6 times as likely as the linear spline model. The probability (Akaike weight, Table 4) that the linear spline model was the best approximating model was slightly under 1, compared with very low probabilities for the simple linear and parallel slopes models. That is, there was very strong evidence for the linear spline model as the best approximating model.

3.3 | ARIMA models for gabapentin and pregabalin

The ARIMA models of the monthly number of prescription items and the monthly dose per prescription item for gabapentin and pregabalin were not part of the original analysis plan, and therefore the results are presented in the supplementary documents only (Supplement 4).

4 | DISCUSSION

I modelled the prescription of gabapentin and pregabalin, in terms of the mean number of monthly prescription items and the mean monthly dose of drug per prescription item, by general practitioners for a 2-year period before and after the reclassification of gabapentinoids in England. For gabapentin, the best fit model for the monthly number of prescription items was a simple linear model, and the monthly dose per prescription item was the parallel slopes model. That is, the number of prescription items being prescribed per month remained constant over the 4-year period, with no stepped or ramped

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TABLE 3 Regression coefficients for models of pregabalin[a]

Model	Variable	Point estimate	95% confidence interval
Monthly number of prescription items			
Spline	Intercept	507 340	488 707 to 525 972
	Month (up to May 2019)	4206	3117 to 5295
	Month (From April 2019)	2522	1376 to 3667
Simple	Intercept	517 642	503 304 to 531 980
	Month	3390	2881 to 3899
Parallel slopes	Intercept	504 588	465 842 to 543 334
	Month	3712	2687 to 4738
	Period (up to May 2019)	10 312	−18 096 to 38 720
Monthly dose per prescription item			
Spline	Intercept	6434	6412 to 6456
	Month (up to May 2019)	−7.73	−9.01 to −6.44
	Month (From April 2019)	−0.04	−1.39 to 1.31
Simple	Intercept	6387	6364 to 6410
	Month	−4.01	−4.82 to −3.19
Parallel slopes	Intercept	6412	6350 to 6473
	Month	−4.62	−6.25 to −2.98
	Period (up to May 2019)	−19.5	−64.8 to 25.8

[a]Models are ordered in descending order of fit (see Table 4 for model fit details).

TABLE 4 Model fits for pregabalin[a]

Model	AICc	ΔAICc from best model	Relative likelihood	Evidence ratio	Akaike weight[b]
Monthly number of prescription items					
Spline	1109.52	0	1	1	0.49
Simple	1110.11	0.59	0.74	1.35	0.36
Parallel slopes	1111.93	2.41	0.30	3.34	0.15
Monthly dose per prescription item					
Spline	462.10	0	1	1	1
Simple	492.03	29.93	3.17×10^{-7}	3.15×10^{6}	3.17×10^{-7}
Parallel slopes	493.62	31.52	1.43×10^{-7}	6.97×10^{6}	1.43×10^{-7}

[a]Models are ordered in descending order of fit.
[b]May not add to 1 because of rounding.

changes in that number of prescription items at or after April 2019. The finding that a parallel slopes model was the best fit model for monthly dose per prescription item indicates that there was a parallel downward shift (a stepped change) in the dose per prescription item after the 1 April reclassification of the drug. In terms of the slope of the number of prescription items model, the interval estimate was consistent with a zero slope. My interpretation of the model is that the number of prescription items of gabapentin per month remained stable and close to zero across time, despite changes to the drug classification. In terms of the monthly dose per prescription item, the interval estimates for the slope and the period effects did not include zero, but the interval estimates also indicated that the changes between the two time periods were minor. If converted to daily dose of gabapentin (assuming a 30-day prescription), the 95% confidence interval of the slope was 0.09 to 0.14 mg per day, and the 95% confidence interval for the intercept for the period effect showed a reduction of between 8.1 and 17.1 mg. My interpretation of the model is that reclassification of gabapentin had little effect on the dose being prescribed per prescription item. These interpretations of the models for monthly number of prescription items and monthly dose per prescription item are substantiated by the results of the ARIMA modelling, where the forecast values closely followed the actual values, except for the small, stepped change in dose per prescription item at April 2019.

For pregabalin, a linear spline model was the best fit model for the number of prescription items per month and the monthly dose of pregabalin per prescription item. The first segment of the linear spline model for the number of prescription items had a positive slope (95% confidence interval: 3117 to 5295 items per month), and this positive slope was maintained, but at a slightly shallower rate (95% confidence

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interval: 1367 to 5295 items per month). My interpretation of the model is that month-on-month increases in prescription items before the change in the classification of pregabalin, continued, although at a marginally lower rate, after the change in April 2019. In terms of the monthly dose per prescription item, the slope of the line before April 2019 was negative, but the effect size was very small (95% confidence interval: −9.01 to −6.44 mg per prescription item per month). This small monthly decrease was halted by the introduction of the rescheduling of pregabalin such that the 95% confidence interval for slope of the line after April 2019 is consistent with a slope of 0 (−1.39 to 1.31 mg per prescription item per month). Considering the shallow slope of the line before April 2019, my interpretation of this linear spline model is that there was very little change in the dose being prescribed over time.

In terms of the ARIMA model of the number of prescription items per month, the forecast is consistent with the actual values such that all the actual values fall within the 90% prediction interval for the forecast. The ARIMA model for the monthly dose of pregabalin per prescription item fared poorly, such that the model forecast a continuing decrease in monthly dose per prescription item, while the actual dose per prescription item levelled off after April 2017, causing a rapid separation of the curves such that the ARIMA model overestimated the rate of dose reduction per prescription item after April 2019.

In 2014, another analgesic, tramadol, was reclassified as a Schedule 3 Controlled Substance in the UK. The reason for the reclassification was similar to those given for the gabapentinoids, that is, concerns about safety and misuse.[25] An analysis of long-term trends in tramadol revealed that while statistically significant decreases were observed across several measures of tramadol use after the reclassification, the extent of these changes was minor.[26]

That there were no meaningful decreases in the dose per prescription item for either gabapentinoids is not unexpected. There is a registered dosing window for each of the drugs, and the lower end of these dose ranges act as limits to how much doses of the respective drugs can be reduced before they become ineffective in the average patient. The rescheduling also does not advocate for changes in drug dose. That is, the reclassification adds an additional safeguard that interferes with the prescription of the two drugs by doctors, the filling of scripts by pharmacists, and the collection of the drugs by patients, but it does affect the dose per prescription item.

The reason for the stabilisation in the number of gabapentin prescription items per month, even before the April 2019 reclassification, while that for pregabalin continued to rise is unclear. It is unlikely that pregabalin is superseding gabapentin because of its better pharmacokinetics because both drugs saw persistent growth in prescriptions after the introduction of pregabalin in the UK in 2003.[5] That the number of pregabalin scripts continued to increase, although at a slower rate, after the April 2019 reclassification, also is perplexing. It has been suggested that the off-label use of the drugs is behind the increase in prescriptions. For example, an analysis revealed that about half of new prescriptions for pregabalin in the UK were for off-label indications, with about 60% of pregabalin prescriptions being for pain other than neuropathic pain.[6] Yet, these data do not explain why prescriptions consistent with the indications of pregabalin (neuropathic pain, focal seizures, and generalised anxiety disorder) increased in parallel to that of off-label use.[7]

A limitation of this study is that it assesses the prescription of gabapentinoids in isolation, and does not look at co-prescription of other substances, such as benzodiazepines and opioids, that are known to be prescribed with gabapentinoids and which may contribute to the morbidity and mortality associated with gabapentinoids.[7] Unfortunately, these are aggregated data, so creating linkages between gabapentinoids use and concomitant use of other drugs at the patient level is not possible with these data. Moreover, these data are only for general practitioners, so it is not clear what the effect of the change in regulation had on prescribing behaviour in specialists such as pain specialists, neurologists, and palliative care specialists. Furthermore, the assumption of the analysis is that the population was relatively stable over the period of assessment, and therefore changes in the number of prescription items reflects prescription habits and not population changes. The population of England did grow between mid-2017 and mid-2021 (increasing by 1.6%),[27] but this increase was lower than the increase in the number of gabapentin and pregabalin prescription items over the same period (3.2% increase for gabapentin, and 30.2% for pregabalin, Supplement 5). Finally, the use of linear regression models for interrupted time series analysis brings in the issue of whether the errors were correlated. Thus, all linear regression models were checked for autoregression of their residuals, and none was detected.

5 | CONCLUSION

The rescheduling of the gabapentinoids made prescribing the drugs more difficult, and was introduced with a view of reducing unnecessary prescribing of the drugs and therefore the misuse and abuse of the drugs.[7] The results of this analysis show that prescribing behaviour (number of prescription items and dose per prescription item) for gabapentinoids was not significantly impacted by the change in drug classification. That is, the change in schedule did not have the desired effect, and given the lack of change for tramadol when it was similarly rescheduled, highlights the limited efficacy of this level of rescheduling on curbing prescribing behaviour.

AUTHOR CONTRIBUTIONS

As sole author of the work, Peter Kamerman was responsible for conceiving the idea for the study, analysing the data, and writing the manuscript.

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CONFLICT OF INTEREST STATEMENT

Peter Kamerman has received consultancy fees from Partners in Research and lecture fees from GlaxoSmithKline.

DATA AVAILABILITY STATEMENT

All analysis scripts and data are available from GitHub (https://github.com/kamermanpr/gabapentinoids) and mirrored on Zenodo (DOI: https://doi.org/10.5281/zenodo.7214845), and a Docker image of the environment in which the code was executed is available from: https://hub.docker.com/r/kamermanpr/gabapentinoids.

ETHICS STATEMENT

The study was conducted using publicly available data, released under a UK Open Government Licence.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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