Received: 8 May 2024 | Revised: 25 September 2024 | Accepted: 8 October 2024

DOI: 10.1002/hup.2912

RESEARCH ARTICLE

WILEY

Patient outcome following selective serotonin reuptake inhibitor prescribing in primary care in Wales (UK)

Shaila Ahmed[1,2] | Katherine Chaplin[2] | Richard S. Young[1] | Paul N. Deslandes[1,2]

[1]Faculty of Life Sciences and Education, University of South Wales, Treforest, UK

[2]All Wales Therapeutics and Toxicology Centre, University Hospital Llandough, Llandough, UK

Correspondence
Paul N. Deslandes.
Email: paul.deslandes@wales.nhs.uk

Funding information
Research Capacity Building Collaboration Wales

Abstract

Objective: This study investigated prescribing patterns of two cohorts of patients treated with selective serotonin reuptake inhibitors (SSRI) in primary care in Wales (UK), to better understand drivers for increased usage.

Methods: This e-cohort study included patients receiving a first READ-coded SSRI prescription in SAIL in either 2005 or 2015. Patients were followed up for 3 years from date of SSRI prescription. Influence of age and other demographic data on prescribing patterns, and details of mental health or medication reviews that took place were identified.

Results: In total 67,006 patients were included across the two cohorts; 29,534 in 2005, and 37,472 in 2015. Citalopram was the most commonly prescribed SSRI in both cohorts. A READ-coded diagnosis relating to SSRI treatment could not be identified in 24,797 patients. The percentage of patients continuing treatment for 3 years was 6.9% and 11.3% in 2005 and 2015, respectively. In total, 21,150 (72%) patients in the 2005 cohort and 23,947 (64%) in the 2015 cohort received at least one medication review during follow-up.

Conclusions: The proportion of patients continuing longer term treatment was small, whilst the number of recorded mental health and medication reviews offers some reassurance that prescribing remained appropriate.

KEYWORDS
antidepressant, drug utilisation, prescribing, selective serotonin reuptake inhibitor

1 | INTRODUCTION

Antidepressant prescribing has increased over the past two decades both in the United Kingdom (Bogowicz et al., 2021; Hafferty et al., 2019; Lockhart & Guthrie, 2011) and elsewhere (Forns et al., 2019; Lipovec et al., 2022). Studies from the UK have suggested that factors contributing to these changes include increasing numbers of patients being prescribed antidepressants, use of higher doses, and longer-term prescribing (Hafferty et al., 2019; Lockhart & Guthrie, 2011; McRea et al., 2016). A trend towards longer-term prescribing has also been noted in The Netherlands and the United States of America (Huijbregts et al., 2017; Mojtabai & Olfson, 2014). Concerns have been expressed that rising prescribing represents over-diagnosis of depression and over-use of antidepressants (Spence, 2013). However, increased prescribing of antidepressants could also indicate a greater awareness and recognition of mental illness or a higher prevalence of depression requiring treatment (Reid, 2013).

In the UK, the 2009 National Institute for Health and Care Excellence (NICE) guideline for depression (CG90; NICE, 2009) recommended the use of antidepressants for the management of moderate to severe major depression in combination with psychological intervention. The guideline recommended use of selective serotonin reuptake inhibitors (SSRIs) over other antidepressants, and the use of an alternative SSRI or an antidepressant from a different class (such as a serotonin-noradrenaline reuptake inhibitor) when switching treatment due to inadequate response. Prescription data from the UK reflects this advice, with SSRIs the most prescribed antidepressant group (Bogowicz et al., 2021; Hafferty et al., 2019). Treatment was recommended for six to 12 months after symptom remission of an initial episode of illness to reduce the risk of relapse (i.e. an overall duration of approximately nine to 15 months in the first instance; NICE, 2009), and this broadly aligns with other clinical guidance (Cleare et al., 2015). Data from the UK has suggested increased treatment duration over time (McRea et al., 2016), with longer-term prescribing (for a period of 15 months or longer) accounting for approximately 50% of treatment episodes in one study (Hafferty et al., 2019).

Whilst antidepressant treatment has been shown to be effective compared to placebo (albeit with small effect sizes; Cipriani et al., 2018), longer term treatment is not without challenges. Possible benefits in relation to relapse prevention (Lewis et al., 2021) must be considered in the context of adverse effects including discontinuation symptoms (Kendrick, 2021). Effective review of treatment with a consideration of the risks and benefits of ongoing prescribing is key to optimal management. The All Wales Medicines Strategy Group provides medicines optimisation advice to Welsh Government, and part of this work involves monitoring medicines usage using Prescribing Indicators (Haines et al., 2021). Previous work has focussed on reducing prescribing of the antidepressant dosulepin due to its toxicity profile in comparison with other antidepressants (Deslandes et al., 2016). However, promoting the wider optimisation of antidepressant use at a national level has proved more challenging, in part due to the dilemma discussed by Spence (2013) and Reid (2013) mentioned above. It was hoped that greater understanding of antidepressant prescribing patterns in Wales could help to inform possible approaches to this process.

This study aimed to investigate prescribing patterns of two cohorts of patients (one from 2005 and another from 2015) treated with an SSRI, who did not have a previously READ coded antidepressant prescription in primary care in Wales (UK). We sought to identify treatment duration and outcome (measured as whether patients continued the initial antidepressant, discontinued treatment, or were switched to an alternative antidepressant during a 3 year follow up period), and evidence of review of treatment or mental illness.

2 | METHOD

2.1 | Study design and data sources

This retrospective study investigated antidepressant prescribing patterns in two cohorts of patients from Wales. Patients were followed up over a 3-year period from date of first READ coded SSRI prescription issued in primary care in either 2005 or 2015. These years were chosen to allow a comparison of prescribing at a 10-year interval prior to and following publication of NICE guideline NG90, and to allow a 3-year follow-up period of the 2015 cohort prior to the onset of the COVID-19 pandemic. Data were obtained from the SAIL databank (www.saildatabank.com); an expanding data repository containing a wide range of anonymised routinely collected person-based data covering the population of Wales. Primary care data were available for ~80% of the Welsh population. Clinical and demographic data are provided from several sources, including primary and secondary care records. Records can be linked at an individual level between datasets for the purposes of research (Ford et al., 2009; Jones et al., 2014; Lyons et al., 2009).

Primary care data relating to diagnoses, antidepressant prescribing, and medication and illness review were extracted from the Welsh Longitudinal General Practice Database by specified READ codes. Demographic data including sex, age, deprivation in fifths (Welsh Index of Multiple Deprivation [WIMD]) were extracted from the Welsh Demographic Data Service (all held as part of the SAIL databank).

2.2 | Study cohorts

Included individuals were resident in Wales and aged 18 years or over at the start of 2005 (cohort one) or 2015 (cohort two), and did not have a previously READ coded antidepressant prescription in primary care prior to January 2005 and January 2015, respectively. A prescription for an SSRI antidepressant must have been subsequently issued during the relevant calendar year. A previous READ code for amitriptyline (10, 25 and 50 mg) was assumed to be for management of pain, and was permitted.

2.3 | Grouping of patients

The date of first READ-coded SSRI prescription identified in the SAIL database during 2005 (cohort one) or 2015 (cohort two) was used as the index timepoint for each patient. An algorithm was used to follow-up patients for 3 years from date of first prescription, and to identify whether prescribing of the first SSRI continued throughout follow-up (defined as < 90-day gap between prescriptions). Alternatively, if a gap (>90-day interval between prescriptions) in SSRI prescribing was identified and another antidepressant initiated within 90 days of the last SSRI prescription, patients' treatment was considered to have been switched. Finally, if a gap (>90-day interval between prescriptions) in SSRI prescribing was identified with no other antidepressant initiated within 90 days of the last SSRI prescription, patients were considered to have been discontinued. Patients in each cohort were therefore classified into one of three groups:

Group 1: The continued group, consisted of patients receiving continued prescriptions (no gaps between prescriptions of >90-

days) for the identified SSRI throughout the 3-year follow up period.

Group 2: The switched group, consisted of patients whose initial SSRI prescription was stopped (>90-day gap between prescriptions) during follow up period, and who subsequently received an alternative antidepressant prescription within 90 days of last SSRI prescription.

Group 3: The discontinued group, consisted of patients whose initial SSRI prescription was stopped (defined as a >90-day gap between prescriptions) during the follow up period, and who did not receive a subsequent prescription for an alternative antidepressant within 90 days of last SSRI prescription.

2.4 | Prescribing outcomes

First SSRI prescribed and choice of any alternative antidepressant prescriptions during follow-up period for each patient were identified by READ code (see Table S1). Prevalence of antidepressant prescriptions by drug class in patients initiated in 2005 and 2015 were analysed, as well as the influence of age and other demographic data on prescribing patterns. Duration of treatment and number of prescriptions issued was identified for the first SSRI prescribed.

2.5 | Mental illness and treatment review

Details of any mental health review or medication review that took place during follow-up were identified by relevant READ code.

2.6 | Statistical analysis

Data were analysed using SPSS software (v28). Categorical outcomes were compared using chi-squared test, and continuous outcomes with one-way ANOVA. A p-value of <0.05 was considered statistically significant.

2.7 | Approval

Approval was gained from the SAIL Information Governance Review Panel (IGRP approval number 1004). This is an independent body including a range of government, regulatory and professional agencies. The IGRP oversees study approvals in line with permissions already granted for the analysis of anonymous data in the SAIL databank.

3 | RESULTS

3.1 | Demographics

Characteristics of the 2005 and 2015 cohorts are outlined in Table 1. From January to December 2005, 29,534 patients received a first READ coded SSRI prescription in primary care and were included in the 2005 cohort. From January to December 2015, 37,472 patients received a first READ coded SSRI prescription in primary care and were included in the 2015 cohort. The mean ages of the 2005 and 2015 cohorts were 44.0 $\pm$ 19.0 years and 40.4 $\pm$ 19.7 years, respectively ($p < 0.01$). Within the 2005 cohort the mean age of continued patients was significantly higher than the other two groups ($p < 0.001$). In the 2015 cohort the mean ages of each group were significantly different to each other ($p < 0.001$). The proportion of females was significantly different in the 2005 and 2015 cohorts (62% and 58%, respectively; $p < 0.01$). In each cohort, similar proportions of females and males continued, switched and discontinued first SSRI.

3.2 | Prescribing patterns

The proportion of patients who were continued, switched to another antidepressant, or discontinued was 7%, 13% and 80% in the 2005 cohort, and 11%, 15% and 74% in the 2015 cohort. In the 2005 cohort, the three most commonly prescribed SSRIs were citalopram (47%), fluoxetine (26%) and escitalopram (18%), which accounted for 92% of SSRI prescriptions. In the 2015 cohort, the three most commonly prescribed SSRIs were citalopram (46%), sertraline (34%) and fluoxetine (18%), which accounted for over 98% of SSRI prescriptions (Table 2). The total number of prescriptions for all antidepressants across the whole study period was 68% higher in the 2015 cohort than in the 2005 cohort (670,336 vs. 399,853). In both the 2005 and 2015 cohorts, SSRI prescriptions accounted for 90% of all antidepressant prescriptions issued during the study period. The majority of patients (>90% in both cohorts) received only one antidepressant (the original SSRI) or two antidepressants (the original SSRI and one other drug) during the 3-year study period.

3.3 | Continued groups

A total of 2038 (6.9%) patients in the 2005 cohort received regular SSRI prescriptions during the 3-year follow-up period compared to 4228 (11.3%) patients in the 2015 cohort. Citalopram was the most commonly prescribed SSRI in both cohorts, with approximately 8% of patients continuing this treatment for the duration of follow-up in 2005, compared with 11% in 2015. Continuation rates of patients prescribed escitalopram and fluoxetine in the 2005 cohort were 4% and 5%, respectively, whilst continuation rates of patients prescribed sertraline and fluoxetine in the 2015 cohort were 12% and 9%, respectively (see Table 2). Of all patients who continued, 117 (6%) in 2005 and 227 patients (5%) in 2015 received a prescription for an additional antidepressant at some point during follow-up.

3.4 | Switched groups

A total of 3736 (12.6%) patients in the 2005 cohort, and 5468 (14.6%) in the 2015 cohort switched treatment. In those who

TABLE 1 Demographics.

2005 cohort	Continued (n = 2038)	Switched (n = 3736)	Discontinued (n = 23,760)	Total (n = 29,534)
Female *n* (%)	1236 (60.6)	2226 (59.6)	14,900 (62.7)	18,362 (62.2)†
Age years				
Mean, s.d.	55.4*** (17.5)	42.7 (18.0)	43.3 (19.0)	44.0 (19.0)
Median (IQR)	55 (42–68)	40 (28–54)	39 (28–56)	40 (28–57)
Deprivation *n*, (%)				
1 most	521 (25.6)	1017 (27.2)	5755 (24.2)	7293 (24.7)
2	461 (22.6)	855 (22.9)	5031 (21.2)	6347 (21.5)
3	395 (19.4)	657 (17.6)	4369 (18.4)	5421 (18.4)
4	313 (15.4)	526 (14.1)	3738 (15.7)	4577 (15.5)
5 least	269 (13.2)	503 (13.5)	3829 (16.1)	4601 (15.6)
Not recorded	79 (3.9)	178 (4.8)	1038 (4.4)	1295 (4.4)
Diagnoses *n*, (%)				
None recorded	967 (47.4)	1211 (32.4)	9425 (39.7)	11,603 (39.3)
Depression	657 (32.2)	1559 (41.7)	9478 (39.9)	11,694 (39.6)
Anxiety/other licenced indication	182 (8.9)	361 (9.6)	1972 (8.2)	2515 (8.5)
Both	232 (11.4)	605 (16.2)	2885 (12.1)	3722 (12.6)
2015 cohort	**Continued (n = 4228)**	**Switched (n = 5468)**	**Discontinued (n = 27,776)**	**Total (n = 37,472)**
Female *n* (%)	2558 (60.5)	3104 (56.8)	16,234 (58.4)	21,896 (58.4)†
Age years				
Mean, s.d.	49.7*** (18.2)	37.8*** (18.9)	39.5 (19.7)	40.4 (19.7)
Median (IQR)	49 (36–62)	31 (22–49)	33 (23–51)	35 (24–53)
Deprivation *n* (%)				
1 most	902 (21.3)	1426 (26.1)	6186 (22.3)	8514 (22.7)
2	889 (21.0)	1158 (21.2)	5540 (19.9)	7587 (20.2)
3	809 (19.1)	1054 (19.3)	5217 (18.8)	7080 (18.9)
4	674 (15.9)	780 (14.3)	4508 (16.2)	5962 (15.9)
5 least	713 (16.9)	776 (14.2)	4628 (16.7)	6117 (16.3)
Not recorded	241 (5.7)	274 (5.0)	1697 (6.1)	2212 (5.9)
Diagnoses *n*, (%)				
None recorded	1770 (41.9)	1467 (26.8)	9957 (35.8)	13,194 (35.2)
Depression	1359 (32.1)	2238 (40.9)	10,377 (37.4)	13,974 (37.3)
Anxiety/other licenced indication	620 (14.6)	774 (14.1)	3876 (13.9)	5270 (14.1)
Both	479 (11.3)	989 (18.1)	3566 (12.8)	5034 (13.4)

switched, the average duration of treatment for initial SSRI was 4.98 ± 7.98 months and 4.40 ± 6.92 months in 2005 and 2015, respectively (Table 3). In the 2005 cohort, of the 3736 who switched, 2112 (57%) switched to an alternative SSRI. The most common alternatives were citalopram (23%) and sertraline (15%; Table 3), whilst 31% switched to one of the 'other' antidepressants and 12% switched to a tricyclic antidepressant. Overall, 59% of those switched only received prescriptions for the first switched to antidepressant during the remainder of the follow-up period (i.e. received no other antidepressant during follow-up). In the 2015 cohort, of those who switched, 3455 (63%) switched to an alternative SSRI, 36% switched to one of the 'other' antidepressants and 0.6% switched to a tricyclic antidepressant. Overall, 58% of those switched only received prescriptions for the first switched to antidepressant during the remainder of the follow-up period (i.e. received no other antidepressant during follow-up); see Table 4.

3.5 | Discontinued groups

A total of 23,760 (80%) patients in the 2005 cohort, and 27,776 (74%) in the 2015 cohort discontinued treatment during follow-up. The mean duration of treatment for initial SSRI in discontinued patients was 3.95 ± 6.29 months in the 2005 cohort and 4.83 ± 7.14 months in the 2015 cohort. In total, 11,280 discontinued patients across both cohorts received only one single SSRI prescription during the 3-year study period (5545 in 2005, and 5735 in 2015). Of the discontinued patients, 14,188 (60%) in 2005 and 15,729 (57%) in 2015 were not prescribed a further antidepressant at any point in the follow-up period. In the 2005 cohort, 6681 (28%) were restarted on the same SSRI they had previously been prescribed, and 2174 (9%) were prescribed an alternative SSRI at some point during the follow-up period. The mean time to starting subsequent treatment was 329 ± 257 days. In 2015, of the patients who discontinued, 8190 (29.4%) were restarted on the same SSRI they had previously been prescribed, and 2800 (10%) were prescribed an alternative SSRI at some point during follow-up. The mean time to starting subsequent treatment was 324 ± 253 days.

TABLE 2 Initial SSRI prescribed and outcome (four most prescribed SSRIs across both cohorts only).

2005	Continued	Switched	Discontinued	Total
Citalopram *N* (%)	1146 (8)	1531 (11)	11,133 (81)	13,810
Escitalopram *N* (%)	225 (4)	936 (17)	4347 (79)	5508
Fluoxetine *N* (%)	401 (5)	974 (12)	6470 (83)	7845
Sertraline *N* (%)	125 (10)	144 (11)	1020 (79)	1289
2015	**Continued**	**Switched**	**Discontinued**	**Total**
Citalopram *N* (%)	1987 (11)	2542 (15)	12,855 (74)	17,384
Escitalopram *N* (%)	23 (13)	33 (18)	124 (69)	180
Fluoxetine *N* (%)	613 (9)	1082 (16)	5016 (75)	6711
Sertraline *N* (%)	1548 (12)	1730 (14)	9504 (74)	12,782

Note: Paroxetine was the initial SSRI prescribed in 1073 and 410 patients in 2005 and 2015, respectively. Fluvoxamine was the initial SSRI prescribed in nine and five patients in 2005 and 2015, respectively. Breakdown by outcome is not shown for these SSRIs as $n < 5$ for some groups. In 2005, 117/2038 continued patients (6%) received combination therapy (remained on initial SSRI and were prescribed an additional antidepressant). In 2015, 227/4228 continued patients (5%) received combination therapy (remained on initial SSRI and were prescribed an additional antidepressant).

3.6 | Mental health and treatment reviews

The number of patients having at least one READ coded mental health review and at least one medication review during follow-up is shown in Table 5. For continued patients who received at least one review, the mean number of mental health reviews and mean number of medication reviews per patient during follow-up was 3.1 ± 2.7 and 6.9 ± 6.4, respectively in 2005, and 2.3 ± 2.1 and 5.7 ± 5.1, respectively in 2015.

4 | DISCUSSION

This study investigated prescribing patterns following first READ coded primary care SSRI prescription in the SAIL database for 67,006 patients across two cohorts in Wales (UK). The number of patients receiving a first READ-coded SSRI prescription was 27% higher in the 2015 cohort compared to the 2005 cohort, and a larger proportion of the 2015 cohort continued treatment for the 3-year follow-up period (11% compared with 7% in 2005). Approximately 77% of all patients discontinued treatment within the 3-year follow-up periods, of whom more than half did not subsequently receive a prescription for another antidepressant. For both cohorts, SSRIs were more likely to be prescribed for patients living in more deprived areas of Wales.

TABLE 3 Initial SSR duration, and average number of antidepressant prescriptions received during 3-year period.

	Continued	Switched	Discontinued	Total
2005				
Treatment duration of first SSRI prescribed:				
Months (s.d)	36	4.98 (7.99)	3.95 (6.29)	6.29 (10.3)
Number of antidepressant prescriptions received during 3-year follow-up:				
Mean (s.d.)	47 (33)	23 (21)	9 (12)	13.5 (18.7)
Median (IQR)	39 (35–43)	18 (7–35)	4 (2–12)	6 (2–19)
2015				
Treatment duration of first SSRI prescribed:				
Months (s.d)	36	4.40 (6.92)	4.83 (7.14)	8.28 (11.9)
Number of antidepressant prescriptions received during 3-year follow-up:				
Mean (s.d.)	48 (27)	27 (27)	11 (15)	17.89 (22.5)
Median (IQR)	40 (37–48)	22 (8–39)	6 (2–16)	10 (3–28)

TABLE 4 First switched to antidepressant.

2005 cohort	Total = 3736 *n* (%)	Received only this antidepressant during follow-up *n* (%)
Citalopram	847 (23)	634 (75)
Mirtazapine	688 (18)	397 (58)
Fluoxetine	552 (15)	336 (62)
Escitalopram	299 (8)	150 (50)
Sertraline	273 (7)	144 (53)
Dosulepin	237 (6)	128 (54)
Venlafaxine	195 (5)	109 (56)
Lofepramine	172 (5)	84 (49)
Duloxetine	149 (4)	79 (53)
Paroxetine	137 (4)	74 (54)
Trazodone	113 (3)	55 (49)
Clomipramine	24 (0.6)	16 (67)
Reboxetine	14 (0.4)	8 (57)
Nortriptyline	10 (0.3)	0
2015 cohort	**Total = 5468 *n* (%)**	**Received only this antidepressant during follow-up *n* (%)**
Sertraline	1542 (28)	941 (61)
Mirtazapine	1521 (28)	832 (55)
Citalopram	948 (17)	564 (59)
Fluoxetine	874 (16)	510 (58)
Venlafaxine	241 (4)	149 (62)
Duloxetine	158 (3)	90 (57)
Paroxetine	63 (1)	32 (51)
Trazodone	57 (1)	31 (54)
Escitalopram	28 (0.5)	16 (57)

Note: Medicines with single digit numbers of switched to patients have not been included in this table. Percentages in the first column represent percentage of switched patients receiving relevant drug. Percentages in second column represent percentage of those treated who only received that drug during subsequent follow-up.

TABLE 5 Illness and treatment reviews.

2005				
Review type	**Continued (*n* = 2038)**	**Switched (*n* = 3736)**	**Discontinued (*n* = 23,760)**	**Total (*n* = 29,534)**
Mental health *n* (%)	277 (14)	473 (13)	1353 (6)	2103 (7)
Medication *n* (%)	1950 (96)	3038 (81)	16,162 (68)	21,150 (72)
2015				
Review type	**Continued (*n* = 4228)**	**Switched (*n* = 5468)**	**Discontinued (*n* = 27,776)**	**Total (*n* = 37,472)**
Mental health *n* (%)	1508 (36)	2867 (52)	8805 (32)	13,180 (35)
Medication *n* (%)	3803 (90)	4007 (73)	16,137 (58)	23,947 (64)

Note: Number and percentage of patients who had at least one READ coded mental health or medication review during follow-up.

Citalopram was the most prescribed antidepressant in each of the study cohorts. In the 2005 cohort, fluoxetine and escitalopram were the next most prescribed, whereas in the 2015 cohort escitalopram prescribing was substantially lower, and sertraline prescribing was substantially higher. Of those who were switched to an alternative antidepressant, the majority were prescribed either a different SSRI or an 'other' class of antidepressant (most commonly mirtazapine) in both cohorts.

This study captured data pertaining to patients receiving a first READ coded SSRI prescription in the SAIL databank in Wales. The point of implementation of, and transfer of information to electronic records (from which data in SAIL is derived) is likely to have varied between General Practices. Therefore, it is possible that a proportion of patients may have received a diagnosis of depression or anxiety and an antidepressant prescription prior to the point at which their data were included in SAIL. If prescription information was not READ coded in their electronic medical record, these patients would have been included in this study despite receiving previous antidepressant treatment. The average age of patients across the cohorts was somewhat higher than the median age of depression diagnosis in one study (Solmi et al., 2022), suggesting that some may have experienced depression or anxiety previously, lending support to this hypothesis. Similarly, the younger mean age of the 2015 cohort may reflect the exclusion of a greater number of older, previously treated patients due to more proportionally complete records compared to the 2005 cohort. The mean age of continuing patients was significantly greater than those who switched or discontinued in both the 2005 and 2015 cohort. This may reflect a perceived need for ongoing treatment in older patients by prescribers, perhaps due to a greater number of previous illness episodes and associated concerns of an increased risk of symptom recurrence. The study was not designed to investigate these aspects, which is a limitation, and further work would be required to address this.

In the 2005 and 2015 cohorts, 52.5% and 58% of patients receiving a first READ coded SSRI prescription in SAIL had a recorded depression or anxiety diagnosis, whilst overall, 35% of patients did not have a recorded diagnosis in the three months prior to and one month following first READ coded SSRI prescription. It must be noted that the current study relied upon READ coding for data extraction, and did not explore prescribing for unlicensed indications, which may be relatively common for certain drugs (Schäfer et al., 2020). Furthermore, patients who might have been prescribed an antidepressant at a point in time predating information in the SAIL database, may have had an earlier recorded diagnosis that was not captured in this study. Nevertheless, it has been suggested that improved indication recording may increase appropriate prescribing (Feather et al., 2023), and interventions to address this may be a consideration for policy makers. A greater proportion of patients in each cohort was female, which probably reflected the influence of sex on depression prevalence (Ferenchick et al., 2019). The magnitude of this effect was smaller in 2015 than in 2005, perhaps due to greater recognition or acceptance of mental illness amongst men. Sex did not appear to have a significant effect on outcome, with similar proportions of men and women in the continued, switched and discontinued groups in each cohort. Depression prevalence and antidepressant prescribing in the UK have been shown to be influenced by socio-economic deprivation (Grigoroglou et al., 2020). The number of patients receiving a first READ coded SSRI was higher in areas of greater deprivation in both of our cohorts. However, it was perhaps notable that the distribution of patients across each deprivation quintile was more even in 2015 (particularly in the continued group), suggesting greater treatment initiation in more affluent areas compared with 2005.

Observed prescribing patterns were largely consistent with those seen in England (Lalji et al., 2021). The proportion of citalopram, escitalopram, and paroxetine prescribing was lower, and sertraline prescribing higher in the 2015 cohort. This perhaps reflected adherence to safety advice and evidence-based guidelines. In 2011 and 2014 the Medicines and Healthcare Regulatory Agency (MHRA) issued warnings about the potential for citalopram and escitalopram to cause QT interval prolongation (MHRA, 2014), whilst paroxetine appears to have the highest incidence of discontinuation symptoms among SSRIs (Cleare et al., 2015; NICE, 2009). Concern amongst prescribers over these adverse effects may explain a reduction in prescribing of escitalopram, citalopram and paroxetine in 2015. NICE and British Association for Psychopharmacology (BAP) guidelines recommended the use of sertraline for patients with a comorbid chronic physical health condition because of a lower risk of drug-drug interactions (Cleare et al., 2015; NICE, 2009). Perceived safety advantages may have driven the higher levels of sertraline prescribing seen in the 2015 cohort.

The majority of patients in both cohorts discontinued treatment within 3 years of first READ coded SSRI prescription. The mean time to discontinuation was between four and five months, and over half of those discontinuing did not restart treatment during follow-up. This suggested that an initial short course of antidepressant treatment was either effective, or patients did not wish to continue further treatment. Approximately 40% of those who were discontinued went on to receive an antidepressant later in the follow-up period. Mean time to restarting treatment was approximately 11 months. This lends support to the high risk of illness recurrence (Cleare et al., 2015), and the need for ongoing monitoring following initial treatment. The larger percentage of patients continuing treatment throughout the 3-year follow-up period and the corresponding lower percentage discontinuing treatment in the 2015 cohort suggested an increase in long-term prescribing over time, consistent with the findings of Hafferty et al. (2019). Concerns over illness relapse and emergence of withdrawal symptoms following treatment discontinuation have been suggested to be barriers to antidepressant discontinuation (Scholten et al., 2020) and may have contributed to this prescribing pattern. Long-term prescribing is indicated for patients with recurrent or relapsing depression and therefore, may be appropriate for certain patients (Cleare et al., 2015). However, a number of patients included in this study would have been likely to be receiving their first SSRI, and may therefore have been experiencing a first episode of depression or anxiety, where long-term antidepressant prescribing might be less likely to be indicated. Where long term prescribing is indicated, review after 2 years to establish the need for

ongoing treatment has been suggested (Kendrick, 2021), whilst NICE Guideline NG222 (NICE, 2022) recommends review of ongoing antidepressant treatment every six months. The mean number of both recorded mental health and medication reviews per continued patient was smaller in 2015 compared to 2005. Data extraction relied upon coding of information in the GP system, and any reviews that took place without being coded would not have been identified. Nevertheless, active review of long-term prescribing is needed to ensure ongoing need (Kendrick, 2021). If the lower mean number of reviews per continued patient in the 2015 cohort is indicative of a decline in patient monitoring this is a concern, and further work to explore the significance of this finding would appear warranted.

In 2005 the most commonly switched to antidepressant was citalopram, and in 2015 it was sertraline. This change may reflect the safety concerns related to QT interval prolongation with citalopram noted above. Mirtazapine was the second most switched to antidepressant in both cohorts, although the proportion of switched patients receiving this drug was substantially greater in 2015 compared with 2005 (28% vs. 18%). Although this study was not designed to investigate reasons for the observed prescribing patterns, it is conceivable that this increase was due to prescribers viewing mirtazapine as a safer second line alternative to tricyclic antidepressants (which were used for very few patients in the 2015 cohort). Treatment effectiveness in clinical practice can be considered in the context of efficacy and tolerability, and treatment continuation (or discontinuation) provides an indicator of this (Cipriani et al., 2009). In patients who were switched to an alternative antidepressant in our study, there were some small differences in the proportions continuing each drug. Of the most commonly switched to drugs, citalopram and fluoxetine had the largest proportion of patients receiving only these drugs following switching in 2005, and venlafaxine and sertraline had the largest proportion of patients receiving only these drugs following switching in 2015. Although escitalopram has been shown to be more efficacious and more tolerable than other antidepressants (Cipriani et al., 2018), this was not reflected in the proportion of patients going on to receive only this drug following switching in our study. The mean time to switching was approximately five months in 2005 and four months in 2015. Assuming switching occurred due to poor response or poor tolerability, this might indicate that patients remained on sub-optimal treatment for a relatively long period of time before a change in prescription was made. This again highlights the need for effective review of treatment. However, it must be noted that this study did not investigate reasons for switching or more detailed dosing patterns, which might have provided further insight into prescribing decision making.

This study identified a greater number of patients receiving a first READ coded SSRI prescription in primary care in Wales and a greater proportion of patients continuing treatment for 3 years in 2015 compared with 2005. Despite this increase, the proportion of patients continuing longer term treatment remained small, and the number of completed mental health and medication reviews might offer some reassurance that prescribing remained appropriate. However, further work to explore the nature and value of these reviews would help to confirm this hypothesis.

AUTHOR CONTRIBUTIONS

Paul N. Deslandes conceived the study. Paul N. Deslandes, Richard S. Young and Shaila Ahmed contributed to the design of the study. Katherine Chaplin extracted the data. Shaila Ahmed and Katherine Chaplin analysed the data. Shaila Ahmed and Paul N. Deslandes drafted the manuscript. All authors reviewed the manuscript and gave approval for publication.

ACKNOWLEDGEMENTS

The authors would like to thank Huw Collins and Hywel Evans at SAIL, and David Barnard for their input and support with this work. SA received funding from a Research Capacity Building Collaboration (RCBC) Wales First into Research Fellowship and a University of South Wales Higher Education Investment and Recovery (HEIR) Fund.

CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to declare in relation to this work.

DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article or uploaded as Supporting Information. Person-level data are not available owing to policies and procedures in place to protect data held in the SAIL databank.

ETHICS STATEMENT

This study used anonymised data only, ethical approval was not required. Approval was granted by the SAIL Information Governance Review Panel (IGRP approval number 1004).

ORCID

Richard S. Young https://orcid.org/0009-0002-0149-7074
Paul N. Deslandes https://orcid.org/0000-0001-6751-9438

REFERENCES

Bogowicz, P., Curtis, H., Walker, A., Cowen, P., Geddes, J., & Goldacre, B. (2021). Trends and variation in antidepressant prescribing in English primary care: A retrospective longitudinal study. *BJGP Open*, *5*(4). BJGPO.2021.0020. https://doi.org/10.3399/BJGPO.2021.0020

Cipriani, A., Furukawa, T. A., Salanti, G., Chaimani, A., Atkinson, L. Z., Ogawa, Y., Leucht, S., Ruhe, H. G., Turner, E. H., Higgins, J. P. T., Egger, M., Takeshima, N., Hayasaka, Y., Imai, H., Shinohara, K., Tajika, A., Ioannidis, J. P. A., & Geddes, J. R. (2018). Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: A systematic review and network meta-analysis. *Lancet*, *391*(10128), 1357–1366. https://doi.org/10.1016/S0140-6736(17)32802-7

Cipriani, A., Furukawa, T. A., Salanti, G., Geddes, J. R., Higgins, J. P. T., Churchill, R., Watanabe, N., Nakagawa, A., Omori, I. M., McGuire, H., Tansella, M., & Barbui, C. (2009). Comparative efficacy and acceptability of 12 new-generation antidepressants: A multiple-treatment meta-analysis. *Lancet*, *373*(9665), 746–758. https://doi.org/10.1016/s0140-6736(09)60046-5

Cleare, A., Pariante, C., Young, A., Anderson, I., Christmas, D., Cowen, P., Dickens, C., Ferrier, I., Geddes, J., Gilbody, S., Haddad, P., Katona, C., Lewis, G., Malizia, A., McAllister-Williams, R., Ramchandani, P., Scott, J., Taylor, D., & Uher, R. (2015). Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British association for psychopharmacology guidelines. *Journal*

of Psychopharmacology, *29*(5), 459–525. https://doi.org/10.1177/0269881115581093

Deslandes, P., Jenkins, K., Haines, K., Hutchings, S., Cannings-John, R., Lewis, T. L., Bracchi, R. C., & Routledge, P. A. (2016). A change in the trend in dosulepin usage following the introduction of a prescribing indicator but not after two national safety warnings. *Journal of Clinical Pharmacy and Therapeutics*, *41*(2), 224–228. https://doi.org/10.1111/jcpt.12376

Feather, C., Appelbaum, N., Darzi, A., & Franklin, B. D. (2023). Indication documentation and indication-based prescribing within electronic prescribing systems: A systematic review and narrative synthesis. *BMJ Quality and Safety*, *32*(6), 357–368. https://doi.org/10.1136/bmjqs-2022-015452

Ferenchick, E. K., Ramanuj, P., & Pincus, H. A. (2019). Depression in primary care: Part 1—screening and diagnosis. *Br Med J*, *365*, l794. https://doi.org/10.1136/bmj.l794

Ford, D., Jones, K., Verplancke, J., Lyons, R. A., John, G., Brown, G., Brooks, C. J., Thompson, S., Bodger, O., Couch, T., & Leake, K. (2009). The SAIL databank: Building a national architecture for e-health research and evaluation. *BMC Health Services Research*, *9*(1), 157. https://doi.org/10.1186/14726963-9-157

Forns, J., Pottegård, A., Reinders, T., Poblador-Plou, B., Morros, R., Brandt, L., Cainzos-Achirica, M., Hellfritzsch, M., Schink, T., Prados-Torres, A., Giner-Soriano, M., Hagg, D., Hallas, J., Cortes, J., Jacquot, E., Deltour, N., Perez-Gutthann, S., Pladevall, M., & Reutfors, J. (2019). Antidepressant use in Denmark, Germany, Spain, and Sweden between 2009 and 2014: Incidence and comorbidities of antidepressant initiators. *Journal of Affective Disorders*, *249*, 242–252. https://doi.org/10.1016/j.jad.2019.02.010

Grigoroglou, C., Munford, L., Webb, R., Kapur, N., Ashcroft, D., & Kontopantelis, E. (2020). Prevalence of mental illness in primary care and its association with deprivation and social fragmentation at the small-area level in England. *Psychological Medicine*, *50*(2), 293–330. https://doi.org/10.1017/s0033291719000023

Hafferty, J. D., Wigmore, E. M., Howard, D. M., Adams, M. J., Clarke, T.-K., Campbell, A. I., MacIntyre, D. J., Nicodemus, K. K., Lawrie, S. M., Porteous, D. J., & McIntosh, A. M. (2019). Pharmaco-epidemiology of antidepressant exposure in a UK cohort record-linkage study. *Journal of Psychopharmacology*, *33*(4), 482–493. https://doi.org/10.1177/0269881119827888

Haines, K., Bracchi, R., Lang, R., Samuels, K., & Routledge, P. A. (2021). The all Wales medicines Strategy group: 18 years' experience of a national medicines optimisation committee. *British Journal of Clinical Pharmacology*, *87*(10), 3961–3970. https://doi.org/10.1111/bcp.14817

Huijbregts, K., Hoogendoorn, A., Slottje, P., van Balkom, A. J., & Batelaan, N. M. (2017). Long-term and short-term antidepressant use in general practice: Data from a large cohort in The Netherlands. *Psychotherapy and Psychosomatics*, *86*(6), 362–369. https://doi.org/10.1159/000480456

Jones, K., Ford, D., Jones, C., Dsilva, R., Thompson, S., Brooks, C. J., Heaven, M. L., Thayer, D. S., McNerney, C. L., & Lyons, R. A. (2014). A case study of the secure anonymous information linkage (SAIL) gateway: A privacy protecting remote access system for health related research and evaluation. *Journal of Biomedical Informatics*, *50*(100), 196–204. https://doi.org/10.1016/j.jbi.2014.01.003

Kendrick, T. (2021). Strategies to reduce use of antidepressants. *British Journal of Clinical Pharmacology*, *87*(1), 23–33. https://doi.org/10.1111/bcp.14475

Lalji, H. M., McGrogan, A., & Bailey, S. (2021). An analysis of antidepressant prescribing trends in England 2015–2019. *J Affect Disord Rep*, *6*, 100205. https://doi.org/10.1016/j.jadr.2021.100205

Lewis, G., Marston, L., Duffy, L., Freemantle, N., Gilbody, S., Hunter, R., Kendrick, T., Kessler, D., Mangin, D., King, M., Lanham, P., Moore, M., Nazareth, I., Wiles, N., Bacon, F., Bird, M., Brabyn, S., Burns, A., Clarke, C. S, … Lewis, G. (2021). Maintenance or discontinuation of antidepressants in primary care. *New England Journal of Medicine*, *385*(14), 1257–1267. https://doi.org/10.1056/NEJMoa2106356

Lipovec, N. C., Anderlic, A., & Locatelli, I. (2022). General antidepressants prescribing trends 2009–2018 in Slovenia: A cross-sectional retrospective database study. *International Journal of Psychiatry in Clinical Practice*, *26*(4), 401–405.

Lockhart, P., & Guthrie, B. (2011). Trends in primary care antidepressant prescribing 1995–2007: A longitudinal population database analysis. *British Journal of General Practice*, *61*(590), 565–572. https://doi.org/10.3399/bjgp11x593848

Lyons, R., Jones, K., John, G., Brooks, C. J., Verplancke, J. P., Ford, D. V., Brown, G., & Leake, K. (2009). The SAIL databank: Linking multiple health and social care datasets. *BMC Medical Informatics and Decision Making*, *9*(1), 3. https://doi.org/10.1186/1472-6947-9-3

McCrea, R. L., Sammon, C. J., Nazareth, I., & Peterson, I. (2016). Initiation and duration of selective serotonin reuptake inhibitor prescribing over time: UK cohort study. *British Journal of Psychiatry*, *209*(5), 421–426. https://doi.org/10.1192/bjp.bp.115.166975

Medicines and Healthcare products Regulatory Agency. (2014). Citalopram and escitalopram: QT interval prolongation. *Drug Safety Update*. https://www.gov.uk/drug-safety-update/citalopram-and-escitalopram-qt-interval-prolongation. Accessed March 2024.

Mojtabai, R., & Olfson, M. (2014). National trends in long-term use of antidepressant medications: Results from the U.S. National health and nutrition examination survey. *The Journal of Clinical Psychiatry*, *75*(2), 169–177. https://doi.org/10.4088/jcp.13m08443

National Institute for Health and Care Excellence (NICE). (2009). Depression in adults: Recognition and management. *NICE Guideline*, CG90.

National Institute for Health and Care Excellence (NICE). (2022). Depression in adults: Treatment and management. *NICE Guideline*, NG222.

Reid, I. (2013). Are antidepressants overprescribed? No. *British Medical Journal*, *346*(jan22 3), f190. https://doi.org/10.1136/bmj.f190

Schäfer, W., Reinders, T., Riedel, O., & Haug, U. (2020). How often are antidepressants prescribed off-label among older adults in Germany? A claims data analysis. *British Journal of Clinical Pharmacology*, *87*(4), 1778–1789. https://doi.org/10.1111/bcp.14564

Scholten, W., Batelaan, N., & Van Balkom, A. (2020). Barriers to discontinuing antidepressants in patients with depressive and anxiety disorders: A review of the literature and clinical recommendations. *Ther Adv Psychopharmacol*, *10*, 1–10. https://doi.org/10.1177/2045125320933340

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Shin, J. I., Kirkbride, J. B., Jones, P., Kim, J. H., Kim, J. Y., Carvalho, A. F., Seeman, M. V., Corell, C. U., & Fusar-Poli, P. (2022). Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*, *27*(1), 281–295. https://doi.org/10.1038/s41380-021-01161-7

Spence, D. (2013). Are antidepressants overprescribed? Yes. *British Medical Journal*, *346*(jan22 3), f191. https://doi.org/10.1136/bmj.f191

SUPPORTING INFORMATION

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

How to cite this article: Ahmed, S., Chaplin, K., Young, R. S., & Deslandes, P. N. (2024). Patient outcome following selective serotonin reuptake inhibitor prescribing in primary care in Wales (UK). *Human Psychopharmacology: Clinical and Experimental*, e2912. https://doi.org/10.1002/hup.2912