SUPPLEMENTARY MATERIAL

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1 METHODS

1.1 DATA SOURCES

CPRD GOLD is an ongoing resource that collects data from consenting primary care sites in the UK that use a specific computer software system called Vision.[1] It is one of the largest primary care datasets in the world, containing over 4 million active patients (around 7% of the whole UK population) that have been shown to be representative of UK residents in terms of age, sex, and ethnicity.[1] Over 670 practices in England, Scotland, Wales, and Northern Ireland have consented to practice- and patient-level data abstraction by CPRD, where each patient has data available on prescriptions (using British National Formulary (BNF) codes), diagnoses (using Read codes), and characteristics collected since their registration date at the practice.[1]

We used linked data, where available. Linkage with the Office for National Statistics (ONS, capturing death registrations) and practice-level Index for Multiple Deprivation scores (IMD, capturing patient and practice-level deprivation using scores predefined by geographical area)[2] are available for all patients in CPRD GOLD. Other sources of linked data, including patient-level IMD scores, those from Hospital Episode Statistics (HES, capturing inpatient hospitalisations) and the Mental Health Services Data Set (MHSDS, capturing inpatient and outpatient contacts with mental health services),[1, 3] are only available for 75% of English practices.[1]

The Pregnancy Register contains all pregnancies for women of child-bearing age in CPRD GOLD, including estimated timings of pregnancy (from multiple dates recorded throughout pregnancy), pregnancy outcome (such as live birth and miscarriage), and maternal age.[4] Close agreement with hospitalization data show that the data included within the Pregnancy Register are well recorded.[4]

A GP is often the first medical professional involved in providing antenatal care; the NHS website recommends that individuals make an appointment with their GP as soon as they know they are pregnant; the GP can then coordinate further appointments with midwifery and obstetric services.[5] However since 2007, women have had the choice between registering their pregnancy with their GP or going directly to register with a midwife.[6] Although notes should be reported back to the GP if the latter occurs, it may not be consistent and may explain the decline in number of pregnancies in CPRD GOLD from around 2010.[6]

1.2 IDENTIFYING PREGNANCIES

Individuals were dropped from the analysis if they did not have at least 12 months of follow-up with an 'up to standard' (UTS) practice. Practices are assigned an UTS date which refers to the date on which the practice started contributing 'high-quality' data and is used in CPRD studies as an internal quality control.[1]

The Pregnancy Register as received from CPRD contains the outcome of the pregnancy (livebirth, stillbirth, miscarriage, etc.). A substantial proportion of the outcome variable consists of "Unspecified loss" and "Outcome unknown" pregnancies, detailed elsewhere.[4] Given that the Pregnancy Register algorithm only used primary care data to identify pregnancy episodes and their outcome, we employed an additional approach to try and convert

unspecified outcomes to know outcomes using secondary care data. If a patient received care in hospital for the resolution of their pregnancy (either miscarriage care or a delivery), we could identify records in HES that are likely to pertain to pregnancy episodes in the Pregnancy Register to recode unknown outcomes to known.

Using the algorithmic approach described by Campbell *et al.*[7], we pulled together episodes from secondary care pertaining to pregnancy where the outcome was known and then aligned the dates with the estimated dates of the pregnancy episode in the Pregnancy Register. In doing so, we could use a combination of the recorded outcome and episode date in HES in place of the unknown outcome and estimated pregnancy end date in the Pregnancy Register, with the imputed gestational length employed by the Pregnancy Register algorithm to estimate an updated pregnancy start (subtracting the imputed length from the episode date in HES).

1.3 ANTIDEPRESSANT PRESCRIBING

Table S1 Drug substances that fall into each class category of antidepressants: SSRIs, SNRIs, TCAs, and 'other'.

Selective serotonin reuptake inhibitors (SSRIs)	(Serotonin-) noradrenaline reuptake inhibitors (SNRI/NRIs)	Tricyclic antidepressants (TCAs)	'Other' antidepressants
Citalopram	Duloxetine	Amitriptyline	Agomelatine
Escitalopram	Reboxetine	Amoxapine	Isocarboxazid
Fluoxetine	Venlafaxine	Clomipramine	Mianserin
Fluvoxamine		Desipramine	Mirtazapine
Paroxetine		Dosulepin	Nefazodone
Sertraline		Doxepin	Phenelzine
		Imipramine	Tranylcypromine
		Lofepramine	Trazodone
		Maprotiline	Tryptophan
		Nortriptyline	Vortioxetine
		Protriptyline	
		Trimipramine	

Given that prescriptions for antidepressants are made in primary care, prescription timing and estimated length of prescription were used in this study to ascertain whether pregnant patients may have been exposed to antidepressants during pregnancy and how their regimens may have changed over the course of pregnancy.

Within CPRD, multiple variables are derived from dosage text, inputted by the GP into the Vision software, namely dose number, dose frequency, and daily dose. Dose number corresponds to the number of doses taken each time the medicine is advised, and dose frequency refers to the number of times a dose should be administered daily; thus, for "2 tablets to be taken twice daily" the dose number would be two and the dose frequency would be two.

Daily dose is the dose number multiplied by the dose frequency, in other words the total number of doses taken each day, so for the above example the daily dose would be four.

Dose number and dose frequency were cleaned to obtain any additional information from dosage text and used to derive a clean daily dose for each prescription. Abnormal values for dose number (0 and >15) were changed to missing so that daily dose could be imputed in a later step. To ascertain each prescriptions length, quantity was also cleaned (the total number of dose unit given for each prescription) to combine with daily dose. Similarly to dose number, abnormal values (< 5 or > 300) were changed to missing and imputed later.

For missing values in daily dose and quantity, a hot-decking imputation approach was used, which employed a stepwise process to impute the modal daily dose and quantity at decreasing levels of specificity. Firstly, modal values were taken from identical prescriptions made in the same person if not missing. If still missing, modal values were taken from identical prescriptions in different people. If still missing, modal values were taken from the same medication prescribed at different quantities/daily doses. This decreasing specificity fills in the last few missing values with modal values of medications in that wider class. Following the hot-decking imputation step, these complete data that contained prescription start and end dates was merged with the Pregnancy Register to align with complementary pregnancy start and end dates. We were then able to identify prescriptions that fell within each period of interest, meaning individuals could be categorised as exposed (having received a prescription) or unexposed (having not received a prescription) during each period (before, during, and after pregnancy).

To identify dose changes, we standardised doses across each medication so they could be compared. We employed an approach that leveraged the distribution of daily doses (in milligrams) within each drug in the data, using the quartile values to assign low, medium, and high. For example, fluvoxamine had a range of 25–600mg per day in our data. We then assigned the lowest 25% of the daily dose "low" (≤25th percentile, 25–50mg), the middle 50% "medium" (>25th and ≤75th percentile, 75–100mg), and the upper quartile "high" (>75th percentile, 112.5–600mg). Some rarely prescribed medications had small distributions due to lack of diversity in the doses prescribed, meaning that the same prescribed dose was accounted for in the quartiles and more stringent thresholds were required. For example, the isocarboxazid distribution contained 20mg in the 25th, 50th, and 75th quartile so the same thresholds were applied as above but with the 25th, 75th, and 90th percentile. For isocarboxazid, "low" pertained to 10–20mg, "medium" to 22.5mg, and "high" to 30–40mg. These were checked against the EMC website to confirm that they aligned with clinical practice. The summary of each dose assignment for each drug is provided at https://github.com/flozoemartin/Patterns/ (Supp_Dose distributions).

Upon inspecting the data, some prescriptions retained needed some additional cleaning. There were prescriptions for the same product that had been made on the same day for the same duration but had different affiliated daily doses. Following clinical input from medical co-authors, these were deemed to be the same prescription where the prescribing clinician was creating a dose amount not available as a singular tablet (for example, to achieve a 30mg dose of citalopram, the prescription would appear across three records: a 20mg and a 10mg). For these prescriptions where the product, prescription length, and prescriptions dates were the same, but the dose was

different for each, the daily doses in milligrams were added together and "duplicates" were removed. The above process of assigning standardised doses was then reapplied to assure that the new combined doses had been given the right category: low, medium, or high.
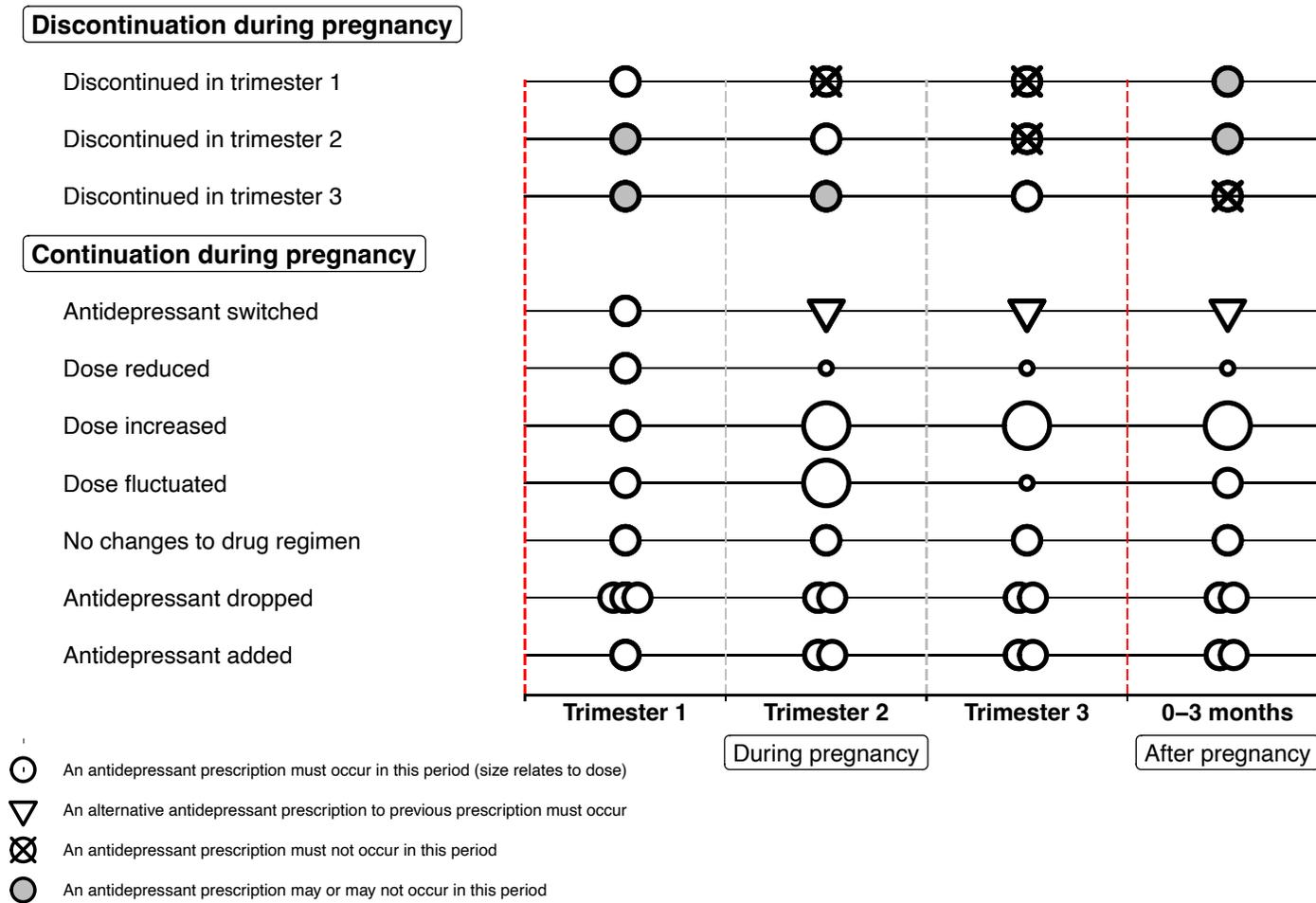
1.4   PATTERNS OF PRESCRIBING

During pregnancy, discontinuation was reported as any during pregnancy and was defined as the 'final' antidepressant prescription ending more than 2 weeks from the end of pregnancy. In sensitivity analysis, trimester of discontinuation was explored among those with at least 27 completed weeks' gestation: trimester one (final prescription during pregnancy ending in between week 14), trimester two (final prescription during pregnancy ending in between week 14 and week 27), and trimester three. Trimester three discontinuation was defined by those with a prescription for antidepressants during trimester three but no prescriptions for antidepressants in the 3 months after the end of pregnancy (**Error! Reference source not found.**). The use of prescribing windows that utilised future prescriptions would not be appropriate for causal analyses but aren't problematic in these descriptive analyses.

We differentiated between single- and multi-drug regimens (mono- and polytherapy) for those who did not discontinue during pregnancy. Those with two prescriptions for different antidepressant products overlapping by more than four weeks were considered to be using a multi-drug regimen (to prevent cross-tapering[8] being wrongly considered as a multi-drug regimen, as opposed to switching within a single-drug regimen), whereas those that did not were classified as individuals prescribed a single-drug regimen.

Among those on a single-drug regimen, we showed product switching (subsequent use of a different antidepressant) and dose changes (increase or decrease with the same product). For patients on a multi-drug regimen, we described product adding to and dropping from the regimen, as well as dose changes within products in the regimen. Example prescription patterns that fulfil the criteria for each pattern are shown in Figure S1.

Figure S1 Examples of pattern definition for those prescribed to antidepressants during pregnancy.

Discontinuation during pregnancy

Discontinued in trimester 1

Discontinued in trimester 2

Discontinued in trimester 3

Continuation during pregnancy

Antidepressant switched

Dose reduced

Dose increased

Dose fluctuated

No changes to drug regimen

Antidepressant dropped

Antidepressant added

Trimester 1   Trimester 2   Trimester 3   0–3 months

During pregnancy   After pregnancy

An antidepressant prescription must occur in this period (size relates to dose)

An alternative antidepressant prescription to previous prescription must occur

An antidepressant prescription must not occur in this period

An antidepressant prescription may or may not occur in this period

1.5　Characteristic derivation

Indication-based lists of Read code were created using the medical dictionaries provided by CPRD. ICD-10 codelists were then created using keyword searches. Both were checked by clinical co-authors and are available in https://github.com/flozoemartin/Patterns/. The Read code lists were then faced to the Clinical and Referral data in CPRD GOLD, and the ICD-10 codelists were faced towards the linked HES data for whom it was available.

Other characteristics were obtained from CPRD and linked data and summarised in Table S2.

Table S2 Details of covariate definitions.

Covariate	Definition	Do file	Codelists
Maternal age at start of pregnancy	Given that only year of birth available in CPRD for anonymisation, a pseudo-date of birth of 1st July in each patient's year of birth is generated and then subtracted from the pregnancy start date	0_data management/ 4_covariates/ 1_covariate derivation	–
Practice IMD (in quintiles)	The Index of Multiple Deprivation (IMD) is a composite measure of several domains that capture 'deprivation': a score is attributed to each practice ID and then all scores are divided into quintiles, with quintile 1 being least deprived and	0_data management/ 4_covariates/ 1_covariate derivation	–

	quintile 5 being most deprived		
Maternal ethnicity	Maternal ethnicity is obtained from both CPRD Clinical data and Hospital Episode Statistics (HES) Patient data	0_data management/ 4_covariates/ 2a_clean_ethnicity_codes_in_HES 2b_clean_ethnicity_codes_in_CPRD	ethnicity_gold_codelist.csv
Maternal body mass index (BMI)	Maternal BMI is obtained hierarchically from the first trimester, if not available within 5 years before pregnancy, if not available in the year after pregnancy (excluding the first three months postpartum), if not available with 10 years either side of pregnancy, if not available more than 10 years after pregnancy	0_data management/ 4_covariates/ 3_alc_smok_bmi 3b_pr_getbmistatus 3c_pr_getallbmirecords 3d_pr_getheightstatus	–
Maternal smoking	Maternal smoking during pregnancy, recorded in Clinical and Additional data, if available; if not the algorithm takes the next nearest record of smoking	0_data management/ 4_covariates/ 3_alc_smok_bmi 3a_pr_getsmok	smoking_codelist.csv

	within 10 years of pregnancy start		
Maternal alcohol intake	Maternal alcohol intake during pregnancy, recorded in Clinical and Additional data, as well as pharmacological treatments for alcohol dependence in Therapy data, if available; if not the algorithm takes the next nearest record of alcohol intake within 10 years of pregnancy start	0_data management/ 4_covariates/ 3_alc_smok_bmi 3e_pr_getalcoholstatus	alcohol_codelist.csv
Maternal illicit drug use	Evidence of illicit drug use any time during pregnancy in the Clinical or Referral data or prescriptions for illicit drug use e.g., methadone any time during pregnancy in the Therapy data	0_data management/ 4_covariates/ 6_cr_illicit_drug_use	illicit_drug_read_codelist.csv illicit_drug_ost_codelist.csv
Maternal gravidity history at start of pregnancy	History of miscarriage, stillbirth, termination of pregnancy, or other losses (ectopic pregnancy, molar	0_data management/ 4_covariates/ 1_covariate derivation	–

	pregnancy, blighted ovum etc.) at the start of pregnancy		
Maternal parity at start of pregnancy	Number of pregnancies carried to more than 20 weeks' gestation (live births, stillbirths, deliveries based on third trimester or late pregnancy records) at the start of pregnancy	0_data management/ 4_covariates/ 1_covariate derivation	–
Number of consultations in CPRD in the 12 months before pregnancy	The number of consultations each patient had in the year prior to pregnancy derived from the CPRD Consultation data	0_data management/ 4_covariates/ 1_covariate derivation	–
Maternal mental health problems ever before or during pregnancy	Evidence of the first diagnosis of mental health disorders e.g., depression, anxiety, bipolar etc. ever before or during pregnancy (i.e., diagnosis made prior to the pregnancy end date) in the Clinical or Referral data, as well as HES for whom it was available	0_data management/ 5_indications/ 1_identifying depression & anxiety 2_identifying indications in hes 3_identifying other indics	ad_indication_icd10_codelist.csv ad_indication_read_codelist.csv

Maternal neurodevelopmental disorders ever before or during pregnancy	Evidence of the first diagnosis of neurodevelopmental disorders e.g., autism spectrum disorder, attention deficit hyperactivity disorder etc. ever before or during pregnancy (i.e., diagnosis made prior to the pregnancy end date) in the Clinical or Referral data	0_data management/ 4_covariates/ 9_cr_mothers_neurodevelopmental_health	adhd_icd10_codelist.csv adhd_medication_codelist.csv adhd_read_codelist.csv autism_icd10_codelist.csv autism_read_codelist.csv id_icd10_codelist.csv id_read_codelist.csv
Possible somatic indications for antidepressants ever or during pregnancy	Evidence of the first diagnosis of other possible somatic indications for antidepressants e.g., pain, tension-type headache, migraine prophylaxis etc. ever before or during pregnancy (i.e., diagnosis made prior to the pregnancy end date) in the Clinical or Referral data	0_data management/ 5_indications/ 2_identifying indications in hes 3_identifying other indics	ad_indication_icd10_codelist.csv ad_indication_read_codelist.csv
Other mental health-related prescriptions during pregnancy	Mental health-related prescriptions including mood stabilisers, benzodiazepines, antipsychotics etc.	0_data management/ 4_covariates/ 4_cr_extract_mental_health_Rx	asm_codelist.csv benzos_codelist.csv antipsychotic_codelist.csv

	made during pregnancy identified from the Therapy data		
Other prescriptions during pregnancy	Other prescriptions of anti-emetics, folic acid and teratogens made during pregnancy identified from the Therapy data	0_data management/ 4_covariates/ 5_cr_extract_other_Rx	Antiemetic_codelist.csv Folic_acid_codelist.csv Teratogens_codelist.csv

2 RESULTS

2.1 STUDY POPULATION

Table S3 Proportion of pregnancy outcomes in eligible sample

Outcome	Proportion	Delivery or loss
Live birth	734,938 (71.1)	Delivery
Stillbirth	3,211 (0.3)	Delivery
Live birth or stillbirth	549 (0.1)	Delivery
Miscarriage	127,521 (12.3)	Loss
Termination of pregnancy (TOP)	39,744 (3.8)	Loss
Probable TOP	99,841 (9.7)	Loss
Ectopic	11,158 (1.1)	Loss
Molar	975 (0.1)	Loss
Blighted ovum	738 (0.1)	Loss
Unspecified loss	6,495 (0.6)	Loss
Delivery based on a third trimester record	6,640 (0.6)	Delivery
Delivery based on a late pregnancy record	1,973 (0.2)	Delivery

Table S4 Proportion of those prescribed antidepressants during pregnancy who were exclusively prescribed each medication, ordered from most to least common. Those in the "multiple" group were prescribed >1 drug substance during pregnancy, those in the citalopram group were only prescribed citalopram during pregnancy, for example.

Drug prescribed	*n* (%)
Total exposed	79,144 (100)
Citalopram	20,077 (25.4)
Fluoxetine	18,040 (22.8)
Sertraline	10,554 (13.3)
Multiple	9,042 (11.4)
Amitriptyline	5,993 (7.6)
Paroxetine	3,614 (4.6)
Venlafaxine	2,967 (3.7)
Mirtazapine	2,545 (3.2)
Escitalopram	1,892 (2.4)
Dosulepin	1,551 (2.0)
Lofepramine	760 (1.0)
Duloxetine	549 (0.7)
Trazodone	476 (0.6)
Clomipramine	369 (0.5)
Nortriptyline	273 (0.3)
Imipramine	190 (0.2)
Reboxetine	53 (0.1)
Moclobemide	49 (0.1)
Trimipramine	41 (0.1)
Doxepin	40 (0.1)
Fluvoxamine	35 (0.0)
Mianserin	13 (0.0)
Agomelatine	10 (0.0)
Vortioxetine	<5
Tranylcypromine	<5
Amoxapine	<5
Maprotiline	<5
Tryptophan	<5
Phenelzine	<5

Table S5 Characteristics table.

Characteristics	Total N (%)	Prescribed antidepressants during pregnancy n (%)	Not prescribed antidepressants during pregnancy n (%)
Total	1,033,783 (100.0)	79,144 (100.0)	954,639 (100.0)
Pregnancy start year			
1996 – 2000	120,490 (11.7)	5,234 (6.6)	115,256 (12.1)
2001 – 2006	306,175 (29.6)	19,738 (24.9)	286,437 (30.0)
2007 – 2012	372,539 (36.0)	28,643 (36.2)	343,896 (36.0)
2013 – 2018	234,570 (22.7)	25,529 (32.3)	209,050 (21.9)
Age at start of pregnancy			
<18	38,836 (3.8)	1,117 (1.4)	37,719 (4.0)
18–24	234,583 (22.7)	19,196 (24.3)	215,387 (22.6)
25–29	265,993 (25.7)	20,632 (26.1)	245,361 (25.7)
30–34	287,482 (27.8)	20,545 (26.0)	266,937 (28.0)
≥35	206,889 (20.0)	17,654 (22.3)	189,235 (19.8)
Practice Index of Multiple Deprivation (IMD)			
1st quintile (least deprived)	163,727 (15.8)	10,316 (13.0)	153,411 (16.1)
2nd quintile	167,765 (16.2)	11,811 (14.9)	155,954 (16.3)
3rd quintile	189,474 (18.3)	14,390 (18.2)	175,084 (18.3)
4th quintile	231,787 (22.4)	18,433 (23.3)	213,354 (22.3)
5th quintile (most deprived)	281,030 (27.2)	24,194 (30.6)	256,836 (26.9)
Ethnicity			
White	639,193 (61.8)	51,322 (64.8)	587,871 (61.6)
South Asian	31,837 (3.1)	959 (1.2)	30,878 (3.2)
Black	16,920 (1.6)	513 (0.6)	16,407 (1.7)
Other	11,235 (1.1)	357 (0.5)	10,878 (1.1)
Mixed	6,657 (0.6)	429 (0.5)	6,228 (0.7)
Missing	327,941 (31.7)	25,564 (32.3)	302,377 (31.7)
Body mass index (kg/m²) at start of or around pregnancy			
Underweight (<18.5)	33,926 (3.3)	2,890 (3.7)	31,036 (3.3)
Healthy weight (18.5–24.9)	470,954 (45.6)	30,986 (39.2)	439,968 (46.1)
Overweight (25.0–29.9)	241,326 (23.3)	18,783 (23.7)	222,543 (23.3)
Obese (≥30.0)	181,912 (17.6)	19,949 (25.2)	161,963 (17.0)
Missing	105,665 (10.2)	6,536 (8.3)	99,129 (10.4)
Smoking status around the start of pregnancy			
Non-smoker	419,921 (40.6)	21,634 (27.3)	398,287 (41.7)
Ex-smoker	251,655 (24.3)	20,905 (26.4)	230,750 (24.2)
Current smoker	308,267 (29.8)	34,362 (43.4)	273,905 (28.7)
Missing	53,940 (5.2)	2,243 (2.8)	51,697 (5.4)
Alcohol intake around the start of pregnancy			
Non-drinker	133,669 (12.9)	9,915 (12.5)	123,754 (13.0)
Current drinker	594,192 (57.5)	45,315 (57.3)	548,877 (57.5)
Ex-drinker	60,462 (5.8)	6,618 (8.4)	53,844 (5.6)
Missing	245,460 (23.7)	17,296 (21.9)	228,164 (23.9)
Illicit drug use			
In the 12 months before pregnancy	3,698 (0.4)	1,362 (1.7)	2,336 (0.2)
During pregnancy	2,378 (0.2)	914 (1.2)	1,464 (0.2)
History of pregnancy loss at the start of pregnancy			
Miscarriage	162,414 (15.7)	15,405 (19.5)	147,009 (15.4)
Stillbirth	6,345 (0.6)	722 (0.9)	5,623 (0.6)

Termination	174,264 (16.9)	19,360 (24.5)	154,904 (16.2)
Other losses	15,969 (1.5)	1,617 (2.0)	14,352 (1.5)
Parity at the start of pregnancy			
0	489,830 (47.4)	29,080 (36.7)	460,750 (48.3)
1	348,858 (33.7)	26,667 (33.7)	322,191 (33.8)
2	132,186 (12.8)	14,754 (18.6)	117,432 (12.3)
3 or more	58,465 (5.7)	8,324 (10.5)	50,141 (5.3)
Primary care consultations in the 12 months before pregnancy			
0	116,218 (11.2)	5,177 (6.5)	111,041 (11.6)
1–3	266,266 (25.8)	5,291 (6.7)	260,975 (27.3)
4–10	426,917 (41.3)	26,633 (33.7)	400,284 (41.9)
≥10	224,382 (21.7)	42,043 (53.1)	182,339 (19.1)
Mental health problems ever before the end of pregnancy			
Depression	263,063 (25.4)	63,795 (80.6)	199,268 (20.9)
Anxiety	164,115 (15.9)	38,266 (48.3)	125,849 (13.2)
Bipolar (depressive episodes)	2,498 (0.2)	888 (1.1)	1,610 (0.2)
Schizophrenia	2,405 (0.2)	883 (1.1)	1,522 (0.2)
Eating disorders[3]	19,635 (1.9)	4,142 (5.2)	15,493 (1.6)
Neurodevelopmental disorder ever before the end of pregnancy			
Autism spectrum disorder (ASD)	312 (0.0)	74 (0.1)	238 (0.0)
Attention deficit hyperactivity disorder (ADHD)	1,822 (0.2)	361 (0.5)	1,461 (0.2)
Intellectual disability (ID)	1,135 (0.1)	206 (0.3)	929 (0.1)
Possible somatic indications for antidepressants ever before the end of pregnancy			
Neuropathic pain/fibromyalgia	48,086 (4.7)	7,263 (9.2)	40,823 (4.3)
Diabetic neuropathy	93 (0.0)	28 (0.0)	65 (0.0)
Stress (urinary) incontinence	13,661 (1.3)	2,213 (2.8)	11,448 (1.2)
Migraine prophylaxis	3,552 (0.3)	638 (0.8)	2,914 (0.3)
Chronic tension-type headache	418 (0.0)	88 (0.1)	330 (0.0)
Other mental health-related prescriptions during pregnancy[1]			
Antipsychotics	579 (0.1)	392 (0.5)	187 (0.0)
Mood stabilisers	11,618 (1.1)	5,265 (6.7)	6,353 (0.7)
Benzodiazepines	4,989 (0.5)	2,968 (3.8)	2,021 (0.2)
Z-drugs	7,768 (0.8)	2,438 (3.1)	5,330 (0.6)
Other prescriptions during pregnancy[1]			
Other drugs not recommended by obstetricians[4]	50,478 (4.9)	9,141 (11.5)	41,337 (4.3)
Folic acid as a multivitamin	212,664 (20.6)	19,104 (24.1)	193,560 (20.3)
High dose folic acid (5mg)	52,724 (5.1)	6,776 (8.6)	45,948 (4.8)
Antiemetics	82,816 (8.0)	13,202 (16.7)	69,614 (7.3)

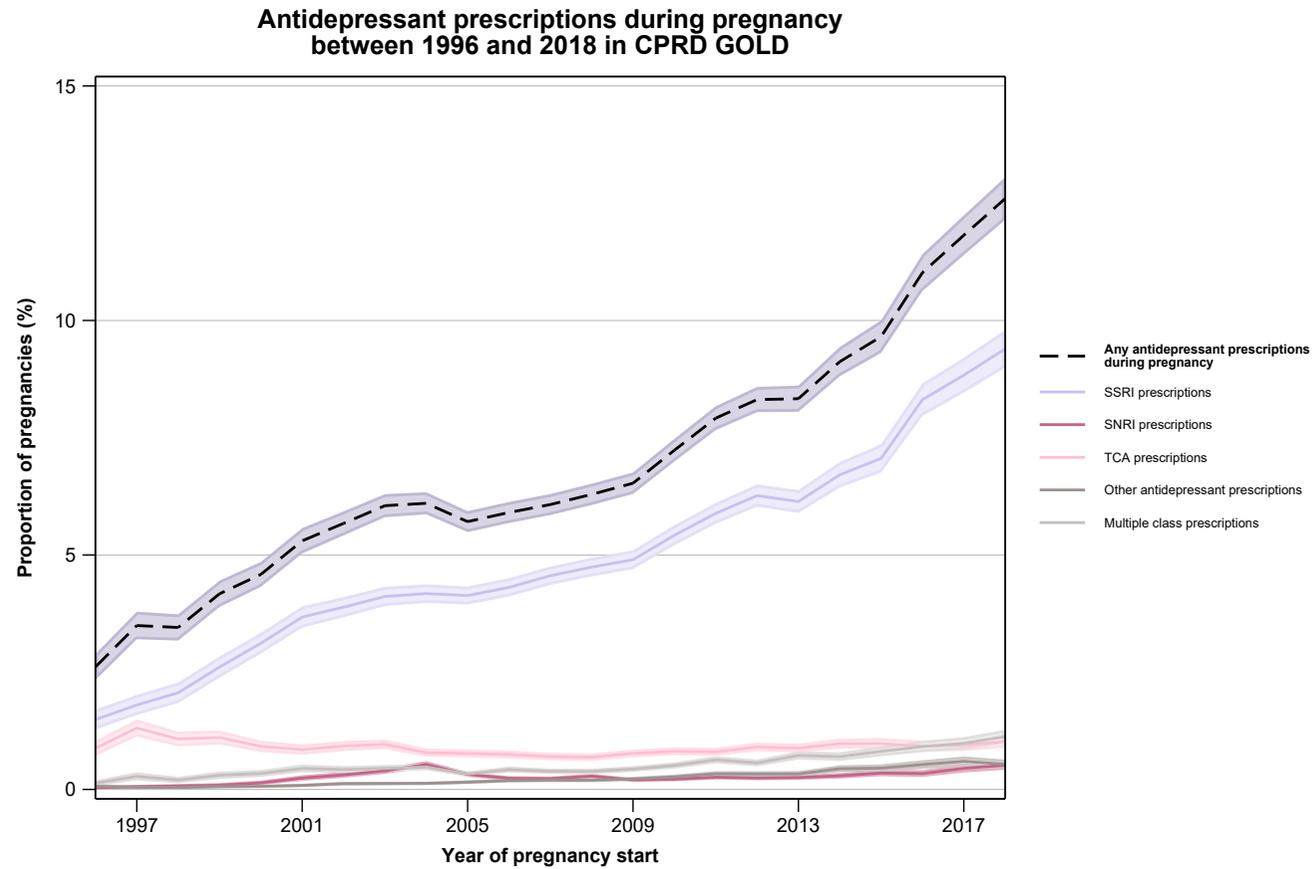[1] A prescription made during or overlapping with pregnancy
[2] No prescription made during or overlapping with pregnancy
[3] Anorexia nervosa, bulimia, and other disordered eating codes (codelist in GitHub repository)
[4] "Classical teratogens" like isotretinoin and ACE inhibitors (codelist in GitHub repository)

2.2   PRESCRIBING OVER TIME AMONG LIVE BIRTHS

Figure S2 Antidepressant prescribing during pregnancy restricted to live births.

Antidepressant prescriptions during pregnancy between 1996 and 2018 in CPRD GOLD

Legend:
- Any antidepressant prescriptions during pregnancy
- SSRI prescriptions
- SNRI prescriptions
- TCA prescriptions
- Other antidepressant prescriptions
- Multiple class prescriptions

X-axis: Year of pregnancy start (1997, 2001, 2005, 2009, 2013, 2017)
Y-axis: Proportion of pregnancies (%) (0, 5, 10, 15)

2.3   PRESCRIBING BY REGION

Table S6 Proportion of pregnancies from each CPRD region prescribed antidepressants during pregnancy.

Practice region	Prescribed / Total n / N	%
East Midlands	1,832 / 27,468	6.7
East of England	4,228 / 66,939	6.3
London	3,606 / 77,744	4.6
North East	1,040 / 15,932	6.5
North West	8,216 / 110,062	7.5
Northern Ireland	5,010 / 53,654	9.3
Scotland	19,056 / 204,963	9.3
South Central	6,030 / 86,163	7.0
South East Coast	6,062 / 86,510	7.0
South West	5,040 / 67,612	7.5
Wales	12,185 / 128,681	9.5
East Midlands	5,348 / 81,697	6.6
Yorkshire & The Humber	1,491 / 26,358	5.7

2.4 PATTERNS OF PRESCRIBING BY YEAR

Table S7 Patterns of prescribing by year window.

Pattern of prescribing during pregnancy	Total prescribed	1996 - 2000	2001 - 2006	2007 - 2012	2013 - 2018
All	79,144 (100.0)	5,234 (100.0)	19,738 (100.0)	28,643 (100.0)	25,529 (100.0)
Discontinued during pregnancy[a]	44,228 (55.9)	3,488 (66.6)	12,021 (60.9)	15,827 (55.3)	12,892 (50.5)
Continued[b] a single drug regimen throughout pregnancy	33,365 (42.2)	1,706 (32.6)	7,489 (37.9)	12,292 (42.9)	11,878 (46.5)
Continued[b] a multi-drug[c] regimen throughout pregnancy	1,551 (2.0)	40 (0.8)	228 (1.2)	524 (1.8)	759 (3.0)
Continued a single drug regimen throughout pregnancy	33,365 (100.0)	1,706 (100.0)	7,489 (100.0)	12,292 (100.0)	11,878 (100.0)
Antidepressant switched	2,776 (8.3)	161 (9.4)	652 (8.7)	1,034 (8.4)	929 (7.8)
Dose reduced	2,237 (6.7)	68 (4.0)	399 (5.3)	875 (7.1)	895 (7.5)
Dose increased	2,236 (6.7)	96 (5.6)	399 (5.3)	805 (6.5)	936 (7.9)
Dose fluctuated	2,422 (7.3)	60 (3.5)	393 (5.2)	903 (7.3)	1,066 (9.0)
More than one regimen change[d]	1,473 (4.4)	56 (3.3)	274 (3.7)	573 (4.7)	570 (4.8)
No changes to drug regimen	22,221 (66.6)	1,265 (74.2)	5,372 (71.7)	8,102 (65.9)	7,482 (63.0)
Continued a multi-drug[c] regimen throughout pregnancy	1,551 (100.0)	40 (100.0)	228 (100.0)	524 (100.0)	759 (100.0)
Antidepressant added	225 (14.5)	5 (12.5)	40 (17.5)	78 (14.9)	102 (13.4)
Antidepressant dropped	207 (13.3)	11 (27.5)	30 (13.2)	73 (13.9)	93 (12.3)
Products added & dropped	294 (19.0)	6 (15.0)	48 (21.1)	106 (20.2)	134 (17.7)
Dose changes	83 (5.4)	0 (0.0)	6 (2.6)	26 (5.0)	51 (6.7)
Multiple changes (to dose & product)	416 (26.8)	12 (30.0)	52 (22.8)	131 (25.0)	221 (29.1)

| No changes to drug regimen | 326 (21.0) | 6 (15.0) | 52 (22.8) | 110 (21.0) | 158 (20.8) |

[a] Evidence of regimen changes before discontinuation *n*=6,998 (15.8%)

[b] Those who had an overlapping prescription with the end of pregnancy

[c] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription

[d] Those who experienced a switch in product as well as at least one dose change

2.5 STRINGENT INCIDENT USE

Table S8 Patterns of prescribing during pregnancy where incident use is defined as no antidepressant prescriptions in the 12 months prior to pregnancy.

Pattern of prescribing during pregnancy	Total prescribed during pregnancy	'Prevalent prescribed'[a]	'Incident prescribed'[b]
All	79,144 (100.0)	68,258 (100.0)	10,886 (100.0)
Discontinued during pregnancy[c]	44,228 (55.9)	37,492 (54.9)	6,736 (61.9)
Continued[d] a single drug regimen throughout pregnancy	33,365 (42.2)	29,251 (42.9)	4,114 (37.8)
Continued[d] a multi-drug[e] regimen throughout pregnancy	1,551 (2.0)	1,515 (2.2)	36 (0.3)
Continued a single drug regimen throughout pregnancy	33,365 (100.0)	29,251 (100.0)	4,114 (100.0)
Antidepressant switched	2,776 (8.3)	2,505 (8.6)	271 (6.6)
Dose reduced	2,237 (6.7)	2,191 (7.5)	46 (1.1)
Dose increased	2,236 (6.7)	1,937 (6.6)	299 (7.3)
Dose fluctuated	2,422 (7.3)	2,339 (8.0)	83 (2.0)
More than one regimen change[f]	1,473 (4.4)	1,401 (4.8)	72 (1.8)
No changes to drug regimen	22,221 (66.6)	18,878 (64.5)	3,343 (81.3)
Continued a multi-drug[e] regimen throughout pregnancy	1,551 (100.0)	1,515 (100.0)	36 (100.0)
Antidepressant added	225 (14.5)	218 (14.4)	7 (19.4)
Antidepressant dropped	207 (13.3)	198 (13.1)	9 (25.0)
Products added & dropped	294 (19.0)	286 (18.9)	8 (22.2)

Dose changes	83 (5.4)	83 (5.5)	0 (0.0)
Multiple changes (to dose & product)	416 (26.8)	409 (27.0)	7 (19.4)
No changes to drug regimen	326 (21.0)	321 (21.2)	5 (13.9)

[a] Those who had at least one prescription for antidepressants in the 12 months prior to pregnancy and during pregnancy
[b] Those who did not have a prescription for antidepressants in the 12 months prior to pregnancy but at least one prescription during pregnancy
[c] Evidence of regimen changes before discontinuation *n*=6,998 (15.8%)
[d] Those who had an overlapping prescription with the end of pregnancy
[e] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription
[f] Those who experienced a switch in product as well as at least one dose change

2.6 PATTERNS BY PARITY

Table S9 Patterns of prescribing by category of parity.

Pattern of prescribing during pregnancy	Total prescribed	Nulliparous	1	2	3+
All	79,144 (100.0)	29,213 (100.0)	26,758 (100.0)	14,809 (100.0)	8,364 (100.0)
Discontinued during pregnancy[a]	44,228 (55.9)	17,197 (58.9)	15,059 (56.3)	7,807 (52.7)	4,165 (49.8)
Continued[b] a single drug regimen throughout pregnancy	33,365 (42.2)	11,514 (39.4)	11,183 (41.8)	6,692 (45.2)	3,976 (47.5)
Continued[b] a multi-drug[c] regimen throughout pregnancy	1,551 (2.0)	502 (1.7)	516 (1.9)	310 (2.1)	223 (2.7)
Continued a single drug regimen throughout pregnancy	33,365 (100.0)	11,514 (100.0)	11,183 (100.0)	6,692 (100.0)	3,976 (100.0)
Antidepressant switched	2,776 (8.3)	898 (7.8)	961 (8.6)	578 (8.6)	339 (8.5)
Dose reduced	2,237 (6.7)	799 (6.9)	785 (7.0)	434 (6.5)	219 (5.5)
Dose increased	2,236 (6.7)	721 (6.3)	752 (6.7)	458 (6.8)	305 (7.7)
Dose fluctuated	2,422 (7.3)	865 (7.5)	822 (7.4)	445 (6.6)	290 (7.3)
More than one regimen change[d]	1,473 (4.4)	461 (4.0)	523 (4.7)	294 (4.4)	195 (4.9)
No changes to drug regimen	22,221 (66.6)	7,770 (67.5)	7,340 (65.6)	4,483 (67.0)	2,628 (66.1)

Continued a multi-drug[c] regimen throughout pregnancy	1,551 (100.0)	502 (100.0)	516 (100.0)	310 (100.0)	223 (100.0)
Antidepressant added	225 (14.5)	69 (13.7)	69 (13.4)	59 (19.0)	28 (12.6)
Antidepressant dropped	207 (13.3)	69 (13.7)	65 (12.6)	41 (13.2)	32 (14.3)
Products added & dropped	294 (19.0)	96 (19.1)	110 (21.3)	49 (15.8)	39 (17.5)
Dose changes	83 (5.4)	26 (5.2)	21 (4.1)	21 (6.8)	15 (6.7)
Multiple changes (to dose & product)	416 (26.8)	138 (27.5)	134 (26.0)	78 (25.2)	66 (29.6)
No changes to drug regimen	326 (21.0)	104 (20.7)	117 (22.7)	62 (20.0)	43 (19.3)

[a] Evidence of regimen changes before discontinuation n=6,998 (15.8%)
[b] Those who had an overlapping prescription with the end of pregnancy
[c] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription
[d] Those who experienced a switch in product as well as at least one dose change

2.7 DISCONTINUATION BY TRIMESTER

Table S10 Patterns of discontinuation among those with at least 27 completed weeks' gestation.

Pattern of discontinuation during pregnancy	Total prescribed during pregnancy[a] n (%)	'Prevalent' user[b] n (%)	'Incident' user[c] n (%)
All	33,988 (100)	26,441 (100)	7,547 (100)
Discontinuation in trimester 1[d]	26,422 (77.7)	21,637 (81.8)	4,785 (63.4)
Discontinuation in trimester 2[e]	5,465 (16.1)	3,713 (14.0)	1,752 (23.2)
Discontinuation in trimester 3[f]	2,101 (6.2)	1,091 (4.1)	1,010 (13.4)

[a] Restricted to those with at least 27 completed weeks' gestation
[b] Those who had at least one prescription for antidepressants in the 3 months prior to pregnancy and during pregnancy
[c] Those who did not have a prescription for antidepressants in the 3 months prior to pregnancy but at least one prescription during pregnancy
[d] Evidence of regimen changes before discontinuation n=3,465 (13.1%)
[e] Evidence of regimen changes before discontinuation n=1,854 (33.9%)
[f] Evidence of regimen changes before discontinuation n=680 (32.4%)

2.8 PATTERNS AMONG DELIVERIES

Table S11 Patterns analysis restricted to delivery outcomes (live birth, stillbirth, live birth or stillbirth, delivery based on a third trimester record, delivery based on a late record).

Pattern of prescribing during pregnancy	Total deliveries prescribed during pregnancy n (%)	'Prevalent' user[b] n (%)	'Incident' user[c] n (%)
All	52,306 (100)	41,635 (100)	10,671 (100)
Discontinued during pregnancy[c]	34,234 (65.4)	26,638 (64.0)	7,596 (71.2)
Continued[d] a single drug regimen throughout pregnancy	17,072 (32.6)	14,043 (33.7)	3,029 (28.4)
Continued[d] a multi-drug[e] regimen throughout pregnancy	1,000 (1.9)	954 (2.3)	46 (0.4)
Continued a single drug regimen throughout pregnancy	17,072 (100)	14,043 (100)	3,029 (100)
Antidepressant switched	1,858 (10.9)	1,571 (11.2)	287 (9.5)
Dose reduced	1,603 (9.4)	1,540 (11.0)	63 (2.1)
Dose increased	1,104 (6.5)	824 (5.9)	280 (9.2)
Dose fluctuated	2,009 (11.8)	1,896 (13.5)	113 (3.7)
More than one regimen change[f]	1,193 (7.0)	1,101 (7.8)	92 (3.0)
No changes to drug regimen	9,305 (54.5)	7,111 (50.6)	2,194 (72.4)
Continued a multi-drug[e] regimen throughout pregnancy	1,000 (100)	954 (100)	46 (100)
Antidepressant added	128 (12.8)	122 (12.8)	6 (13.0)
Antidepressant dropped	125 (12.5)	116 (12.2)	9 (19.6)
Products added & dropped	210 (21.0)	199 (20.9)	11 (23.9)
Dose changes	57 (5.7)	57 (6.0)	<5
Multiple changes (to dose & product)	329 (32.9)	317 (33.2)	12 (26.1)
No changes to drug regimen	326 (21.0)	314 (21.1)	12 (19.7)

[a] Those who had at least one prescription for antidepressants in the 3 months prior to pregnancy and during pregnancy
[b] Those who did not have a prescription for antidepressants in the 3 months prior to pregnancy but at least one prescription during pregnancy
[c] Evidence of regimen changes before discontinuation n=6,041 (17.6%)
[d] Those who had an overlapping prescription with the end of pregnancy
[e] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription
[f] Those who experienced a switch in product as well as at least one dose change

2.9 PATTERNS AMONG LOSSES

Table S12 Patterns analysis restricted to loss outcomes (miscarriage, TOP, probable TOP, ectopic, molar, blighted ovum, unspecified loss).

Pattern of prescribing during pregnancy	Total losses prescribed during pregnancy n (%)	'Prevalent' user[b] n (%)	'Incident' user[c] n (%)
All	26,838 (100)	21,776 (100)	5,062 (100)
Discontinued during pregnancy[c]	9,994 (37.2)	8,163 (37.5)	1,831 (36.2)
Continued[d] a single drug regimen throughout pregnancy	16,293 (60.7)	13,077 (60.1)	3,216 (63.5)
Continued[d] a multi-drug[e] regimen throughout pregnancy	551 (2.1)	536 (2.5)	15 (0.3)
Continued a single drug regimen throughout pregnancy	16,293 (100)	13,077 (100)	3,216 (100)
Antidepressant switched	918 (5.6)	758 (5.8)	160 (5.0)
Dose reduced	634 (3.9)	608 (4.6)	26 (0.8)
Dose increased	1,132 (6.9)	955 (7.3)	177 (5.5)
Dose fluctuated	413 (2.5)	386 (3.0)	27 (0.8)
More than one regimen change[f]	280 (1.7)	258 (2.0)	22 (0.7)
No changes to drug regimen	12,916 (79.3)	10,112 (77.3)	2,804 (87.2)
Continued a multi-drug[e] regimen throughout pregnancy	551 (100)	536 (100)	15 (100)
Antidepressant added	97 (17.6)	93 (17.4)	<5
Antidepressant dropped	82 (14.9)	77 (14.4)	5 (33.3)
Products added & dropped	84 (15.2)	82 (15.3)	<5
Dose changes	26 (4.7)	26 (4.9)	<5
Multiple changes (to dose & product)	87 (15.8)	87 (16.2)	<5
No changes to drug regimen	326 (21.0)	314 (21.1)	12 (19.7)

[a] Those who had at least one prescription for antidepressants in the 3 months prior to pregnancy and during pregnancy
[b] Those who did not have a prescription for antidepressants in the 3 months prior to pregnancy but at least one prescription during pregnancy
[c] Evidence of regimen changes before discontinuation n=957 (9.6%)
[d] Those who had an overlapping prescription with the end of pregnancy
[e] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription
[f] Those who experienced a switch in product as well as at least one dose change

2.10   RESTRICTED TO >1 PRESCRIPTION

Table S13 Restricting exposed to those with at least two prescriptions during pregnancy.

Pattern of prescribing during pregnancy	Total losses prescribed during pregnancy n (%)	'Prevalent' user[b] n (%)	'Incident' user[c] n (%)
All	60,446 (100)	51,124 (100)	9,322 (100)
Discontinued during pregnancy[c]	27,118 (44.9)	23,233 (45.4)	3,885 (41.7)
Continued[d] a single drug regimen throughout pregnancy	31,777 (52.6)	26,401 (51.6)	5,376 (57.7)
Continued[d] a multi-drug[e] regimen throughout pregnancy	1,551 (2.6)	1,490 (2.9)	61 (0.7)
Continued a single drug regimen throughout pregnancy	31,777 (100)	26,401 (100)	5,376 (100)
Antidepressant switched	2,614 (8.2)	2,211 (8.4)	403 (7.5)
Dose reduced	2,177 (6.9)	2,091 (7.9)	86 (1.6)
Dose increased	2,224 (7.0)	1,771 (6.7)	453 (8.4)
Dose fluctuated	2,421 (7.6)	2,281 (8.6)	140 (2.6)
More than one regimen change[f]	1,464 (4.6)	1,351 (5.1)	113 (2.1)
No changes to drug regimen	20,877 (65.7)	16,696 (63.2)	4,181 (77.8)
Continued a multi-drug[e] regimen throughout pregnancy	1,551 (100)	1,490 (100)	~60 (100)
Antidepressant added	225 (14.5)	215 (14.4)	10 (16.4)
Antidepressant dropped	207 (13.3)	193 (13.0)	14 (23.0)
Products added & dropped	294 (19.0)	281 (18.9)	13 (21.3)
Dose changes	83 (5.4)	83 (5.6)	<5
Multiple changes (to dose & product)	416 (26.8)	404 (27.1)	12 (19.7)
No changes to drug regimen	326 (21.0)	314 (21.1)	12 (19.7)

[a] Those who had at least one prescription for antidepressants in the 3 months prior to pregnancy and at least two prescriptions during pregnancy
[b] Those who did not have a prescription for antidepressants in the 3 months prior to pregnancy but at least two prescriptions during pregnancy
[c] Evidence of regimen changes before discontinuation n=6,796 (25.1%)
[d] Those who had an overlapping prescription with the end of pregnancy
[e] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription
[f] Those who experienced a switch in product as well as at least one dose change

2.11   PATTERNS AMONG THOSE WITH HES

Table S14 Patterns of prescribing stratified by pre-pregnancy use among those with linked secondary care (HES) data.

Pattern of prescribing during pregnancy	Total prescribed during pregnancy n (%)	'Prevalent' user[a] n (%)	'Incident' user[b] n (%)
All	33,736	26,410	7,326
Discontinued during pregnancy[c]	19,044 (56.5)	14,611 (55.3)	4,433 (60.5)
Continued[d] a single drug regimen throughout pregnancy	14,078 (41.7)	11,217 (42.5)	2,861 (39.1)
Continued[d] a multi-drug[e] regimen throughout pregnancy	614 (1.8)	582 (2.2)	32 (0.4)
Continued a single drug regimen throughout pregnancy	14,078 (100)	11,217 (100)	2,861 (100)
Antidepressant switched	1,247 (8.9)	1,026 (9.1)	221 (7.7)
Dose reduced	908 (6.4)	870 (7.8)	38 (1.3)
Dose increased	885 (6.3)	689 (6.1)	196 (6.9)
Dose fluctuated	942 (6.7)	881 (7.9)	61 (2.1)
More than one regimen change[f]	574 (4.1)	526 (4.7)	48 (1.7)
No changes to drug regimen	9,522 (67.6)	7,225 (64.4)	2,297 (80.3)
Continued a multi-drug[e] regimen throughout pregnancy	614 (100)	582 (100)	32 (100)
Antidepressant added	614 (100)	582 (100)	32 (100)
Antidepressant dropped	106 (17.3)	99 (17.0)	7 (21.9)
Products added & dropped	88 (14.3)	81 (13.9)	7 (21.9)
Dose changes	121 (19.7)	113 (19.4)	8 (25.0)
Multiple changes (to dose & product)	29 (4.7)	29 (5.0)	<5
No changes to drug regimen	143 (23.3)	138 (23.7)	5 (15.6)

[a] Those who had at least one prescription for antidepressants in the 3 months prior to pregnancy and during pregnancy
[b] Those who did not have a prescription for antidepressants in the 3 months prior to pregnancy but at least one prescription during pregnancy
[c] Evidence of regimen changes before discontinuation n=2,729 (14.3%)
[d] Those who had an overlapping prescription with the end of pregnancy
[e] Those prescribed at least two, differing antidepressant products >5 days from the end of their current prescription
[f] Those who experienced a switch in product as well as at least one dose change

2.12   POST-PREGNANCY PRESCRIBING

Table S15 Proportion of patients who initiated or resumed antidepressant treatment in the 12 months after pregnancy.

Previous prescription pattern	Total N	Prescribed after pregnancy n (%)	Not prescribed after pregnancy n (%)
All	1,033,783 (100)	162,947 (15.8)	870,836 (84.2)
Continued throughout pregnancy	34,916 (100)	34,916 (100)	–
Discontinued during pregnancy	44,228 (100)	23,457 (53.0)	20,771 (47.0)
Discontinued in the 12 months prior to pregnancy	74,559 (100)	25,532 (34.2)	49,027 (65.8)
No use before or during pregnancy	880,080 (100)	79,042 (9.0)	801,038 (91.0)

Table S16 Proportion of patients who initiated or resumed antidepressant treatment in the 12 months after pregnancy restricted to first pregnancies.

Previous prescription pattern	Total N	Prescribed after pregnancy n (%)	Not prescribed after pregnancy n (%)
All	347,929 (100.0)	43,898 (12.6)	304,031 (87.4)
Continued throughout pregnancy	7,305 (100.0)	7,305 (100.0)	0 (0.0)
Discontinued during pregnancy	11,155 (100.0)	5,271 (47.3)	5,884 (52.7)
Discontinued in the 12 months prior to pregnancy	18,910 (100.0)	5,586 (29.5)	13,324 (70.5)
No use before or during pregnancy	310,559 (100.0)	25,736 (8.3)	284,823 (91.7)

Table S17 Proportion of individuals who were prescribed antidepressants in the 12 months after pregnancy stratified by previous use, among deliveries (postnatal use) and losses (post-pregnancy use)

Previous prescription pattern	Total N	Prescribed after pregnancy n (%)	Not prescribed after pregnancy n (%)
Deliveries			
All	747,311 (100)	113,506 (15.2)	633,805 (84.8)
Continued throughout pregnancy	18,072 (100)	18,072 (100)	–
Discontinued during pregnancy	34,234 (100)	17,642 (51.5)	16,592 (48.5)
Discontinued in the 12 months prior to pregnancy	51,059 (100)	17,789 (34.8)	33,270 (65.2)
No use before or during pregnancy	643,946 (100)	60,003 (9.3)	583,943 (90.7)
Losses			
All	286,472 (100)	49,441 (17.3)	237,031 (82.7)
Continued throughout pregnancy	16,844 (100)	16,844 (100)	–
Discontinued during pregnancy	9,994 (100)	5,815 (58.2)	4,179 (41.8)
Discontinued in the 12 months prior to pregnancy	23,500 (100)	7,743 (32.9)	15,757 (67.1)
No use before or during pregnancy	236,134 (100)	19,039 (8.1)	217,095 (91.9)

Table S18 Proportion of individuals who initiated or resumed antidepressant treatment in the 12 months after pregnancy among those that had at least 12 months follow-up post-pregnancy.

Previous prescription pattern	Total N	Prescribed after pregnancy n (%)	Not prescribed after pregnancy n (%)
All	921,521 (100)	151,454 (16.4)	770,067 (83.6)
Continued throughout pregnancy	31,105 (100)	31,105 (100)	–
Discontinued during pregnancy	38,992 (100)	21,742 (55.8)	17,250 (44.2)
Discontinued in the 12 months prior to pregnancy	65,816 (100)	23,849 (36.2)	41,967 (63.8)
No use before or during pregnancy	785,608 (100)	74,758 (9.5)	710,850 (90.5)

2.13 INDICATIONS

Table S19 Incident depression and anxiety at different times in relation to pregnancy.

Indication	Total N	Prescribed during pregnancy n (%)	Not prescribed during pregnancy n (%)
	1,033,783 (100)	79,144 (100)	954,639 (100)
Depression			
Depression started more than 12 months before pregnancy	223,775 (21.6)	49,447 (62.5)	174,328 (18.3)
Depression started 12 months before pregnancy	31,339 (3.0)	10,482 (13.2)	20,857 (2.2)
Depression started during pregnancy	7,949 (0.8)	3,866 (4.9)	4,083 (0.4)
Depression started in the 12 months post-pregnancy	48,011 (4.6)	2,360 (3.0)	45,651 (4.8)
Anxiety			
Anxiety started more than 12 months before pregnancy	136,469 (13.2)	29,941 (37.8)	106,528 (11.2)
Anxiety started 12 months before pregnancy	19,661 (1.9)	5,937 (7.5)	13,724 (1.4)
Anxiety started during pregnancy	7,985 (0.8)	2,388 (3.0)	5,597 (0.6)
Anxiety started in the 12 months post-pregnancy	20,050 (1.9)	2,551 (3.2)	17,499 (1.8)

Table S20 Prevalence of other indications among those prescribed to antidepressants during pregnancy with depression and/or anxiety.

	Total prescribed n (%)	Depression n (%)	Anxiety n (%)	Depression and anxiety n (%)	Neither depression nor anxiety n (%)
Total	79,144 (100)	32,204 (100)	6,675 (100)	31,591 (100)	8,674 (100)
Depression	63,795 (80.6)	32,204 (100)	–	31,591 (100)	–
Anxiety	38,266 (48.3)	–	6,675 (100)	31,591 (100)	–
Other mood disorders*	51 (0.1)	22 (0.1)	<5	27 (0.1)	<5
Eating disorders	4,142 (5.2)	1,468 (4.6)	234 (3.5)	2,177 (6.9)	263 (3.0)
Pain	7,263 (9.2)	2,542 (7.9)	482 (7.2)	3,544 (11.2)	695 (8.0)
Diabetic neuropathy	28 (0.0)	16 (0.0)	<5	7 (0.0)	<5
Stress incontinence	2,213 (2.8)	834 (2.6)	124 (1.9)	1,145 (3.6)	110 (1.3)
Migraine prophylaxis	638 (0.8)	215 (0.7)	46 (0.7)	308 (1.0)	69 (0.8)
Tension-type headache	88 (0.1)	34 (0.1)	<5	43 (0.1)	7 (0.1)
No evidence of an antidepressant indication	7,578 (9.6)	–	–	–	7,578 (87.4)

2.14   MISSING DATA

Table S21 Likelihood of having missing data in ethnicity, BMI, smoking status, alcohol use status having discontinued.

Variable	Discontinuers with missing	Continuers with missing	Likelihood of missing data [aOR[a] (95% CI)]
Maternal ethnicity	14,490/44,228 (32.76)	11,074/34,916 (31.72)	1.03 (1.00-1.06)
Maternal BMI around the start of pregnancy	3,868/44,228 (8.75)	2,668/34,916 (7.64)	1.18 (1.12-1.25)
Smoking status around the start of pregnancy	1,431/44,228 (3.24)	812/34,916 (2.33)	1.11 (1.01-1.21)
Alcohol consumption around the start of pregnancy	10,110/44,228 (22.86)	7,181/34,916 (20.57)	1.14 (1.10-1.18)

[a] adjusted for year of pregnancy start

3 References

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