

1 Supplementary Appendices

2 eTable 1 Medication categories recorded in NIMATS and the years in 3 which they were recorded during the study period

NIMATS Medication category	Years category used in NIMATS	BNF chapter and section codes^a used to create equivalent medication categories in EPD
None	2010-2016	None
Analgesics	2010-2016	4.7
Antacid	2010-2016	1.1.1
Antiasthmatics	2010-2016	3.1, 3.2 and 3.3
Antibiotics	2010-2016	5.1, 13.10.1 and 11.3.1
Anticoagulant	2010-2016	2.8.1, 2.8.2 and 2.9.0 ^b
Antidepressants	2010-2016	4.3
Antiemetic	2010-2016	4.6
Antiepileptic	2010-2016	4.8
Antihistamines	2010-2016	3.4.1
Antihypertensive	2010-2016	2.5, 2.6.2 and tadalafil
Antivirals	2015-2016	5.3, 13.10.3 and 11.3.3
Cardiac	2010-2016	2 and tadalafil
Diuretics	2010-2016	2.2
Drug abuse	2010-2014	4.10.1, 4.10.3, acamprosate, disulfiram, calcium carbimide, nalmefene, buprenorphine, methadone, lofexidine, naltrexone, and levacetylmethadol hydrochloride.
Folic Acid - commenced pre-conception ^c	2010-2016	Not available
Folic Acid - commenced post-conception	2010-2016	9.1.2
Hormonal	2010-2016	6., 7.3, 8.3.1 and 8.3.2
Immunosuppressants	2010-2016	8.2.1, 8.2.2 and 1.5.3
Iron	2010-2016	9.1.1

Insulin	2010-2016	6.1.1
Laxatives	2010-2016	1.6
Sedatives	2010-2016	4.1.1
Steroids	2010-2016	1.5.2, 3.2, 6.3, 10.1.2, 11.4.1, 13.4, 12.2.1 beclometasone, 12.2.1 betamethasone, 12.2.1 budesonide, 12.2.1 fluticasone, 12.2.1 mometasone, 12.2.1 triamcinolone, 12.3.1 betamethasone, 12.3.1 hydrocortisone
Thyroxine	2010-2016	6.2.1
Tranquillisers	2010-2014	4.1.2
Vitamins ^d	2010-2016	9.6
Other	2010-2014	All other codes not listed above

NIMATS= Northern Ireland Maternity System, BNF= British National Formulary

^a Some medications could not be identified by the BNF code alone. Instead, the generic drug name and BNF code were combined, or the generic drug name was used to determine exposures.

^b Antiplatelets are included in BNF codes after review of initial results and input from AL, a consultant midwife/data expert.

^c Pre-conception folic acid was not available in the data as the prescriptions started at the date of the LMP. This information would be available in the EPD if a wider exposure window were used when creating the dataset.

^d other than folic acid

14 eTable 2 Calculation of Sensitivity, and Specificity, PPV and NPV

		Reference / 'gold standard'	
		EPD	
		Yes	No
NIMATS	Yes	A	B
	No	C	D

- 15 Sensitivity - proportion of true positives correctly identified as such
- 16
$$= (\text{True positives (A)} / \text{True positives (A)} + \text{False negatives (C)}) \times 100$$
- 17 Specificity - proportion of true negatives correctly identified as such
- 18
$$= (\text{True negative (D)} / \text{False positive (B)} + \text{True negative (D)}) \times 100$$
- 19 Positive predictive value - proportion of positives which are truly positive
- 20
$$= (\text{True Positives (A)}) / (\text{True Positives (A)} + \text{False Positives (B)}) \times 100$$
- 21 Negative predictive value - proportion of negatives which are truly negative
- 22
$$= (\text{True Negatives (D)}) / (\text{True Negatives (D)} + \text{False Negatives (C)}) \times 100$$

eTable 3 The number of pregnancies with each medication recorded in NIMATS, EPD, NIMATS only, EPD only, both NIMATS and the EPD and in NIMATS or EPD

Medication	NIMATS (%)	EPD (%)	NIMATS only (%)	EPD only (%)	NIMATS and EPD (%)	NIMATS or EPD (%)
Any medication	103,816	88,693	32,636	17,513	71,180	121,329
Only vitamins, iron and folic acid	78,373	20,698	62,926	5,251	15,447	83,624
Medication excluding vitamins, iron and folic acid	25,443	67,995	4,757	47,309	20,686	72,752
Available over the counter or by prescription^a						
Pregnancy-related						
Low dose folic acid (400 mcg)	31,424	37,654	25,382	31,612	6,042	63,036
Vitamins	28,463	1,994	27,586	1,117	877	29,580
Antiemetic	4,403	12,187	690	8,474	3,713	12,877
Antacid	1,638	124	1,621	107	17	1,745
Iron	1,290	2,580	908	2,198	382	3,488
Laxatives	231	5,431	74	5,274	157	5,505
Intermittent use						
Analgesics	1,777	9,640	939	8,802	838	10,579
Antihistamines	509	3,554	232	3,277	277	3,786
Antivirals^b	16	173	Redacted	Redacted	Redacted	Redacted
Available by prescription only						
Pregnancy-related						
High dose folic acid (5mg)	2,847	8,985	926	7,064	1,921	9,911
Chronic use/Pregnancy related						
Anticoagulant^c	1,937	2,490	544	1,097	1,393	3,034
Intermittent use						
Antibiotics	1,460	18,230	446	17,216	1,014	18,676
Tranquilisers^d	283	1,366	169	1,252	114	1,535
Sedatives	647	1,170	476	999	171	746
Chronic use						
Hormonal	1,871	9,592	512	8,233	1,359	10,104
Antidepressants	830	8,574	111	7,855	719	8,685
Steroids - all	149	6,647	65	6,563	84	6,712
Antiasthmatics	3,466	5,614	1,667	3,815	1,799	7,281
Cardiac	49	4,733	11	4,695	38	4,744
Thyroxine	725	2,926	125	2,326	600	3,051
Antiepileptic	167	1,261	32	1,126	135	1,293
Insulin	147	782	19	654	128	801
Antihypertensive	526	480	246	200	280	726
Immunosuppressants	73	152	45	124	28	197
Diuretics	Redacted	97	Redacted	Redacted	Redacted	Redacted
Other medications						

Other^d	10,115	22,722	6,693	19,300	3,422	29,415
Drug abuse^{d,e}	53	87	Redacted	Redacted	Redacted	Redacted

^a Some medication subtypes can be obtained either OTC or by prescription; others are classes that contain prescription-only medications as well as medications available OTC or by prescription.

^b Comparison restricted to 2015-2016 as this medication category was introduced to NIMATS in 2015.

^c Based on expert advice, the EPD exposure included antiplatelets and aspirin used for its antiplatelet effect (BNF code 2.9.0).

^d Comparison restricted to 2010-2014 as this medication category was removed from NIMATS in 2015.

^e EPD exposures represent drugs used for substance dependence, such as methadone for opioid dependence. NIMATS exposures may also include illicit drug use.

eTable 4 The number and proportion of pregnancies with each medication recorded in NIMATS, EPD, NIMATS only, EPD only, both NIMATS and the EPD, NIMATS or EPD, Cohen's kappa, the strength of agreement, sensitivity and specificity, PPV and NPV with different definitions of 'anticoagulants'.

Medication	Anticoagulant n (%)	Anticoagulant including antiplatelets and aspirin ^a n (%)	Anticoagulant including antiplatelets and all aspirin ^b n (%)
NIMATS	1,937 (1.4)	1,937 (1.4)	1,937 (1.4)
EPD	1,002 (0.7)	2,490 (1.8)	10,793 (7.7)
NIMATS only	1,167 (0.8)	544 (0.4)	523 (0.4)
EPD only	232 (0.2)	1,097 (0.8)	9,379 (6.7)
NIMATS and EPD	77 (0.6)	1,393 (1)	1,414 (1)
NIMATS or EPD	2,169 (1.6)	3,034 (2.2)	11,316 (8.1)
Cohen's kappa (95% CI)	0.52 (0.50, 0.54)	0.62 (0.61-0.64)	0.20 (0.19-0.21)
Strength of agreement	Moderate	Moderate	Slight
Sensitivity	7.7	55.9	13.1
Specificity	99.2	99.6	99.6
PPV	6.2	71.9	73.0
NPV	99.8	99.2	93.2

NIMATS= Northern Ireland Maternity System, EPD=Enhanced Prescribing Database

^a This included aspirin used for its antiplatelet effect (British National Formulary (BNF) code 2.9.0) but not aspirin used as an analgesic (BNF code 4.7.1).

^b This included aspirin used for its antiplatelet effect (BNF code 2.9.0) and aspirin used as an analgesic (BNF code 4.7.1).