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Medication use from conception to the first antenatal appointment: agreement between maternal self-report to midwife and prescribing records in Northern Ireland in 2011-2016

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Abstract

Introduction

Data reliability must be considered before using administrative healthcare databases to study medication utilisation and safety during pregnancy.

Objectives

To compare medication use reported by the mother and recorded by midwives at the first antenatal visit in the Northern Ireland (NI) Maternity System (NIMATS) to dispensed prescriptions recorded in the Enhanced Prescribing Database (EPD).

Methods

A population-based linked cohort study including all resident women in NI who gave birth between 01/01/2011 and 31/12/2016. Prescriptions dispensed in the EPD between the last menstrual period and the first antenatal visit were compared to medications recorded in NIMATS. The number and proportion of pregnancies with medications in each data source were calculated along with Cohen's kappa, sensitivity and specificity.

Results

Of the 139,687 pregnancies in NIMATS (106,206 women), 74.3% reported taking medication, including supplements, and 63.5% had prescriptions dispensed (with 86.9% reporting taking medication or having a prescription dispensed). Excluding supplements, 18.2% reported medication use, while 48.7% had prescriptions dispensed. In NIMATS, 20.4% of pregnancies had vitamins and 1.2% antacids compared to 1.4% and 0.1% respectively in EPD. All other medications were more commonly prescribed than reported, with moderate agreement for antiemetics (kappa 0.42, 95% CI 0.41-0.43), anticoagulants (kappa 0.62, 95% CI 0.61-0.64) and antihypertensives (kappa 0.62, 95% CI 0.61-0.64). Agreement was lowest for 400mg folic acid (kappa -0.09, 95% CI -0.10 - -0.09). There was considerable underreporting of medicines for chronic use, such as antiepileptics, at the first antenatal appointment.

Conclusions

Medication use during early pregnancy was common. Women obtained vitamins and antacids over the counter rather than by prescription, but all other medications were prescribed more. Non-compliance and discontinuation may explain some of the disagreement, but reporting of prescribed medicines for chronic illnesses was incomplete in antenatal records. To identify all medication use, combining maternal reporting with prescribing data is recommended.

Highlights

- Medication use in early pregnancy is common in Northern Ireland based on maternal reports or prescribing records.
- Agreement between maternal report and prescribing records was, at best, moderate, even for medications taken for chronic conditions.
- There was evidence of considerable underreporting of medicines for chronic diseases, such as antiepileptics, at the first antenatal appointment.
- A combination of maternal reports and prescribing data is recommended to identify all medication use.

Keywords

Pregnancy; Pharmaceutical Preparations; Information Storage and Retrieval; Self-Report

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Introduction

Medication use during pregnancy is common [1] and has been increasing over time [2, 3]. Despite this, just 5% of medications have been adequately monitored, tested, and labelled with safety information for use in pregnant and breastfeeding women [4] as pregnant women are usually excluded from premarketing clinical trials of new medications [5]. Instead, information on medication safety in pregnancy is mainly based on post-marketing surveillance using pregnancy registries or electronic healthcare databases [6–8].

When evaluating medication utilisation or the safety of medications taken during pregnancy, the reliability of medication exposure data in electronic healthcare databases is an important consideration. There is no 'gold standard' to assess maternal medication exposure, and each source of information is prone to bias. Prescription databases do not include over-the-counter (OTC) medicines, medicines bought online, or medicines given to hospital inpatients, outpatients, or in Accident & Emergency departments. They may also over-estimate medication exposure if patients do not redeem issued prescriptions [9, 10] and if dispensed prescriptions are not taken or are taken much later [11]. Self-reported data may be susceptible to recall [12] or social desirability bias, [13] and accuracy of recall may be influenced by factors such as questionnaire design, potential stigma, time between use and interview, age, education level, route of administration, and presence and severity of comorbidities [14–18]. The recall of intermittently used medications is lower than those used daily for chronic conditions [15, 16, 19–23].

Two Northern Ireland (NI) electronic healthcare databases may be suitable for medication utilisation or safety research. The Northern Ireland Maternity System (NIMATS) database captures pregnancy and perinatal information for all women giving birth in NI. At the first antenatal visit (typically 10–12 weeks gestation), a midwife records pregnancy and general health-related information, including the medications a woman reports taking, using a standardised reporting template. All women have a booking interview conducted by a midwife whether they go on to be cared for by a midwife or obstetrician during their pregnancy. This is potentially a rich source of medication information, as it should include OTC, hospital-prescribed medications, and general practitioner (GP)-prescribed medications. The NI Enhanced Prescribing Database (EPD) records GP-prescribed medicines dispensed by pharmacists. Neither of these datasets were developed for research purposes, meaning the quality of the data must first be assessed to determine if they are "fit for purpose". In an earlier study, [24] we examined the prevalence of prescriptions dispensed in the EPD between 2010 and 2016. We found that, excluding supplements, almost half of pregnant women in NI had prescriptions for medications in early pregnancy. There was evidence for variation in medication use with maternal age and area-based deprivation. Younger and older mothers and those living in the most deprived areas were more likely to have medications recorded in the EPD [24].

This study aimed to compare medication use reported by the mother and recorded by midwives at the first antenatal visit in NIMATS to dispensed prescriptions recorded in the

EPD in the context of the potential use of these databases for drug utilisation and safety studies.

Methods

The detailed methodology of this population-based linked cohort study has been described previously [24]. Women resident in NI who gave birth between 1st January 2011 and 31st December 2016 were identified in the NIMATS database. Information extracted from NIMATS included medication recorded at the first antenatal visit (known as the booking interview), gestational age at delivery, and the delivery date. These NIMATS maternity data were linked to the EPD prescription dispensation data using the mother's Health and Care Number (HCN) or hospital number if the HCN was unavailable, and to the NI Multiple Deprivation Measure (MDM) 2017, based on the mother's postcode at the booking interview. The linked NIMATS-EPD data included prescriptions issued from 1st April 2010 to 30th June 2016 to cover the early pregnancy period for mothers who gave birth between January 2011 and December 2016. During the study period, 13.8% of prescriptions to the NI population, not just to pregnant women, could not be matched to a unique HCN by the data provider. Prescribed medications were free of charge in NI from the start of the study period [25].

Medication exposures

There are 28 categories in NIMATS to record medication use, including an option for 'no medication' (eTable 1). Three medication categories were removed at the end of 2014, and one was added. A separate variable records the dose of folic acid taken. The EPD database uses the British National Formulary (BNF) classification system for prescribed medications. EPD exposures equivalent to the NIMATS medication categories were created by combining relevant BNF codes and doses for folic acid. Some medicines 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. To aid in interpreting the results, the medication categories were organised based on their use (i.e. pregnancy-related, acute/intermittent, or chronic) [26] and source (i.e. available by 'prescription-only' or 'OTC or by prescription'). As we are restricted by the medication categories used in NIMATS, some of the 'OTC or by prescription' medication categories consist of medications available via both sources, such as vitamins. Others include some medications only available via prescription while the rest of the category is available in both 'OTC or by prescription' such as antiemetics or antivirals. The 'other' medication category in NIMATS, which included any medication not included in any of the other NIMATS medication categories, and the NIMATS drug abuse category were examined separately.

The medication exposure period of interest was between the Last Menstrual Period (LMP), calculated from the date of delivery minus the gestational age at delivery, and the date of the booking interview. Prescriptions dispensed during this period for each pregnancy were extracted from the

EPD and linked to the NIMATS record. Medications with a dispensing record outside this period i.e. before the LMP or after the booking interview were not identified in the EPD. For the medication categories explored each pregnancy was considered to either have the medication recorded/not recorded in NIMATS and either dispensed/not dispensed in the EPD.

This study included all pregnancies recorded at the maternity booking appointment resulting in either live birth, still birth or fetal death. Only one observation was included in the dataset for women with multiple births, as the mother's details are the same for both births. Some pregnancies (0.04%) were excluded from the dataset due to a missing date of booking interview. Births with a gestational age at booking <1 week (0.02%), >20 weeks (3.0%), or with a gestational age at delivery ≥ 44 weeks (0.06%) were excluded due to concerns

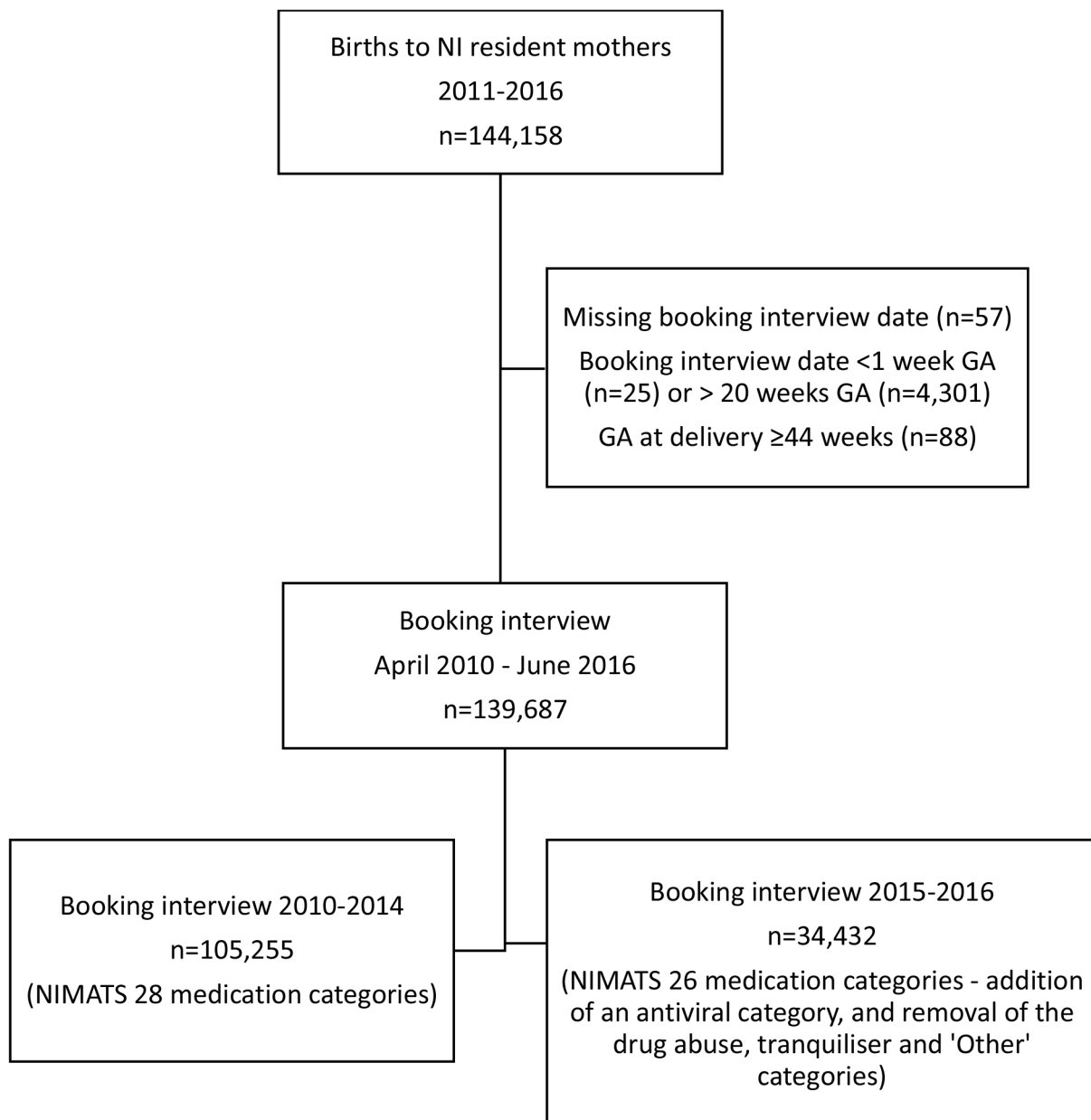
about data validity (Figure 1). Terminations of pregnancy were illegal in NI during the study period.

Statistical analysis

Descriptive statistics were used to describe the cohort.

For each medication, the number and proportion of pregnancies with: i) the medication recorded in NIMATS, ii) prescriptions in EPD, iii) the medication recorded in NIMATS only, iv) prescriptions in the EPD only, v) the medication in both NIMATS and the EPD and vi) medication recorded in NIMATS or prescriptions in the EPD. The agreement, corrected for that expected by chance alone, was calculated using Cohen's kappa [27]. The kappa statistic was interpreted based on the suggested cut-off values of Landis and Koch (1977) [28]. Sensitivity, specificity, positive

Figure 1: Flow chart detailing exclusions and final population



NI = Northern Ireland; GA = Gestational age; NIMATS = Northern Ireland Maternity System.

predictive value (PPV), and negative predictive value (NPV) were also calculated. When calculating these measures of agreement, it was necessary to choose a reference for maternal medication exposure. While neither the EPD nor maternal report would be considered the gold standard, the EPD was used here as the reference. Sensitivity is the proportion of medications/prescriptions correctly identified (true positives) while specificity is the proportion correctly identified as not having medications/prescriptions (true negatives). PPV is the proportion of those positive for a medication/prescription which are truly positive, and NPV is the proportion of negatives which are truly negative. The calculations for these measures are described in eTable 2. Comparisons between NIMATS and EPD were limited to years when the medication was recorded in NIMATS, for example, 2015–2016 for antivirals.

Stata/SE, version 16 [29] was used for all analyses. Kappa, sensitivity and specificity were not provided if there was a risk of disclosure due to small numbers.

Ethics approval

This study was approved by the Ulster University Nursing and Health Research Ethics Filter Committee, the Health Research Authority (reference: 17/NS/0047), and the Honest Broker Governance Board (HBS Reference 21). As the Honest Broker Service provided only anonymised data, individual consent was not required.

Results

Between 2010 and 2016, there were 139,687 pregnancies booked by 106,206 women; see Table 1 for sample characteristics. The mean gestational age at booking was 10.7 weeks (range <5–20 weeks), with 86.0% of pregnancies booked by 12 weeks. The mean maternal age was 29.3 years, and the mean gestational age at delivery was 39.0 weeks. Most women (71.9%) had one pregnancy during the period, with a quarter (24.9%) having two and the rest (3.4%) 3+ pregnancies recorded during the period.

In NIMATS, 74.3% of pregnancies had a medication reported at the booking appointment compared to 63.5% with a prescription dispensed in the EPD, see Table 2 (and eTable 3 for numbers). Combining both data sources, 86.9% of women reported taking medication or had a prescription dispensed. Vitamins, iron or folic acid were the only medications reported in NIMATS in 56.1% of pregnancies compared to 14.8% of pregnancies in the EPD. Excluding vitamins, iron, and folic acid, 18.2% of pregnancies had a medication reported in NIMATS compared to 48.7% with a prescription in the EPD. These represented slight to fair agreement based on Cohen's kappa but the PPV was 81.3%, see Table 3.

Medications available OTC or by prescription

The medications available OTC or by prescription (Table 2), were all taken for pregnancy-related or acute/intermittent use. Low-dose folic acid (400mcg) was reported in 22.5% of pregnancies in NIMATS, with a similar proportion (27.0%) having low-dose folic acid prescribed. However, the reported

and prescribed records agreed in less than a fifth of cases with Cohen's kappa, indicating just chance agreement between the two sources and a PPV of 19.2%, see Table 3. Combining the two data sources, almost half of women (45.1%) took low-dose folic acid (Table 2).

Vitamins and antacids were the only medications available OTC that were more commonly reported in NIMATS than prescribed in EPD. In 20.4% of pregnancies women reported vitamins in NIMATS compared to only 1.4% with prescriptions in EPD, with a PPV of just 3.1%. More than 95% of those who reported using vitamins did not have a prescription. More than half of those who obtained vitamins by prescription did not report their use in NIMATS. Antacids were reported in NIMATS in 1.2% of pregnancies and prescribed in just 0.1% of pregnancies, with sensitivity just 13.7% and PPV of 1.0%. Almost all of those who reported using antacids obtained these OTC. Of those prescribed antacids, just over one-tenth reported their use in NIMATS.

The only OTC medications with moderate agreement based on Cohen's kappa were the antiemetics, with a PPV of 84.3%. After supplements, antiemetics are the most common medication reported in NIMATS (3.2%). More than double the proportion of pregnancies had an antiemetic prescribed in EPD (8.7%), with less than a third of those with a prescription reporting their use.

The remaining OTC medication groups were all more commonly prescribed in EPD than reported in NIMATS, with PPV ranging from 29.6% to 68.0%. In each of these cases, a low proportion of the women reported taking the prescribed medications in NIMATS.

Prescription-only medications

In contrast to low-dose folic acid, high-dose folic acid (5mg) is available by prescription only in NI. It was reported by 2% of women in NIMATS but had been prescribed to 6.4% of women, see Table 2. Approximately one-third of the reports in NIMATS could not be corroborated in the prescription data. Agreement based on Cohen's kappa was fair, but sensitivity was low at 21.4% and a PPV of 67.5%.

Anticoagulants may be used chronically or started during pregnancy. Expert advice indicated that midwives recorded antiplatelet agents, particularly aspirin, in the anticoagulant category in NIMATS. Anticoagulants were reported in 1.4% of pregnancies and prescribed in 1.8%, with more than half of those prescribed anticoagulants reporting their use resulting in moderate agreement and a PPV of 71.9%. See eTable 4 for the agreement between NIMATS and EPD for anticoagulants alone and anticoagulants, antiplatelet agents, and aspirin.

All prescription-only medications were more commonly prescribed than reported, with antibiotics being the most common prescription-only medication in EPD (13.1%). Antibiotics were much less widely reported in NIMATS (1.0%), with almost 95% of prescribed antibiotics not reported in NIMATS. Agreement based on kappa was slight and antibiotics had one of the lowest sensitivities of 5.6%, and a PPV of 69.5%.

Of the chronically used medications, antihypertensives and antiasthmatics had the highest proportion of prescribed medication reported to NIMATS, 58.3% and 32.0%,

Table 1: Characteristics of included pregnancies

		Number of pregnancies	Percent of pregnancies
Booking year	2010 (from April)	11,148	8.0
	2011	24,059	17.2
	2012	23,492	16.8
	2013	23,314	16.7
	2014	23,242	16.6
	2015	23,344	16.7
	2016 (to June)	11,088	7.9
Maternal age at booking	<20	6,452	4.6
	20-24	21,871	15.7
	25-29	40,897	29.3
	30-34	44,908	32.1
	35-39	21,517	15.4
	40+	4,042	2.9
NIMDM Quintile	1 (Most deprived)	30,629	21.9
	2	29,618	21.2
	3	28,601	20.5
	4	27,425	19.6
	5 (Least deprived)	22,162	15.9
	Missing	1,252	0.9
Pregnancy planning	Planned pregnancy	99,295	71.1
	Unplanned pregnancy	37,531	26.9
	Planning status unknown	2,861	2.0

NIMDM = Northern Ireland Multiple Deprivation Measure.

respectively. For the other chronically used medications, typically fewer than 20% of prescribed medication was reported to NIMATS. Antihypertensives also had moderate agreement based on Cohen's kappa and a PPV of 53.2%. Hormonal medications, antiasthmatics, thyroxine, insulin and immunosuppressants showed fair agreement between NIMATS and the EPD, with PPV ranging from 38.4% (immunosuppressants) to 87.1% (insulin). For the antidepressants, steroids, cardiac, and antiepileptic medications, agreement was slight, with 89.3% (antiepileptic) to 99.2% (steroids) of these prescribed medications not reported in NIMATS. For these conditions, PPV ranged from 56.4% (steroids) to 86.6% (antidepressants).

Discussion

In this large population-based linked cohort study we compared medication data reported by the mother and recorded by midwives to dispensed prescription data for all resident mothers in NI. We found that NIMATS commonly records the use of vitamins, iron, and folic acid during early pregnancy. However, less than a fifth of women reported taking non-supplement medications in NIMATS. This compares to just under half of women with prescriptions for non-supplement medication in the EPD. Both the proportion of pregnancies with maternal self-report and dispensed prescriptions in early pregnancy are in keeping with that seen in early pregnancy in other countries [2, 15, 26, 30–33]. However, it is evident

that a greater range of medications are recorded in the EPD than NIMATS and that relying on NIMATS would underestimate the proportion of women exposed to non-supplement medications, assuming that the women took the dispensed medications.

The context of prescribing is essential when interpreting data. In NI, prescribed medications are free, and women may prefer to obtain medications that are available OTC by prescription, but this entails a GP visit. GPs may encourage pregnant women to take supplements by prescribing them. GPs may also prescribe medications for early pregnancy symptoms before women have their booking appointments. Our results show that more women buy vitamins and antacids than request prescriptions, suggesting that prescription records should not be relied upon solely to identify their use. A combination of maternal report and prescribing records would also be recommended to identify the use of folic acid. Agreement between maternal report and prescribing records for low-dose folic acid was no better than chance, with >80% of those with a prescription not reporting their low-dose folic acid use in NIMATS. A similar proportion of those reporting low-dose folic acid had no prescription recorded, suggesting they bought it OTC or inaccurate reporting as a result of social desirability bias. While about a quarter of women would be identified as having used low-dose folic acid based on NIMATS (22.5%) or EPD (27.0%) alone, combining them, 45.1% of women had either reported or prescribed or both reported and prescribed low-dose folic acid. If the dose of folic acid taken is important to a research study, prescribing records are vital to identify

Table 2: The proportion of 139,687 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	74.3	63.5	23.4	12.5	51.0	86.9
Only vitamins, iron and folic acid	56.1	14.8	45.0	3.8	11.1	59.9
Medication excluding vitamins, iron and folic acid	18.2	48.7	3.4	33.9	14.8	52.1
Available over the counter or by prescription^a						
Pregnancy-related						
Low dose folic acid (400 mcg)	22.5	27.0	18.2	22.6	4.3	45.1
Vitamins	20.4	1.4	19.7	0.8	0.6	21.2
Antiemetic	3.2	8.7	0.5	6.1	2.7	9.2
Antacid	1.2	0.1	1.2	0.1	0.0	1.2
Iron	0.9	1.8	0.7	1.6	0.3	2.5
Laxatives	0.2	3.9	0.1	3.8	0.1	3.9
Intermittent use						
Analgesics	1.3	6.9	0.7	6.3	0.6	7.6
Antihistamines	0.4	2.5	0.2	2.3	0.2	2.7
Antivirals^b	0.0	0.5	Redacted	Redacted	Redacted	Redacted
Available by prescription only						
Pregnancy-related						
High dose folic acid (5mg)	2.0	6.4	0.7	5.1	1.4	7.1
Chronic use/Pregnancy related						
Anticoagulant^c	1.4	1.8	0.4	0.8	1.0	2.2
Intermittent use						
Antibiotics	1.0	13.1	0.3	12.3	0.7	13.4
Tranquilisers^d	0.3	1.3	0.2	1.2	0.1	1.5
Sedatives	0.5	0.8	0.3	0.7	0.1	0.5
Chronic use						
Hormonal	1.3	6.9	0.4	5.9	1.0	7.2
Antidepressants	0.6	6.1	0.1	5.6	0.5	6.2
Steroids - all	0.1	4.8	0.0	4.7	0.1	4.8
Antiasthmatics	2.5	4.0	1.2	2.7	1.3	5.2
Cardiac	0.0	3.4	0.0	3.4	0.0	3.4
Thyroxine	0.5	2.1	0.1	1.7	0.4	2.2
Antiepileptic	0.1	0.9	0.0	0.8	0.1	0.9
Insulin	0.1	0.6	0.0	0.5	0.1	0.6
Antihypertensive	0.4	0.3	0.2	0.1	0.2	0.5
Immunosuppressants	0.1	0.1	0.0	0.1	0.0	0.1
Diuretics	Redacted	0.1	Redacted	Redacted	Redacted	Redacted
Other medications						
Other^d	9.6	21.6	6.4	18.3	3.3	27.9
Drug abuse^{d,e}	0.1	0.1	Redacted	Redacted	Redacted	Redacted

NIMATS= Northern Ireland Maternity System; EPD= Enhanced Prescribing Database.

^aSome 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.

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

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

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

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

Table 3: Cohen's kappa, strength of agreement, sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) for each medication category explored

Medication	Cohen's kappa (95% CI)	Strength of agreement	Sensitivity	Specificity	PPV	NPV
Any medication	0.17 (0.17-0.18)	Slight	80.3	36.0	68.6	51.2
Only vitamins, iron and folic acid	0.10 (0.10-0.10)	Slight	74.6	47.1	19.7	91.4
Medication excluding vitamins, iron and folic acid	0.24 (0.24-0.25)	Fair	30.4	93.4	81.3	56.8
Available over the counter or by prescription^a						
Pregnancy-related						
Low dose folic acid (400 mcg)	-0.09 (-0.10--0.09)	Chance	16.0	75.1	19.2	70.8
Vitamins	0.03 (0.03-0.04)	Slight	44.0	88.0	3.1	99.0
Antiemetic	0.42 (0.41-0.43)	Moderate	30.5	99.5	84.3	93.7
Antacid	0.02 (0.01-0.03)	Slight	13.7	98.8	1.0	99.9
Iron	0.19 (0.17-0.20)	Slight	14.8	99.3	29.6	98.4
Laxatives	0.05 (0.04-0.06)	Slight	2.9	99.9	68.0	96.2
Intermittent use						
Analgesics	0.13 (0.12-0.14)	Slight	8.7	99.3	47.2	93.6
Antihistamines	0.13 (0.12-0.15)	Slight	7.8	99.8	54.4	97.6
Available by prescription only						
Pregnancy-related						
High dose folic acid (5mg)	0.30 (0.29-0.31)	Fair	21.4	99.3	67.5	94.8
Chronic use/Pregnancy related						
Anticoagulant^b	0.62 (0.61-0.64)	Moderate	55.9	99.6	71.9	99.2
Intermittent use						
Antibiotics	0.09 (0.08-0.09)	Slight	5.6	99.6	69.5	87.5
Tranquilisers^c	0.13 (0.11-0.16)	Slight	8.3	99.8	40.3	99.1
Sedatives	0.18 (0.16-0.21)	Slight	14.6	99.7	26.4	99.3
Chronic use						
Hormonal	0.22 (0.21-0.23)	Fair	14.2	99.6	72.6	94.0
Antidepressants	0.14 (0.13-0.15)	Slight	8.4	99.9	86.6	94.3
Steroids - all	0.02 (0.02-0.03)	Slight	1.3	100	56.4	95.3
Antiasthmatics	0.38 (0.36-0.39)	Fair	32.0	98.8	51.9	97.2
Cardiac	0.02 (0.01-0.02)	Slight	0.8	100	77.6	96.6
Thyroxine	0.32 (0.30-0.34)	Fair	20.5	99.9	82.8	98.3
Antiepileptic	0.19 (0.16-0.22)	Slight	10.7	100	80.8	99.2
Insulin	0.27 (0.24-0.31)	Fair	16.4	100	87.1	99.5
Antihypertensive	0.56 (0.52-0.59)	Moderate	58.3	99.8	53.2	99.9
Immunosuppressants	0.25 (0.17-0.32)	Fair	18.4	100	38.4	99.9
Other medications						
Other^c	0.09 (0.08-0.09)	Slight	15.1	94.3	33.8	85.1

Note: It was not possible to calculate agreement between NIMATS and EPD for antivirals, diuretics and drug abuse due to small number restrictions.

NIMATS = Northern Ireland Maternity System; EPD = Enhanced Prescribing Database.

^aSome medication subtypes can be obtained either OTC or by prescription; others are classes that contain prescription-only medications and medications available OTC or by prescription.

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

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

high-dose folic (5 mg) acid use as this dose can only be obtained by prescription. There were more than three times as many pregnancies with prescribed high-dose folic acid as with

reported high-dose folic acid. These findings have important implications beyond the NI context, as maternal folic acid use is a crucial covariate [34] in medication safety research

in pregnancy, particularly in relation to the risk of congenital anomalies.

For all medications, except vitamins and antacids, prescribing records suggested more use than maternal reports. Self-report of prescribed medication was particularly low for laxatives, antivirals, antibiotics, antidepressants, steroids, and cardiac medications, with more than ten times as many prescriptions dispensed as reported in NIMATS. Some apparent underreporting in NIMATS for medications such as laxatives likely reflects their intermittent use, as women may not require them following their prescription. However, the underreporting of antiepileptic and cardiac medications, thyroxine, and insulin in NIMATS is surprising, given that agreement between reported and prescribed use of chronic medications is typically good [15, 16, 19–23]. There appears to be substantial underreporting of chronic medication use during pregnancy in antenatal records at booking in NI. While antenatal records may be updated in subsequent appointments, their incompleteness at booking needs investigation as it may impact care.

Some of the discordance between maternity data and prescription records may also reflect non-compliance. In medication utilisation or safety studies, non-compliance is typically less of an issue for dispensed prescriptions, as in the EPD, than for issued prescriptions [10]. However, pregnant women are a unique population, and women may discontinue their medications when they find out they are pregnant due to perceived risk [35]. In terms of the use of data for medication safety studies, very early pregnancy use before discontinuation is still relevant to risk.

Discontinuation of antidepressants may be contributing to the lower-than-expected [19, 21, 22] agreement between self-report and prescription records. It is estimated that 70%–80% of women discontinue their antidepressants during their pregnancy, [36–38] with antidepressant use typically returning to pre-pregnancy levels, or higher, after delivery [36, 39]. The decision to use antidepressants during pregnancy is complex. The risk of continuing antidepressants for the child must be weighed against the risks for both mother and child of untreated depression. Unfortunately, it is impossible to tell from the data whether medications were discontinued, and if so, if this decision was made in discussion with healthcare providers. There may also be an element of non-disclosure of mental illness due to perceived stigma, [40] which is of concern as it could lead to a lack of or delayed support.

Discontinuation in early pregnancy may also be contributing to the lack of agreement for hormonal medications such as contraceptives. About a quarter of women of reproductive age in NI use the combined oral contraceptive pill or the progesterone-only pill [41]. In trials, it has been estimated that there will be 2.59 pregnancies per 100 women-years [42] using these methods, but there may be as much as a 4–7% failure rate in the first 12 months of typical use [43, 44]. For some planned pregnancies, conception may have occurred immediately after cessation of contraceptives. Contraceptives may also be prescribed to treat polycystic ovary syndrome, and hormones may have been prescribed as part of fertility treatment. These would be discontinued as soon as the woman realised she was pregnant, and so would not be reported to midwives, but would still appear in the EPD record.

In contrast, prescriptions for chronic conditions such as asthma, which may be dispensed with a 90-day supply in the UK, may not be recorded in the EPD if a woman conceived after she redeemed her last prescription, particularly if she had her first antenatal visit before 12 weeks. The additional information in NIMATS is, therefore, useful in such situations. Increasing the time window used here, to include 30 or 90 days before the LMP may increase the agreement for chronically used medications with long dispensing windows and some intermittently used medications such as laxatives. It would however, decrease the agreement for intermittently used medications such as antibiotics. It is therefore important that in medication utilisation or safety studies in pregnancy, the time window used to identify medication use is tailored to the medication of interest.

As with most prescribing databases, the EPD does not record medications dispensed by hospital pharmacies. Inpatient stays would be expected to be rare before booking, and administration of medication while in hospital has been shown to detrimentally impact the ability of mothers to know and recall medication use [22]. However, women may attend early pregnancy clinics, emergency departments or dentists and be discharged home with medications. These would then be reported to midwives, and recorded in NIMATS, but not recorded in the EPD. This may explain some of the reported pregnancy-related or intermittently used medications not present in the EPD, such as antibiotics or antiemetics. In Canada and Europe, antibiotics are the most prescribed medication in pregnancy, with first-trimester prescriptions ranging from 9.7%–12.0% [2, 18, 23] in keeping with what is seen in NI. Indeed, in Australia, Havard et al. (2021) found that antibiotics are used disproportionately more among pregnant women relative to women of childbearing age [45]. As antibiotics are intermittently and briefly used, agreement between reported and prescribed antibiotic use is typically poor to moderate [15, 16, 18, 19, 21, 22, 46] as seen here.

The potential to combine NIMATS and EPD data to examine the use of medications in pregnancy is limited by the categories available in NIMATS to record medication use. To be useful for medication utilisation or safety studies, maternity data should collect information on medicines at the individual drug level and record whether women continued or discontinued their medication upon finding out they were pregnant. The potential for under-reporting of medication use also needs to be considered. There is an option for midwives to record textual information relating to medications, such as medication name or dose. These variables have not been made available for research in NI due to concerns that individuals could be identified from textual data. If they could be made available, approaches such as text-mining could be used to extract additional information from maternal reports of medication use [47], vastly increasing the potential utility of NIMATS for medication utilisation or safety studies.

Strengths and limitations

A major strength of the present study is the use of a population-based cohort comprising all pregnancies to NI resident mothers during the study period. There was no prescription charge in NI during the study period, meaning

that all women should have equal ability to access medications prescribed to them.

A limitation of the study is that in addition to being restricted to dispensed GP prescriptions, the EPD also underestimates medication use due to problems matching dispensed prescriptions to a patient's unique HCN. The data provider estimated that this affected 13.8% of prescriptions to the NI population, not just to pregnant women, during the 2010-2016 study period i.e. this proportion is not specific to pregnant women, but applies to all men, women and children. The issue with unmatched records was completely random and occurred when the scanners, used to process prescription charges, failed to pick up the patient's HCN from the paper prescription [48]. It has the potential to affect agreement in early pregnancy for intermittently used medications more than chronically used medications with frequent prescriptions. While randomly missing prescriptions would not affect sensitivity, they would lead to an underestimation of specificity and PPV and an overestimation of NPV.

The information in NIMATS was prospectively recorded in early pregnancy, so the risk of recall bias is limited. However, how a woman is asked about her medication use will impact the information she provides. It has been shown that the more detailed information a questionnaire asks for, the better it will compare with records of dispensed drugs [49]. This would suggest that if a midwife asks a woman if she is on any medications, the midwife will get much less information than if they specifically ask about each medication recorded in NIMATS. Understanding how healthcare professionals phrase questions to women regarding medication usage and record data is essential to improving medical records and their usefulness in patient care and research. This could, in turn, lead to improvements in patient care, and the quality of data for service evaluation and research [50].

Conclusion

Medication use during early pregnancy was common in NI, with 86.9% of women reporting medication use or having a prescription dispensed. Maternal reports indicated that women buy, rather than request, prescriptions for vitamins and antacids. For non-supplement medications, there were more dispensed prescriptions than maternal reports. While some women may be non-compliant or discontinue their medications during pregnancy, the reporting of prescribed medications to midwives for chronic illnesses was very incomplete, even for medications for chronic illnesses that may impact care. A combination of maternal report and prescribing data is recommended to identify all medication use in drug safety studies, particularly for folic acid.

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those of the author and do not necessarily represent those of the BSO.

Statement on conflicts of interest

None declared.

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Ethics statement

This study was approved by the Ulster University Nursing and Health Research Ethics Filter Committee, the Health Research Authority (reference: 17/NS/0047), and the Honest Broker Governance Board (HBS Reference 21). As the Honest Broker Service provided only anonymised data, individual consent was not required.

Data availability statement

All relevant data are within the paper and its supporting information files. The raw data is available to accredited researchers upon application to the Honest Broker Service: <https://bsc.hscni.net/directorates/digital/honest-broker-service/>.

Author contributions

ML and HD conceptualised the study and obtained funding. ML obtained ethical approval, developed the methodology, and supervised the work. JG was responsible for formal analysis and produced the first draft. All authors reviewed and edited draft manuscripts, aided in interpreting the results, and approved the submitted article.

References

1. Daw JR, Hanley GE, Greyson DL, Morgan SG. Prescription drug use during pregnancy in developed countries: a systematic review. *Pharmacoepidemiol Drug Saf* 2011;20:895–902. <https://doi.org/10.1002/pds.2184>
2. Smolina K, Hanley GE, Mintzes B, Oberlander TF, Morgan S. Trends and Determinants of Prescription Drug Use during Pregnancy and Postpartum in British Columbia, 2002–2011: A Population-Based Cohort Study. *PLoS One* 2015;10:e0128312. <https://doi.org/10.1371/journal.pone.0128312>

3. Bjørn, Norgaard, Hundborg H, Nohr, Ehrenstein V. Use of prescribed drugs among primiparous women: an 11-year population-based study in Denmark. *Clin Epidemiol* 2011;3:149. <https://doi.org/10.2147/CLEP.S17747>
4. Mazer-Amirshahi M, Samiee-Zafarghandy S, Gray G, Van Den Anker JN. Trends in pregnancy labeling and data quality for US-approved pharmaceuticals. *Am J Obstet Gynecol* 2014;211:690.e1-690.e11. <https://doi.org/10.1016/j.ajog.2014.06.013>
5. Sharrar RG, Dieck GS. Monitoring product safety in the postmarketing environment. *Ther Adv Drug Saf* 2013;4:211–9. <https://doi.org/10.1177/2042098613490780>
6. Charlton RA, Neville AJ, Jordan S, Pierini A, Damase-Michel C, Klungsøyr K, et al. Healthcare databases in Europe for studying medicine use and safety during pregnancy. *Pharmacoepidemiol Drug Saf* 2014;23:586–94. <https://doi.org/10.1002/pds.3613>
7. Colvin L, Slack-Smith L, Stanley FJ, Bower C. Linking a pharmaceutical claims database with a birth defects registry to investigate birth defect rates of suspected teratogens. *Pharmacoepidemiol Drug Saf* 2010;19:1137–50. <https://doi.org/10.1002/pds.1995>
8. Gelperin K, Hammad H, Leishear K, Bird ST, Taylor L, Hampf C, et al. A systematic review of pregnancy exposure registries: examination of protocol-specified pregnancy outcomes, target sample size, and comparator selection. *Pharmacoepidemiol Drug Saf* 2017;26:208–14. <https://doi.org/10.1002/pds.4150>
9. Tamblyn R, Egale T, Huang A, Winslade N, Doran P. The Incidence and Determinants of Primary Nonadherence With Prescribed Medication in Primary Care. *Ann Intern Med* 2014;160:441. <https://doi.org/10.7326/M13-1705>
10. Eriksson I, Ibáñez L. Secondary data sources for drug utilization research. In: Elseviers M, Wettermark B, Almarsdottir AB, Andersen M, Benko R, Bennie M, et al., editors. *Drug Utilization Research*. First Edit, Chichester, UK: John Wiley & Sons, Ltd; 2016, p. 39–48. <https://doi.org/10.1002/9781118949740.ch4>
11. Schneeweiss S, Avorn J. A review of uses of health care utilization databases for epidemiologic research on therapeutics. *J Clin Epidemiol* 2005;58:323–37. <https://doi.org/10.1016/j.jclinepi.2004.10.012>
12. Fraser FC. Recall bias in case control studies of malformed infants. *Teratology* 2000;62:371–371. [https://doi.org/10.1002/1096-9926\(200012\)62:6<371::AID-TERA1>3.0.CO;2-H](https://doi.org/10.1002/1096-9926(200012)62:6<371::AID-TERA1>3.0.CO;2-H)
13. van de Mortel TF. Faking It: Social Desirability Response Bias in Self-report Research. *The Australian Journal of Advanced Nursing* 2008;25:40–8.
14. Mitchell AA, Cottler LB, Shapiro S. Effect of questionnaire design on recall of drug exposure in pregnancy. *Am J Epidemiol* 1986;123:670–6. <https://doi.org/10.1093/oxfordjournals.aje.a114286>
15. Pisa FE, Casetta A, Clagnan E, Michelesio E, Vecchi Brumatti L, Barbone F. Medication use during pregnancy, gestational age and date of delivery: Agreement between maternal self-reports and health database information in a cohort. *BMC Pregnancy Childbirth* 2015;15:1–14. <https://doi.org/10.1186/s12884-015-0745-3>
16. Sarangarm P, Young B, Rayburn W, Jaiswal P, Dodd M, Phelan S, et al. Agreement between self-report and prescription data in medical records for pregnant women. *Birth Defects Res A Clin Mol Teratol* 2012;94:153–61. <https://doi.org/10.1002/bdra.22888>
17. Nielsen MW, Søndergaard B, Kjølner M, Hansen EH. Agreement between self-reported data on medicine use and prescription records vary according to method of analysis and therapeutic group. *J Clin Epidemiol* 2008;61:919–24. <https://doi.org/10.1016/j.jclinepi.2007.10.021>
18. Van Gelder MMHJ, Van Rooij IALM, De Walle HEK, Roeleveld N, Bakker MK. Maternal recall of prescription medication use during pregnancy using a paper-based questionnaire: A validation study in the Netherlands. *Drug Saf* 2013;36:43–54. <https://doi.org/10.1007/s40264-012-0004-8>
19. Olesen C, Søndergaard C, Thrane N, Lauge Nielsen G, De Jong-Van Den Berg L, Olsen J. Do pregnant women report use of dispensed medications? *Epidemiology* 2001;12:497–501. <https://doi.org/10.1097/00001648-200109000-00006>
20. Palmsten K, Hulugalle A, Bandoli G, Kuo GM, Ansari S, Xu R, et al. Agreement Between Maternal Report and Medical Records During Pregnancy: Medications for Rheumatoid Arthritis and Asthma. *Paediatr Perinat Epidemiol* 2018;32:68–77. <https://doi.org/10.1111/ppe.12415>
21. Cheung K, El Marroun H, Elfrink ME, Jaddoe VWV, Visser LE, Stricker BHC. The concordance between self-reported medication use and pharmacy records in pregnant women. *Pharmacoepidemiol Drug Saf* 2017;26:1119–25. <https://doi.org/10.1002/pds.4264>
22. Howley MM, Fisher SC, Fuentes MA, Werler MM, Tracy M, Browne ML. Agreement between maternal report and medical records on use of medications during early pregnancy in New York. *Birth Defects Res* 2023;498–509. <https://doi.org/10.1002/bdr2.2151>
23. Stephansson O, Granath F, Svensson T, Haglund B, Ekblom A, Kieler H. Drug use during pregnancy in Sweden - Assessed by the prescribed drug register and the medical birth register. *Clin Epidemiol* 2011;3:43–50. <https://doi.org/10.2147/CLEP.S16305>

24. Given J, Casson K, Dolk H, Loane M. Sociodemographic variation in prescriptions dispensed in early pregnancy in Northern Ireland 2010–2016. *PLoS One* 2022;17:1–15. <https://doi.org/10.1371/journal.pone.0267710>
25. Black L-A. Prescriptions: Costs and charges in the UK and Republic of Ireland. Belfast: 2014.
26. Bakker MK, Jentink J, Vroom F, Van Den Berg PB, De Walle HEK, De Jong-Van Den Berg LTW. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006;113:559–68. <https://doi.org/10.1111/j.1471-0528.2006.00927.x>
27. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 1960;20:37–46. <https://doi.org/10.1177/001316446002000104>
28. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
29. StataCorp. Stata Statistical Software: Release 16 2019.
30. Mitchell AA, Gilboa SM, Werler MM, Kelley KE, Louik C, Hernández-Díaz S. Medication use during pregnancy, with particular focus on prescription drugs: 1976–2008. *Am J Obstet Gynecol* 2011;205:51.e1–51.e8. <https://doi.org/10.1016/j.ajog.2011.02.029>
31. Cleary BJ, Butt H, Strawbridge JD, Gallagher PJ, Fahey T, Murphy DJ. Medication use in early pregnancy-prevalence and determinants of use in a prospective cohort of women. *Pharmacoepidemiol Drug Saf* 2010;19:408–17. <https://doi.org/10.1002/pds.1906>
32. Axelsdottir TO, Sigurdsson EL, Gudmundsdottir AM, Kristjansdottir H, Sigurdsson JA. Drug use during early pregnancy: Cross-sectional analysis from the childbirth and health study in primary care in Iceland. *Scand J Prim Health Care* 2014;32:139–45. <https://doi.org/10.3109/02813432.2014.965884>
33. Espnes MG, Bjørge T, Engeland A. Comparison of recorded medication use in the Medical Birth Registry of Norway with prescribed medicines registered in the Norwegian Prescription Database. *Pharmacoepidemiol Drug Saf* 2011;20:243–8. <https://doi.org/10.1002/pds.2085>
34. Damase-Michel C, Wurst KE, Beau A-B, Bromley R, Cooney M, Coste F, et al. Core evidence elements for generating medication safety evidence for pregnancy using population-based data: Core data elements, design and analytical foundations 2020:1–112.
35. Mulder B, Bijlsma M, Schuiling-Veninga C, Morssink L, van Puijenbroek E, Aarnoudse J, et al. Risks versus benefits of medication use during pregnancy: what do women perceive? *Patient Prefer Adherence* 2017;Volume 12:1–8. <https://doi.org/10.2147/PPA.S146091>
36. Margulis A V., Kang EM, Hammad TA. Patterns of Prescription of Antidepressants and Antipsychotics Across and Within Pregnancies in a Population-Based UK Cohort. *Matern Child Health J* 2014;18:1742–52. <https://doi.org/10.1007/s10995-013-1419-2>
37. Ververs T, Kaasenbrood H, Visser G, Schobben F, De Jong-Van Den Berg L, Egberts T. Prevalence and patterns of antidepressant drug use during pregnancy. *Eur J Clin Pharmacol* 2006;62:863–70. <https://doi.org/10.1007/s00228-006-0177-0>
38. Bénard-Larivière A, Pambrun E, Sutter-Dallay AL, Gautier S, Hurault-Delarue C, Damase-Michel C, et al. Patterns of antidepressant use during pregnancy: a nationwide population-based cohort study. *Br J Clin Pharmacol* 2018;84:1764–75. <https://doi.org/10.1111/bcp.13608>
39. Charlton RA, Jordan S, Pierini A, Garne E, Neville AJ, Hansen A V., et al. Selective serotonin reuptake inhibitor prescribing before, during and after pregnancy: A population-based study in six European regions. *BJOG* 2015;122:1010–20. <https://doi.org/10.1111/1471-0528.13143>
40. Smith MS, Lawrence V, Sadler E, Easter A. Barriers to accessing mental health services for women with perinatal mental illness: Systematic review and meta-synthesis of qualitative studies in the UK. *BMJ Open* 2019;9:1–9. <https://doi.org/10.1136/bmjopen-2018-024803>
41. Given JE, Gray A-M, Dolk H. Use of prescribed contraception in Northern Ireland 2010–2016. *The European Journal of Contraception & Reproductive Health Care* 2020;25:106–13. <https://doi.org/10.1080/13625187.2020.1723539>
42. Mansour D, Inki P, Gemzell-Danielsson K. Efficacy of contraceptive methods: A review of the literature. *European Journal of Contraception and Reproductive Health Care* 2010;15:4–16. <https://doi.org/10.3109/13625180903427675>
43. Sundaram A, Vaughan B, Kost K, Bankole A, Finer L, Singh S, et al. Contraceptive Failure in the United States: Estimates from the 2006–2010 National Survey of Family Growth. *Perspect Sex Reprod Health* 2017;49:7–16. <https://doi.org/10.1363/psrh.12017>
44. Bradley SEK, Polis CB, Bankole A, Croft T. Global Contraceptive Failure Rates: Who Is Most at Risk? *Stud Fam Plann* 2019;50:3–24. <https://doi.org/10.1111/sifp.12085>
45. Havard A, Barbieri S, Hanly M, Perez-Concha O, Tran DT, Kennedy D, et al. Medications used disproportionately during pregnancy: Priorities for research on the risks and benefits of medications when used during pregnancy. *Pharmacoepidemiol Drug Saf* 2021;30:53–64. <https://doi.org/10.1002/pds.5131>
46. de Jonge L, Garne E, Gini R, Jordan SE, Klungsoyr K, Loane M, et al. Improving Information on Maternal

- Medication Use by Linking Prescription Data to Congenital Anomaly Registers: A EUROmediCAT Study. *Drug Saf* 2015;38:1083–93. <https://doi.org/10.1007/s40264-015-0321-9>
47. McTaggart S, Nangle C, Caldwell J, Alvarez-Madrado S, Colhoun H, Bennie M. Use of text-mining methods to improve efficiency in the calculation of drug exposure to support pharmacoepidemiology studies. *Int J Epidemiol* 2018;47:617–24. <https://doi.org/10.1093/IJE/DYX264>
48. McDowell B. Family Practitioner Services Background Quality Report General Pharmaceutical Services Statistics Contents. Belfast: 2024.
49. Gama H, Correia S, Lunet N. Questionnaire design and the recall of pharmacological treatments: a systematic review. *Pharmacoepidemiol Drug Saf* 2009;18:175–87. <https://doi.org/10.1002/pds.1703>
50. McGuckin T, Crick K, Myroniuk TW, Setchell B, Yeung RO, Campbell-Scherer D. Understanding challenges of using routinely collected health data to address clinical care gaps: a case study in Alberta, Canada. *BMJ Open Qual* 2022;11:e001491. <https://doi.org/10.1136/bmjopen-2021-001491>

