Dispensed drugs during pregnancy in outpatient care between 2015 and 2021 in Switzerland: a retrospective analysis of Swiss healthcare claims data

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Summary

AIM OF THE STUDY: We aimed to evaluate the utilisation of all prescribed drugs during pregnancy dispensed in outpatient care in Switzerland between 2015 and 2021.

METHODS: We conducted a descriptive study using the Swiss Helsana claims database (2015-2021). We established a cohort of pregnancies by identifying deliveries and estimating the date of the last menstrual period. We analysed the drug burden during a 270-day pre-pregnancy period, during pregnancy (overall and by trimester), and during a 270-day postpartum period. Subsequently, we quantified 1) the median number of drug dispensations (total vs. unique drug claims); and 2) the prevalence of exposure to at least one dispensed drug and the number of dispensed drugs (0, 1, 2, 3, 4, and ≥5); and 3) the 15 most frequently dispensed drugs were identified during each period, overall and stratified by maternal age.

RESULTS: Among 34,584 pregnant women (5.6% of all successful pregnancies in Switzerland), 87.5% claimed at least one drug (not including vitamins, supplements, and vaccines), and 33.3% claimed at least five drugs during pregnancy. During trimester 1 alone, 8.2% of women claimed at least five distinct drugs. The proportion of women who claimed prescribed drugs was lower pre-pregnancy (69.1%) and similar postpartum (85.6%) when compared to during pregnancy (87.5%). The most frequently claimed drugs during pregnancy were meaningfully different during pregnancy than before and after.

CONCLUSIONS: This study suggests that 8 of 10 women in Switzerland are exposed to prescribed drugs during pregnancy. Most drugs dispensed during pregnancy are comparatively well investigated and are considered safe. However, the high drug burden in this vulnerable patient population underlines the importance of evidence on the benefit-risk profile of individual drugs taken during pregnancy.

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Introduction

Many women require drug treatment during pregnancy to treat pre-existing or incident diseases, or obstetric complications. However, the safety of many drugs during pregnancy is not well understood [1–3] because pregnant women are excluded from most randomized controlled trials (RCTs). Despite this limitation, post-marketing studies allow possible teratogenicity to be evaluated for drugs that have been on the market for a long time. However, for new or rarely used drugs, evidence of *in utero* safety is insufficient or absent. In these situations, clinicians need to weigh benefits and risks to the pregnant woman and the unborn child based on insufficient evidence. In Switzerland, the use of prescribed drugs during pregnancy is not well understood, partly due to the fragmented health data landscape and the underdeveloped digitalization in the healthcare sector. It is important to understand which drugs are used during pregnancy in clinical practice to understand the medical needs and potential unknown risks to this vulnerable patient population. In a multinational web-based survey [4], 81% of pregnant women reported taking at least one drug during pregnancy, whether prescribed or over the counter (OTC), between 2011 and 2012. Of the 618 Swiss women who took part in the survey, 83% took at least one drug during pregnancy (excluding iron, mineral supplements, vitamins, herbal remedies, and any type of complementary medicine). However, this data is over a decade old and may be affected by volunteer bias. Three studies based on the Helsana claims database (2014–2018) quantified disease-specific utilisation of drugs to treat selected acute or chronic conditions during pregnancy [5–7], but did not evaluate the overall drug burden during pregnancy in Switzerland.

In this retrospective descriptive study based on the Swiss Helsana claims database, we evaluated the utilisation of all prescribed drugs dispensed during pregnancy in outpatient care in Switzerland between 2015 and 2021.

Methods

Study design and data source

We conducted a retrospective study using the anonymized Helsana claims database for the years 2015–2021. The Helsana group is one of Switzerland's leading health insurance companies, covering around 1.2 million individuals with mandatory health insurance from all 26 cantons (approximately 15% of the Swiss population). The database captures demographics, outpatient healthcare services, outpatient drug dispensations, as well as bundled diagnostic codes for hospitalizations (SwissDRG, Swiss Diagnoses Related Groups). For dispensation of prescription drugs, the corresponding codes of the Anatomical Therapeutic Chemical (ATC) classification system are recorded.
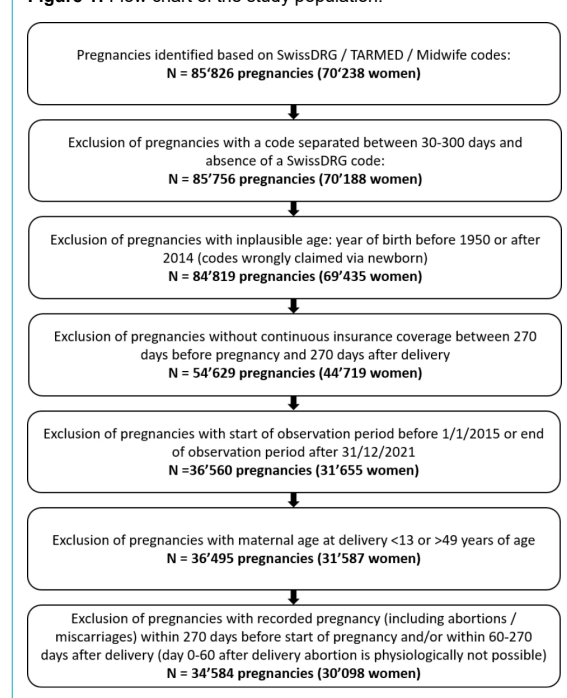
This retrospective observational study using anonymous data did not require an ethics committee approval.

Patient consent was waived due to use of anonymous data.

Study population

Our study population included pregnant women between 13 and 49 years of age at delivery between 2015 and 2021. All women were (1) continuously insured with Helsana's mandatory health insurance during the entire observation period (270 days before the start of pregnancy until 270 days after the delivery date), and (2) not pregnant during the pre-pregnancy or postpartum period (determined by recorded codes for delivery or abortion, reported in table S1 in the appendix). A woman may have contributed more than one pregnancy to the study population. A flow chart of cohort enrolment is shown in figure 1.

Figure 1: Flow chart of the study population.

Pregnancies identified based on SwissDRG / TARMED / Midwife codes:
N = 85'826 pregnancies (70'238 women)

Exclusion of pregnancies with a code separated between 30-300 days and absence of a SwissDRG code:
N = 85'756 pregnancies (70'188 women)

Exclusion of pregnancies with inplausible age: year of birth before 1950 or after 2014 (codes wrongly claimed via newborn)
N = 84'819 pregnancies (69'435 women)

Exclusion of pregnancies without continuous insurance coverage between 270 days before pregnancy and 270 days after delivery
N = 54'629 pregnancies (44'719 women)

Exclusion of pregnancies with start of observation period before 1/1/2015 or end of observation period after 31/12/2021
N =36'560 pregnancies (31'655 women)

Exclusion of pregnancies with maternal age at delivery <13 or >49 years of age
N = 36'495 pregnancies (31'587 women)

Exclusion of pregnancies with recorded pregnancy (including abortions / miscarriages) within 270 days before start of pregnancy and/or within 60-270 days after delivery (day 0-60 after delivery abortion is physiologically not possible)
N = 34'584 pregnancies (30'098 women)

Identification of pregnancies and definition of the delivery date

We identified inpatient and outpatient deliveries, and both live and stillbirths, covered by mandatory health insurance in the Helsana claims database between 01/01/2015 and 31/12/2021. Inpatient deliveries were captured by recorded SwissDRG codes, and outpatient deliveries by recorded TARMED codes (billing system for outpatient services in Switzerland) or billed deliveries by midwifes (table S1 in the appendix). In case there were multiple delivery codes recorded within a period of 30 days, these were regarded as pertaining to the same pregnancy [8], and the first recorded code was set as the date of delivery. Delivery codes separated by more than 300 days were considered as two separate pregnancies. When two successive codes were separated by between 30 and 300 days, the delivery date was set as the inpatient SwissDRG code, and were excluded if only outpatient codes were recorded [5–7]. Deliveries of twins were treated as one single pregnancy. A flow chart showing the number of excluded pregnancies is displayed in figure 1.

Identification of the date of the last menstrual period and pregnancy trimesters

We estimated the date of the last menstrual period (i.e., start of pregnancy) because gestational length or start of pregnancy were not recorded in Swiss healthcare claims data during the study period. According to an algorithm validated in US claims data [9], the date of the last menstrual period was assigned to be 245 days before the date of delivery for pregnancies with a SwissDRG code indicating preterm delivery (<37 weeks, O01A, O01B, O01C, O01D, or O60A), and 270 days before the date of delivery for all other pregnancies. This algorithm has been used in previous studies evaluating pregnancies in the Helsana claims database [5–7].

Observation period and time windows

We observed each pregnancy from 270 days before the last menstrual period (start of observation period) until 270 days after the delivery date (end of observation period). The observation period was divided into the following periods: a) pre-pregnancy period (270-day period before last menstrual period), b) pregnancy, and c) postpartum period (270-day period after the delivery date). Pregnancy was divided into trimesters of 90 days, and trimester 3 was shortened in case of a preterm delivery.

Covariates and drug exposure

We captured maternal age at delivery. We identified reimbursed dispensing of any drugs based on recorded ATC codes [10]. Analysis omitted ATC codes not representing pharmacological treatment (e.g., prophylactic agents, surgical aids, or diagnostic agents; see full list with ATC codes in table S2 in the appendix). Due to the data structure of Swiss electronic claims data, we were not able to identify the indications for individual drugs.

Statistical analysis

Median (SD) number of drug dispensations

We quantified the median (interquartile range, IQR) total number of drug dispensations (and the median (IQR) number of distinct drug dispensations separately) during the pre-pregnancy period, during pregnancy (overall and by trimester), and during the postpartum period. Analyses were conducted overall and within maternal age strata (<26, 26–35, and ≥36 years at delivery). We quantified the results with and without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines (ATC codes in appendix: table S2), as most women are exposed to those drugs during pregnancy.

Prevalence of exposure to at least one dispensed drug and number of dispensed drugs (0, 1, 2, 3, 4, and ≥5)

We quantified (a) the proportion of pregnancies exposed to at least one dispensed drug (prevalence of exposure), and (b) the cumulative number of distinct dispensed drugs (0, 1, 2, 3, 4, and ≥5) per pregnancy during each period and within maternal age strata. Prevalence of exposure was quantified both with and without the dispensing of vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines. For all other analyses, we did not consider those treatments.

Prevalence of exposure to the 15 most frequently dispensed drugs

We identified the 15 most frequently dispensed drugs (ATC 7 digits), quantified as the absolute number of exposed pregnancies divided by the total number of enrolled pregnancies, during the pre-pregnancy period, during pregnancy (overall, by trimester, and by maternal age strata), and during the postpartum period.

For all results, weighted numbers are shown in the appendix. Weighted results account for the demographic distribution of the population with mandatory insurance with Helsana relative to the Swiss population [5–7]. Weighting factors included calendar year, canton, age, and sex. All analyses were conducted using *Python 3.11.0* [11].

Results

Demographics

The dataset included 34,584 pregnancies of 30,098 women (figure 1) with a median maternal age at delivery of 32 years (IQR = 29–36), 10.2% aged <26 years, 62.4% aged between 26–35 years, and 27.4% aged ≥36 years at delivery.

Median (IQR) number of drug dispensations

The median number of claimed drug dispensations during pregnancy was 8 (IQR = 5–13) and 6 (IQR = 3–8) in the case of distinct drugs. After excluding vitamins, supplements, and vaccines, these numbers decreased to 4 (IQR = 2–8) and 3 (IQR = 1–5). The median number of dispensed drugs (not including vitamins, supplements, and vaccines) during pregnancy (table 1) was highest among women aged <26 years at delivery (5, IQR = 2–9; distinct drug dispensations median = 4, IQR = 2–6) and similar for women aged 26–35 (median = 4, IQR = 1–8; distinct drug dispensations median = 3, IQR = 1–5) and for women aged ≥36 (median = 4, IQR = 2–9; distinct drug dispensations median = 3, IQR = 1–6).

Prevalence of exposure to at least one dispensed drug

Figure 2 shows the prevalence of exposure to at least one dispensed drug by period and within maternal age strata, with and without considering vitamins, supplements, and vaccines. During pregnancy, 87.5% of women claimed at least one drug (97.8% when including vitamins, supplements, and vaccines), with increasing proportions over the course of pregnancy (66.7% in trimester 3 vs. 59.2% and 58.6% in trimesters 1 and 2, respectively). Compared to older women, women aged <26 years more frequently claimed at least one drug during pregnancy (91.4% vs. 86.9% in 26–35 and 87.5% in ≥36 years).

Table 1:
Median (IQR) number of drug dispensations by period and within maternal age strata.

Age at delivery (years)	N pregnancies	Pre-pregnancy period		Pregnancy		Trimester 1		Trimester 2		Trimester 3		Postpartum	
		Median (IQR) number of drug claims	Median (IQR) number of distinct drug claims*	Median (IQR) number of drug claims	Median (IQR) number of distinct drug claims*	Median (IQR) number of drug claims	Median (IQR) number of distinct drug claims*	Median (IQR) number of drug claims	Median (IQR) number of distinct drug claims*	Median (IQR) number of drug claims	Median (IQR) number of distinct drug claims*	Median (IQR) number of drug claims	Median (IQR) number of distinct drug claims*
All drug dispensations													
Total	34584	3 (0–8)	3 (0–6)	8 (5–13)	6 (3–8)	2 (1–4)	2 (1–3)	2 (1–4)	2 (1–4)	3 (1–5)	2 (1–4)	5 (2–8)	4 (2–7)
<26	3513	4 (1–9)	3 (1–7)	9 (5–13)	6 (4–9)	2 (1–4)	2 (1–4)	3 (1–5)	2 (1–4)	3 (1–5)	2 (1–4)	5 (2–9)	4 (2–7)
26–35	21592	3 (0–7)	2 (0–6)	8 (4–13)	5 (3–8)	2 (0–4)	2 (0–3)	2 (1–4)	2 (1–4)	3 (1–5)	2 (1–4)	4 (2–8)	4 (2–6)
≥36	9479	3 (1–8)	3 (1–6)	9 (5–14)	6 (3–8)	2 (0–4)	2 (0–3)	2 (1–5)	2 (1–4)	3 (2–6)	3 (1–4)	5 (2–9)	4 (2–7)
Without vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines													
Total	34584	2 (0–7)	2 (0–5)	4 (2–8)	3 (1–5)	0 (1–3)	1 (0–2)	0 (1–2)	1 (0–2)	0 (1–3)	1 (0–2)	4 (2–7)	3 (2–5)
<26	3513	3 (0–8)	3 (0–6)	5 (2–9)	4 (2–6)	1 (0–3)	1 (0–3)	1 (0–3)	1 (0–3)	1 (0–3)	1 (0–3)	4 (2–8)	3 (2–6)
26–35	21592	2 (0–6)	2 (0–5)	4 (1–8)	3 (1–5)	1 (0–3)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–3)	1 (0–2)	3 (2–7)	3 (2–5)
≥36	9479	3 (0–7)	2 (0–5)	4 (2–9)	3 (1–6)	1 (0–3)	1 (0–2)	1 (0–3)	1 (0–2)	1 (0–3)	1 (0–3)	4 (2–7)	3 (2–5)

IQR: interquartile range.

* Number of distinct drugs (distinct ATC-7 level) claimed during the indicated period, overall and within age strata.

During the pre-pregnancy period, less women (69.1%) claimed at least one drug, whereas during the postpartum period, drug exposure was similar to that during pregnancy (85.6% and 87.5%, respectively). Further numerical data is given in figure 2 and table S3 in the appendix.

Number of dispensed drugs

Overall, 71.9% of pregnant women claimed two or more distinct drugs during pregnancy (table 2). This is 15.8% more than during the pre-pregnancy period (56.1%), and 4.4% less than during the postpartum period (76.3%). In total, 33.3% of pregnant women claimed at least five distinct drugs during pregnancy (vs. 28.5% before pregnancy and 32.6% after pregnancy), of whom 8.2% claimed at least five distinct drugs during trimester 1 alone (vs. 6.8% and 7.8% in trimesters 2 and 3, respectively).

Figure 3 shows the prevalence of exposure to 0, 1, 2, 3, 4, and ≥5 distinct drugs within maternal age strata. Pregnant women <26 years most frequently claimed at least two drugs (79.3%) followed by women ≥36 years (72.4%) and those between 26–35 years (70.5%). The same pattern was observed for exposure to at least five drugs (<26: 41.2%, 26–35: 31.6%, and ≥36: 34.2%).

Prevalence of exposure to the 15 most frequently dispensed drugs

Paracetamol was dispensed to the largest proportion of women during pregnancy (29.8% vs. 22.0% before pregnancy and 63.3% after pregnancy, table 3).

In trimester 1, after paracetamol, metoclopramide (12.7%) was the second most prevalent prescription followed by progesterone (10.9%), topical dequalinium (vaginal antiseptic, 6.6%), levothyroxine (5.5%), ibuprofen (3.8%), amoxicillin (3.7%), low-dose acetylsalicylic acid (ASA, 3.3%), pantoprazole (3.1%), estriol (2.7%), fosfomycin (2.6%), ordinary salt combinations (antacids, 2.2%), clotrimazole (1.6%), and oestradiol (1.6%).

Dequalinium, levothyroxine, amoxicillin, pantoprazole, fosfomycin, and ordinary salt combinations (antacids) were also among the 15 most frequently claimed drugs during trimesters 2 and 3. In trimesters 2 and 3, anti-D (rh) immunoglobulin was also among the 15 most frequently dispensed drugs (3.5% and 8.2% of pregnancies, respectively). In trimester 3, proton pump inhibitors and H2 blockers (omeprazole 3.4%, ranitidine 3.3%, esomeprazole 3.0%), nifedipine (3.2%), and insulin detemir (2.5%) were also among the 15 most frequently dispensed drugs.

Figure 2: Prevalence of exposure to at least one dispensed drug during the pre-pregnancy, pregnancy (overall and by trimester), and postpartum periods, overall and within maternal age strata, with and without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines. See table S3 in the appendix for exact values and for weighted results.
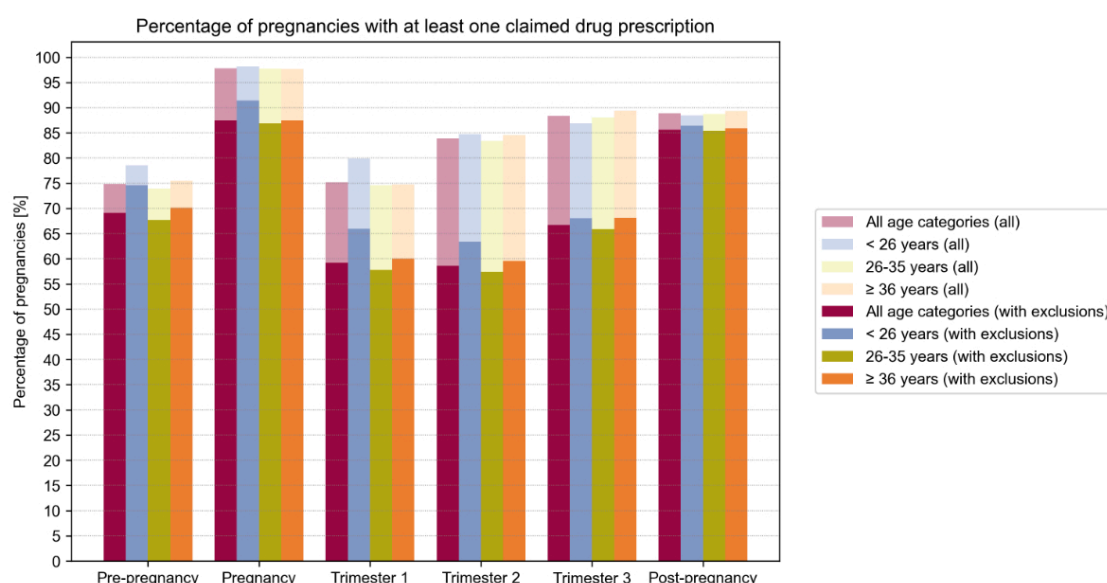
Table 2:

Prevalence of exposure to 0, 1, 2, 3, 4, and ≥5 drug dispensations during pre-pregnancy, pregnancy (overall and by trimester), and postpartum periods without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines. See table S4 in the appendix for weighted results.

Number of distinct drug claims*	Pre-pregnancy period N pregnancies (%)	Pregnancy N pregnancies (%)	Trimester 1 N pregnancies (%)	Trimester 2 N pregnancies (%)	Trimester 3 N pregnancies (%)	Postpartum N pregnancies (%)
0	10695 (30.9)	4324 (12.5)	14101 (40.8)	14306 (41.4)	11509 (33.3)	4968 (14.4)
1	4501 (13.0)	5395 (15.6)	7738 (22.4)	8362 (24.2)	8910 (25.8)	3224 (9.3)
2	3707 (10.7)	5127 (14.8)	4912 (14.2)	4898 (14.2)	5765 (16.7)	5943 (17.2)
3	3187 (9.2)	4535 (13.1)	3157 (9.1)	2918 (8.4)	3666 (10.6)	5134 (14.8)
4	2632 (7.6)	3702 (10.7)	1828 (5.3)	1739 (5.0)	2034 (5.9)	4032 (11.7)
≥5	9862 (28.5)	11501 (33.3)	2848 (8.2)	2361 (6.8)	2700 (7.8)	11283 (32.6)

ATC: Anatomical Therapeutic Chemical.

* ATC-7 level.

During the postpartum period, non-opioid analgesics were the predominantly claimed drugs, with paracetamol (63.3%) being the most prevalent followed by ibuprofen (50.4%), mefenamic acid (16.3%), diclofenac (7.0%), and metamizole (4.1%). Further commonly dispensed drugs after pregnancy were pantoprazole (12.2%), amoxicillin (10.7%), heparin (5.6%), agents used for treatment of constipation based on paraffin (5.1%), macrogol (4.7%), levothyroxine (4.7%), topical dequalinium (4.5%), cabergoline (4.2%), and fluconazole (4.1%).

During pre-pregnancy, commonly prescribed analgesics were also the most prevalent claims, although at a much lower proportion than in the postpartum period (paracetamol 22.0% vs. 63.3% of pregnancies, ibuprofen 20.0% vs. 50.4%, diclofenac 5.4% vs. 7.0%, mefenamic acid 5.2% vs. 16.3%, respectively). Additionally, progesterone was among the most frequently dispensed drugs before pregnancy (5.3%).

By maternal age strata

To further evaluate pregnant women <26 years of age, who had the highest exposure to at least one dispensed drug during pregnancy (see section "Mean (SD) number of drug dispensations"), we evaluated in a post-hoc analysis the prevalence of the 15 most prevalent drug dispensations within maternal age strata (table 4). Dispensation of most drugs was more prevalent to women <26 years of age than to those between 26–35 and ≥36 years of age, except for progesterone, anti-D (rh) immunoglobulin, levothyroxine sodium, omeprazole, and low dose ASA, which were more prevalent in the older age groups.

Discussion

This study used Swiss health care claims data to evaluate the overall drug burden and pattern of utilisation of prescribed drugs before, during, and after pregnancy dispensed in outpatient care in Switzerland between 2015 and 2021. Our study population of 34,584 pregnancies (30,098 women) represents 5.6% of all pregnancies in Switzerland during this period [12–14].

Most women (87.5%) claimed at least one drug during pregnancy, not including vitamins, supplements, and vaccines. The median number of distinct drugs dispensed during pregnancy was 3 (IQR = 1–5), and one third of women claimed five or more distinct drugs. Even during the vulnerable trimester 1, during which organogenesis takes place, almost 1 of 10 women claimed five or more distinct drugs. Thus, our results show that drug use during pregnancy is common. This was expected, given that pregnant women are in close contact with the healthcare system and many pregnancy symptoms and complications may require medical treatment. These results highlight the need to understand which drugs are prescribed in routine care during pregnancy. Future studies should evaluate if the claimed drugs were medically indicated, which is not possible to determine from our data source due to the lack of diagnostic codes.

In a web-based survey [4], 83% of 618 pregnant women from Switzerland reported having used at least one drug (prescribed or OTC) during pregnancy, excluding iron, mineral supplements, vitamins, herbal remedies, and any type of complementary medicine. This survey population may have been affected by volunteer and recall bias, sample size was smaller than in our study, and results may be outdated (study period: 2011–2012). In our larger study, 88% of women claimed at least one prescribed drug during

Figure 3: Prevalence of exposure to 0, 1, 2, 3, 4, and ≥5 drug dispensations during pre-pregnancy, pregnancy (overall and by trimester), and postpartum periods, overall and within age strata, without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines. Exact values and weighted results are shown in table S5 in the appendix.
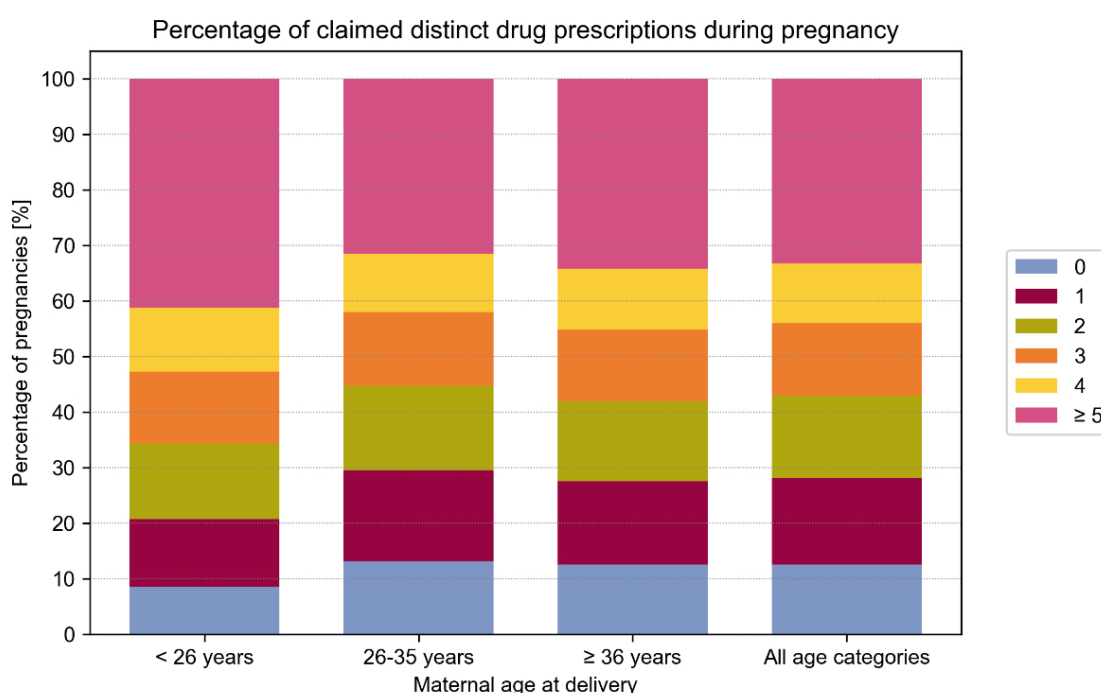
pregnancy, and the longitudinal nature of the data prevented recall bias. However, despite possible limitations, both studies suggest that more than 4 out of 5 women in Switzerland are exposed to drugs during pregnancy. Pregnant women aged <26 years most frequently claimed more than one drug during pregnancy (91.4% vs. 86.9–87.5% for ≥26 years). This may be because a pregnancy at a younger age is likely to be a first-time pregnancy and women may seek more medical advice than in subsequent pregnancies, resulting in more frequent prescriptions. However, channelling by socioeconomic status may also explain some of this difference, with younger women having undergone less education. In a large study among 19,874 Danish women, use of prescription drugs during pregnancy inversely correlated with the duration of education [15]. Younger women may also have lower incomes and may purchase less OTC drugs. However, the extent of OTC drug use cannot be evaluated in this data source.

Evidence on drug use in vulnerable populations such as pregnant women in Switzerland is of great relevance to public health but has only started to emerge in the past decade [16–19]. This is largely due to the fragmented health data landscape and underdeveloped digitalization in the healthcare sector. Other high-income countries, such as all Scandinavian countries, France, and the US, have used healthcare claims data for surveillance of drug use

and safety, also during pregnancy, for decades [20–22]. However, inference on drug use in Switzerland from studies based on health care systems from other countries must be made very cautiously due to differences in reimbursement systems. For example, using comparable methodology, a study based on German claims data by the BARMER health insurer reported that 62.9% of 67,920 pregnant women in 2018 claimed at least one drug during pregnancy [23]. This almost 25% lower prevalence of pregnant women who had any drugs reimbursed is likely explained by the fact that, in Germany, health insurance almost exclusively reimburses prescription drugs. Thus, commonly used drugs such as paracetamol, which can be reimbursed in Switzerland, are not reimbursed in Germany, and thus went unrecorded. Thus, it is important to conduct studies evaluating the use of drugs during pregnancy using Swiss data.

Reassuringly, the 15 most frequently dispensed drugs recorded in our Helsana population have a relatively well-investigated safety profile [24]. The drugs most commonly taken during pregnancy are indicated to treat common acute and chronic conditions and are generally considered safe during pregnancy [5, 6]. These include paracetamol (29.8% of pregnancies), antibiotics (mainly amoxicillin [11.4%] and fosfomycin [7.3%]), vaginal disinfectants (dequalinium, 16.8%) [25], and levothyroxine (7.9%). Low-

Table 3:

Prevalence of exposure to the 15 most frequently dispensed drugs during pre-pregnancy, pregnancy (overall and by trimester), and postpartum periods, without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines. See table S6 in the appendix for weighted results.

	Pre-pregnancy period		Pregnancy		Trimester 1		Trimester 2		Trimester 3		Postpartum	
Rank	Drug substance (ATC code)	%*	Drug substance (ATC code)	%*	Drug substance (ATC code)	%*	Drug substance (ATC code)	%*	Drug substance (ATC code)	%*	Drug substance (ATC code)	%*
1	Paracetamol (N02BE01)	22.0	Paracetamol (N02BE01)	29.8	Paracetamol (N02BE01)	13.1	Paracetamol (N02BE01)	14.1	Paracetamol (N02BE01)	12.0	Paracetamol (N02BE01)	63.3
2	Ibuprofen (M01AE01)	20.0	Dequalinium (G01AC05)	16.8	Metoclopramide (A03FA01)	12.7	Dequalinium (G01AC05)	6.6	Anti-D (rh) immunoglobulin (J06BB01)	8.2	Ibuprofen (M01AE01)	50.4
3	Pantoprazole (A02BC02)	9.0	Metoclopramide (A03FA01)	16.0	Progesterone (G03DA04)	10.9	Levothyroxine sodium (H03AA01)	6.1	Dequalinium (G01AC05)	7.3	Mefenamic acid (M01AG01)	16.3
4	Amoxicillin and enzyme inhibitor (J01CR02)	7.1	Progesterone (G03DA04)	13.4	Dequalinium (G01AC05)	6.6	Amoxicillin and enzyme inhibitor (J01CR02)	4.5	Ordinary salt combinations (A02AD01)	5.9	Pantoprazole (A02BC02)	12.2
5	Metamizole sodium (N02BB02)	6.7	Amoxicillin and enzyme inhibitor (J01CR02)	11.4	Levothyroxine sodium (H03AA01)	5.5	Ordinary salt combinations (A02AD01)	3.8	Levothyroxine sodium (H03AA01)	5.6	Amoxicillin and enzyme inhibitor (J01CR02)	10.7
6	Diclofenac (M01AB05)	5.4	Anti-D (rh) immunoglobulin (J06BB01)	11.1	Ibuprofen (M01AE01)	3.8	Metoclopramide (A03FA01)	3.5	Pantoprazole (A02BC02)	5.2	Diclofenac (M01AB05)	7.0
7	Progesterone (G03DA04)	5.3	Ordinary salt combinations (A02AD01)	10.3	Amoxicillin and enzyme inhibitor (J01CR02)	3.7	Anti-D (rh) immunoglobulin (J06BB01)	3.5	Amoxicillin and enzyme inhibitor (J01CR02)	4.4	Heparin, combinations (C05BA53)	5.6
8	Mefenamic acid (M01AG01)	5.2	Pantoprazole (A02BC02)	9.4	Low-dose acetylsalicylic acid (B01AC06)	3.3	Low-dose acetylsalicylic acid (B01AC06)	3.3	Omeprazole (A02BC02)	3.4	Liquid paraffin (A06AA01)	5.1
9	Diclofenac (M02AA15)	4.6	Levothyroxine sodium (H03AA01)	7.9	Pantoprazole (A02BC02)	3.1	Pantoprazole (A02BC02)	3.1	Ranitidine (A02BA02)	3.3	Macrogol, combinations (A06AD65)	4.7
10	Levothyroxine sodium (H03AA01)	4.5	Fosfomycin (J01XX01)	7.3	Estriol (G03CC06)	2.7	Fosfomycin (J01XX01)	2.9	Nifedipine (C08CA05)	3.2	Levothyroxine sodium (H03AA01)	4.7
11	Dequalinium (G01AC05)	4.5	Estriol (G03CC06)	7.0	Fosfomycin (J01XX01)	2.6	Estriol (G03CC06)	2.9	Esomeprazole (A02BC05)	3.0	Dequalinium (G01AC05)	4.5
12	Fluconazole (J02AC01)	4.4	Ibuprofen (M01AE01)	6.2	Ordinary salt combinations (A02AD01)	2.2	Progesterone (G03DA04)	2.5	Fluconazole (J02AC01)	2.8	Diclofenac (M02AA15)	4.4
13	Fosfomycin (J01XX01)	4.3	Clotrimazole (D01AC01)	5.9	Clotrimazole (D01AC01)	1.9	Clotrimazole (D01AC01)	2.4	Fosfomycin (J01XX01)	2.8	Cabergoline (G02CB03)	4.2
14	Xylometazoline (R01AA07)	4.3	Fluconazole (J02AC01)	5.6	Clotrimazole (G01AF02)	1.6	Fluconazole (J02AC01)	2.2	Estriol (G03CC06)	2.7	Metamizole sodium (N02BB02)	4.1
15	Acetylcysteine (R05CB01)	4.0	Omeprazole (A02BC01)	5.4	Estradiol (G03CA03)	1.6	Ibuprofen (M01AE01)	2.1	Insulin detemir (A10AE05)	2.5	Fluconazole (J02AC01)	4.1

*: % of exposed pregnancies; ATC: Anatomical Therapeutic Chemical.

dose ASA was among the most prevalent drugs in trimesters 1 (3.3%) and 2 (3.3%). The Swiss Society for Gynaecology and Obstetrics (SGGG) recommends low-dose ASA between weeks 12 and 36 for the prevention of preeclampsia, in the presence of specific risk factors [26]. In trimester 3, ASA was not among the 15 most frequently dispensed drugs (1.8%), but true use in trimester 3 likely continued as ASA packages are large in Switzerland (90 pills/package [27]) and some women may not have required a prescription refill in trimester 3 [26].

As expected, antiemetics were among the most prevalent drugs in trimester 1, especially metoclopramide (12.7%). Nausea was also among the leading medication indications in the web-based survey of 628 women in Switzerland (2011–2012) [4]. The true use of antiemetics during trimester 1 is likely much higher than that captured in our study because the first-line antihistaminic antiemetic meclozine with pyridoxine, Itinerol®, is not reimbursed in Switzerland. In 2021, doxylamine (another antihistamine) with pyridoxine (Cariban®) was approved for the treatment of nausea and vomiting during pregnancy and is reimbursed [28]. Additionally in trimester 1, several hormones (progesterone, estriol, and oestradiol) were identified among the most prevalent drug exposures. These were likely prescribed in the context of assisted reproductive technology (ART) or in case of hormone insufficiencies. In contrast to the relatively well-investigated safety profile of the previously discussed drugs used during trimester 1, fluconazole (an antifungal) is discussed more critically in the literature suggesting an increased risk of congenital malformations [30]. A US study also reported that fluconazole was among the most frequently dispensed drugs among pregnant women. Our results reinforce the authors' recommendation that future research should focus on commonly used anti-infectives not limited to antibiotics

[31]. Among the 15 most frequently dispensed drugs were also anti-D (rh) immunoglobulins (3.5% in trimester 2 and 8.2% in trimester 3), which are indicated from gestational week 28–30 (earlier in case of an injury) to prevent rejection reactions in case of rhesus factor incompatibility between the mother and the unborn child [33].

In trimester 3, the use of drugs for acid related disorders increased (ordinary salt combinations, or antacids 5.9%, proton pump inhibitors 11.6%, and ranitidine 3.3%), which was expected given that gastro-oesophageal reflux affects between 30% and 50% of pregnant women and is an increasingly common problem as pregnancy progresses [34]. Insulin (2.5%) and the antihypertensive nifedipine (3.2%) were also among the most claimed drugs in trimester 3. Insulin is the treatment of choice for gestational diabetes, which usually manifests between weeks 24 and 28 [35], and is also the first-line treatment for pre-existing diabetes during pregnancy. Further valuable information on anti-diabetic drugs during pregnancy can be found in a Swiss study based on CSS health insurance claims data [36]. Nifedipine is considered safe during pregnancy and is used as an antihypertensive [37] and as a short-term tocolytic drug in the management of preterm labour (off-label) [38].

Drug use before and after pregnancy meaningfully differed from that during pregnancy. Before pregnancy, we mainly observed drugs which are commonly prescribed in routine care to treat frequent ailments such as pain and viral and bacterial infections. Additionally, progesterone was among the most frequently dispensed drugs, which was likely prescribed either in the context of ART or for a hormone deficiency in women who planned to get pregnant. After pregnancy, the vast majority of drug claims were oral analgesics (paracetamol 63.3%, ibuprofen 50.4%, mefenamic acid 16.3%, diclofenac 7.0%, and metamizole sodium 4.1%), which is expected postpartum. We further identified

Table 4:

Prevalence of exposure to the 15 most prevalent drug dispensations during pregnancy within maternal age strata (without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines). See table S7 in the appendix for weighted results.

	<26 years (n = 3513)		26–35 years (n = 21592)		≥36 years (n = 9479)	
Rank	Drug substance (ATC code)	% of exposed pregnancies	Drug substance (ATC code)	% of exposed pregnancies	Drug substance (ATC code)	% of exposed pregnancies
1	Paracetamol (N02BE01)	42.9	Paracetamol (N02BE01)	29.4	Paracetamol (N02BE01)	25.8
2	Metoclopramide (A03FA01)	24.5	Dequalinium (G01AC05)	17.0	Progesterone (G03DA04)	19.5
3	Dequalinium (G01AC05)	24.3	Metoclopramide (A03FA01)	16.2	Dequalinium (G01AC05)	13.7
4	Amoxicillin and enzyme inhibitor (J01CR02)	15.6	Progesterone (G03DA04)	11.4	Metoclopramide (A03FA01)	12.5
5	Ordinary salt combinations (A02AD01)	12.4	Anti-D (rh) immunoglobulin (J06BB01)	11.1	Anti-D (rh) immunoglobulin (J06BB01)	11.4
6	Fosfomycin (J01XX01)	12.3	Amoxicillin and enzyme inhibitor (J01CR02)	11.0	Amoxicillin and enzyme inhibitor (J01CR02)	10.7
7	Pantoprazole (A02BC02)	12.1	Ordinary salt combinations (A02AD01)	10.3	Levothyroxine sodium (H03AA01)	10.0
8	Anti-D (rh) immunoglobulin (J06BB01)	11.0	Pantoprazole (A02BC02)	9.3	Ordinary salt combinations (A02AD01)	9.4
9	Eestriol (G03CC06)	9.5	Levothyroxine sodium (H03AA01)	7.4	Pantoprazole (A02BC02)	8.6
10	Progesterone (G03DA04)	8.8	Fosfomycin (J01XX01)	7.3	Low-dose acetylsalicylic acid (B01AC06)	7.8
11	Clotrimazole (D01AC01)	8.3	Estriol (G03CC06)	7.0	Estriol (G03CC06)	6.2
12	Ibuprofen (M01AE01)	8.1	Ibuprofen (M01AE01)	6.0	Ibuprofen (M01AE01)	5.7
13	Azithromycin (J01FA10)	7.7	Clotrimazole (D01AC01)	5.7	Clotrimazole (D01AC01)	5.6
14	Fluconazole (J02AC01)	7.5	Fluconazole (J02AC01)	5.6	Fosfomycin (J01XX01)	5.6
15	Clotrimazole (G01AF02)	6.5	Omeprazole (A02BC01)	5.2	Omeprazole (A02BC01)	5.4

ATC: Aanatomical Therapeutic Chemical.

drugs to treat postpartum conditions such as cabergoline for ablactation, or laxatives to facilitate bowel movement. Recorded drug use was higher after pregnancy than before (median number of distinct dispensed drugs after pregnancy = 3 (IQR = 2–5) vs. 2 (IQR = 0–5) before pregnancy), and slightly higher than during pregnancy (median = 3, IQR = 1–5). This was mainly driven by increased postpartum use of analgesics, likely reflecting treatment of pain caused by the delivery. However, women are exempt from the deductible in the compulsory basic insurance between the 13th week of gestation and the 8th week after delivery in Switzerland. Thus, some drugs may not be billed to health insurance in the pre-pregnancy period if the deductible has not been reached [39].

The following limitations need to be considered. First, healthcare claims data do not provide information on whether any or all the tablets of a filled prescription were taken. Thus, our results draw the larger picture of overall drug prescribing during pregnancy in Switzerland, but they may not depict exact absolute levels of drug intake, especially because we also do not capture OTC medication intake. Second, results must be interpreted carefully, as they were estimated based on the 5.6% of all pregnant women in Switzerland who were insured with Helsana during this period. Furthermore, the study population was restricted to women with continuous insurance with Helsana between 270 days before until 270 days after pregnancy (810 days total). Thus, our study population was restricted to loyal customers of Helsana who did not change insurance during this time. Furthermore, the women in our study population may not be entirely representative of women in Switzerland in terms of socio-economic factors. However, maternal age is a known proxy for socio-economic status [40], and the age profile of our population was consistent with that provided by the Swiss Federal Statistical Office during our study period. Third, health care claims data do not capture OTC drug use. In a web-based survey study among 1293 pregnant women who were insured with the German health insurer BARMER in 2020, 75% of women who returned the questionnaire indicated having used at least one OTC drug during pregnancy. Swiss health insurance reimburses somewhat more drugs during pregnancy than German health insurance, but it can be assumed that unrecorded OTC drug use was also high in Switzerland. Fourth, as characteristics of Swiss billing codes did not allow inclusion of pregnancies which ended in termination or abortion into our study population, our prevalence of drug exposure is underestimated. The underestimation range is however difficult to predict, as the prevalence of spontaneous abortions in Switzerland is unknown and in case of terminations the last menstrual period cannot be accurately estimated in our data source. Finally, the start of pregnancy was estimated because it is not recorded in our data. This may have led to inaccurate start of pregnancy dates in some women, which could lead to some misclassification of the exposure time window.

In conclusion, this study suggests that 8 out of 10 women are exposed to prescribed drugs during pregnancy. Reassuringly, most drugs dispensed during pregnancy are comparatively well investigated and are generally considered safe. The frequent use of drugs during pregnancy highlights the importance of evidence on the benefit-risk profile of the individual drugs used. Healthcare claims databases are a valuable tool to study drug utilisation during pregnancy in Switzerland, but they have not been used to their full potential.

Data availability statement

The datasets analysed during the current study are confidential and not publicly available. The analysis code is publicly available here: https://github.com/ebolac/dispensed-drugs-during-pregnancy-in-outpatient-care-between-2015-and-2021-in-Switzerland

Poster presentations of this study

This study was presented as a poster at the 39th International Conference on Pharmacoepidemiology & Therapeutic Risk Management (August 23–27, 2023; Halifax, Nova Scotia, Canada) and at the session "Wenn Schwangere und ihre Kinder Medikamente benötigen – Hotspots" (engl. "When pregnant women and their children need medication – hotspots") organized by "Schweizerische Akademie für Perinatale Pharmakologie" (SAPP; November 2, 2023; Zurich, Switzerland).

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Appendix

Table S1: Inpatient and outpatient codes for identification of deliveries in the health care claims database of the Helsana group and identification of pregnancies during the pre-pregnancy period and postpartum (exclusion criteria)

Identification of deliveries	
Source	**Codes**
TARMED	22.2110, 22.2120, 22.2130, 22.2140, 22.2150, 22.2160, 22.2170, 22.2180, 22.2190, 22.2200, 22.2210, 22.2410, 22.2420
SwissDRG	O01A, O01B, O01C, O01D, O01E, O01F, O01G, O01H, O02A, O02B, O60A, O60B, O60C, O60D
Midwife	B1, B2, B3, B4
Identification of pregnancies during the pre-pregnancy period and postpartum (exclusion criteria)	
TARMED	TARMED codes from above (identification of deliveries) and the following codes (abortions): 22.1240, 22.1250, 22.1260, 22.1270, 22.1280, 22.1290, 22.1300
SwissDRG	SwissDRG codes from above (identification of deliveries) and the following codes (abortions): O03Z, O04Z, O40Z, O61Z, O63Z
Midwife	Midwife codes from above (identification of deliveries)

Table S2: ATC codes which were not considered in this study. Basic exclusions: not considered during entire study. Vitamins, minerals, iron preparations, iodide, and vaccinations: excluded when explicitly stated. The characters «.-» mean that any character or number can follow.

	ATC code and description
Basic exclusions	A01AA.- Caries prophylactic agents
	A07CA Oral rehydration salt formulations
	B05.- Blood substitutes and perfusion solutions
	D02.- Emollients and protectives
	D09AX Soft paraffin dressings
	P03B.- Insecticides and repellents
	S01J.- Diagnostic agents
	S01K.- Surgical aids
	S01XA20 Artificial tears and other indifferent preparations
	V.- except V03.- without: - V03AK Tissue adhesives - V03AM Drugs for embolisation - V03AN.- Medical gases - V03AB16 Ethanol - V03AZ01 Ethanol
Vitamins, minerals, iron preparations, iodide, and vaccinations	A11.- Vitamins
	A12.- Mineral supplements
	B03A.- Iron preparations
	B03B.- Vitamin B12 and folic acid
	H03C.- Iodine therapy
	J07.- Vaccines

Table S3: Prevalence of exposure to at least dispensed drug during the pre-pregnancy period, during pregnancy (overall and by trimester), and during the postpartum overall and within maternal age strata, as well as with vs. without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines.

	Maternal age at delivery [years]	N total	Pre-pregnancy period		Pregnancy		Trimester 1		Trimester 2		Trimester 3		Postpartum	
			N	%	N	%	N	%	N	%	N	%	N	%
Not weighted results														
With vitamins, minerals, iron preparations, iodide, and vaccinations	All (13-49)	34584	25868	74.8	33813	97.8	25995	75.2	29003	83.9	30551	88.3	30733	88.9
	<26	3513	2758	78.5	3449	98.2	2807	79.9	2975	84.7	3053	86.9	3107	88.4
	26-35	21592	15957	73.9	21107	97.8	16104	74.6	18009	83.4	19021	88.1	19156	88.7
	≥36	9479	7153	75.5	9257	97.7	7084	74.7	8019	84.6	8477	89.4	8470	89.4
Without vitamins, minerals, iron preparations, iodide, and vaccinations	All (13-49)	34584	23889	69.1	30260	87.5	20483	59.2	20278	58.6	23075	66.7	29616	85.6
	<26	3513	2620	74.6	3212	91.4	2317	66.0	2226	63.4	2392	68.1	3035	86.4
	26-35	21592	14620	67.7	18755	86.9	12479	57.8	12404	57.4	14222	65.9	18440	85.4
	≥36	9479	6649	70.1	8293	87.5	5687	60.0	5648	59.6	6461	68.2	8141	85.9
Weighted results														
With vitamins, minerals, iron preparations, iodide, and vaccinations	All (13-49)	502100	371508	74.0	490325	97.7	374485	74.6	419398	83.5	443455	88.3	446986	89.0
	<26	51244	39449	77.0	50141	97.8	40463	79.0	43031	84.0	44373	86.6	45245	88.3
	26-35	330177	241480	73.1	322235	97.6	244490	74.6	273960	83.0	290790	88.1	293394	88.9
	≥36	120679	90579	75.1	117949	97.7	89531	74.2	102406	84.9	108291	89.7	108347	89.8
Without vitamins, minerals, iron preparations, iodide, and vaccinations	All (13-49)	502100	342493	68.2	437912	87.5	294325	58.6	293319	58.4	333455	66.4	431066	85.9
	<26	51244	37236	72.7	46266	90.3	33335	65.1	31854	62.2	34823	68.0	44217	86.3
	26-35	330177	220943	66.9	286468	86.8	189436	57.4	189804	57.5	216913	65.7	282513	85.6
	≥36	120679	84314	69.9	105179	87.2	71554	59.3	71661	59.6	81719	67.7	104336	86.5

Table S4: Prevalence of exposure to 0, 1, 2, 3, 4, and ≥5 drug dispensations/s during the pre-pregnancy period, during pregnancy (overall and by trimester), and during the postpartum without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines (weighted results).

Number of distinct drug claims*	Pre-pregnancy period	Pregnancy	Trimester 1	Trimester 2	Trimester 3	Postpartum
	N pregnancies (%)	N pregnancies (%)	N pregnancies (%)	N pregnancies (%)	N pregnancies (%)	N pregnancies (%)
0	159608 (31.8)	64188 (12.8)	207775 (41.4)	208781 (41.6)	168645 (33.6)	71034 (14.1)
1	64592 (12.9)	79903 (15.9)	111856 (22.3)	121070 (24.1)	130737 (26.0)	46640 (9.3)
2	53444 (10.6)	74715 (14.9)	71695 (14.3)	70736 (14.1)	83727 (16.7)	87929 (17.5)
3	45340 (9.0)	66256 (13.2)	44742 (8.9)	42622 (8.5)	52599 (10.5)	75164 (15.0)
4	38934 (7.8)	53270 (10.6)	25658 (5.1)	24963 (5.0)	28883 (5.8)	58507 (11.7)
≥5	140183 (27.9)	163768 (32.6)	40375 (8.0)	33928 (6.8)	37509 (7.5)	162826 (32.4)

*ATC-7 level

Table S5: Prevalence of exposure to 0, 1, 2, 3, 4, and ≥5 drug dispensation/s during the pre-pregnancy period, during pregnancy (overall and by trimester), and during the postpartum overall and within maternal age strata, without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines.

N distinct claimed prescription fills (ATC-7 level)	All age categories		<26 years		26-35 years		≥36 years	
	N pregnancies	% of exposed pregnancies	N pregnancies	% of exposed pregnancies	N pregnancies	% of exposed pregnancies	N pregnancies	% of exposed pregnancies
Not weighted results								
0	4324	12.5	301	8.6	2837	13.1	1186	12.5
1	5395	15.6	426	12.1	3540	16.4	1429	15.1
2	5127	14.8	480	13.7	3287	15.2	1360	14.3
3	4535	13.1	454	12.9	2861	13.3	1220	12.9
4	3702	10.7	405	11.5	2254	10.4	1043	11.0
≥5	11501	33.3	1447	41.2	6813	31.6	3241	34.2
Weighted results								
0	64188	12.8	4978	9.7	43710	13.1	15500	12.8
1	79903	15.9	6143	12.0	55073	16.4	18688	15.5
2	74715	14.9	7111	13.9	50132	15.2	17472	14.5
3	66256	13.2	6575	12.8	44262	13.3	15419	12.8
4	53270	10.6	5701	11.1	34735	10.4	12834	10.6
≥5	163768	32.6	20736	40.5	102266	31.6	40766	33.8

Table S6: Prevalence of exposure to the 15 most frequently dispensed drugs during the pre-pregnancy period, during pregnancy (overall and by trimester), and during the postpartum, without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines (weighted results).

Rank	Pre-pregnancy period Drug substance (ATC code)	% of exposed pregnancies	Pregnancy Drug substance (ATC code)	% of exposed pregnancies	Trimester 1 Drug substance (ATC code)	% of exposed pregnancies	Trimester 2 Drug substance (ATC code)	% of exposed pregnancies	Trimester 3 Drug substance (ATC code)	% of exposed pregnancies	Postpartum Drug substance (ATC code)	% of exposed pregnancies
1	paracetamol (N02BE01)	22.1	paracetamol (N02BE01)	29.7	paracetamol (N02BE01)	13.0	paracetamol (N02BE01)	14.4	paracetamol (N02BE01)	11.9	paracetamol (N02BE01)	63.5
2	ibuprofen (M01AE01)	19.6	dequalinium (G01AC05)	16.7	metoclopramide (A03FA01)	12.9	dequalinium (G01AC05)	6.5	anti-D (rh) immunoglobulin (J06BB01)	7.9	ibuprofen (M01AE01)	49.7
3	pantoprazole (A02BC02)	8.9	metoclopramide (A03FA01)	16.1	progesterone (G03DA04)	10.5	levothyroxine sodium (H03AA01)	5.8	dequalinium (G01AC05)	7.4	mefenamic acid (M01AG01)	16.6
4	amoxicillin and enzyme inhibitor (J01CR02)	6.9	progesterone (G03DA04)	13.0	dequalinium (G01AC05)	6.4	amoxicillin and enzyme inhibitor (J01CR02)	4.4	ordinary salt combinations (A02AD01)	5.7	pantoprazole (A02BC02)	12.0
5	metamizole sodium (N02BB02)	6.5	amoxicillin and enzyme inhibitor (J01CR02)	11.1	levothyroxine sodium (H03AA01)	5.3	ordinary salt combinations (A02AD01)	3.8	levothyroxine sodium (H03AA01)	5.3	amoxicillin and enzyme inhibitor (J01CR02)	10.5
6	diclofenac (M01AB05)	5.2	anti-D (rh) immunoglobulin (J06BB01)	10.9	ibuprofen (M01AE01)	3.7	metoclopramide (A03FA01)	3.5	pantoprazole (A02BC02)	5.4	diclofenac (M01AB05)	7.5
7	mefenamic acid (M01AG01)	5.2	ordinary salt combinations (A02AD01)	10.0	amoxicillin and enzyme inhibitor (J01CR02)	3.7	anti-D (rh) immunoglobulin (J06BB01)	3.4	amoxicillin and enzyme inhibitor (J01CR02)	4.2	heparin, combinations (C05BA53)	5.3
8	progesterone (G03DA04)	5.0	pantoprazole (A02BC02)	9.6	low-dose acetyl-salicylic acid (B01AC06)	3.2	low-dose acetyl-salicylic acid (B01AC06)	3.2	omeprazole (A02BC01)	3.5	levothyroxine sodium (A06AD65)	4.5
9	diclofenac (M02AA15)	4.6	fosfomycin (J01XX01)	7.6	pantoprazole (A02BC02)	3.2	pantoprazole (A02BC02)	3.1	nifedipine (C08CA05)	3.2	macrogol, combinations (A06AD65)	4.4

10	dequalinium (G01AC05)	4.4	levothyroxine sodium (H03AA01)	7.5	fosfomycin (J01XX01)	2.8	fosfomycin (J01XX01)	3.1	esomeprazole (A02BC05)	3.1	liquid paraffin (A06AA01)	4.3
11	levothyroxine sodium (H03AA01)	4.3	estriol (G03CC06)	7.1	estriol (G03CC06)	2.7	estriol (G03CC06)	3.0	fosfomycin (J01XX01)	2.9	dequalinium (G01AC05)	4.3
12	xylometazoline (R01AA07)	4.3	ibuprofen (G03CC06)	6.1	ordinary salt combinations (A02AD01)	2.0	progesterone (G03DA04)	2.5	ranitidine (A02BA02)	2.8	diclofenac (M02AA15)	4.3
13	fluconazole (J02AC01)	4.2	clotrimazole (D01AC01)	5.9	clotrimazole (D01AC01)	2.0	clotrimazole (D01AC01)	2.4	estriol (G03CC06)	2.8	fluconazole (J02AC01)	4.2
14	fosfomycin (J01XX01)	4.1	fluconazole (J02AC01)	5.5	clotrimazole (G01AF02)	1.6	fluconazole (J02AC01)	2.3	fluconazole (J02AC01)	2.7	cabergoline (G02CB03)	4.1
15	acetylcysteine (R05CB01)	4.0	omeprazole (A02BC01)	5.5	anti-D (rh) immunoglobulin (J06BB01)	1.5	ibuprofen (M01AE01)	2.1	insulin detemir (A10AE05)	2.3	metamizole sodium (N02BB02)	4.1

Table S7: Prevalence of exposure to the 15 most prevalent drug dispensations during pregnancy within maternal age strata (without considering vitamins, mineral supplements, iron preparations, vitamin B12, folic acid, iodine therapy, and vaccines) (weighted results).

	<26 years (N = 51244)		26-35 years (N = 330177)		≥36 years (N = 120679)	
Rank	Drug substance (ATC code)	% of exposed pregnancies	Drug substance (ATC code)	% of exposed pregnancies	Drug substance (ATC code)	% of exposed pregnancies
1	paracetamol (N02BE01)	41.3	paracetamol (N02BE01)	29.2	paracetamol (N02BE01)	26.0
2	dequalinium (G01AC05)	24.2	dequalinium (G01AC05)	16.7	progesterone (G03DA04)	19.1
3	metoclopramide (A03FA01)	23.9	metoclopramide (A03FA01)	16.1	dequalinium (G01AC05)	13.4
4	amoxicillin and enzyme inhibitor (J01CR02)	15.1	progesterone (G03DA04)	11.5	metoclopramide (A03FA01)	13.0
5	ordinary salt combinations (A02AD01)	12.2	anti-D (rh) immunoglobulin (J06BB01)	11.0	anti-D (rh) immunoglobulin (J06BB01)	10.8
6	fosfomycin (J01XX01)	11.7	amoxicillin and enzyme inhibitor (J01CR02)	10.7	amoxicillin and enzyme inhibitor (J01CR02)	10.4
7	pantoprazole (A02BC02)	11.6	ordinary salt combinations (A02AD01)	10.0	levothyroxine sodium (H03AA01)	9.9
8	anti-D (rh) immunoglobulin (J06BB01)	10.7	pantoprazole (A02BC02)	9.5	pantoprazole (A02BC02)	9.1
9	estriol (G03CC06)	9.9	fosfomycin (J01XX01)	7.5	ordinary salt combinations (A02AD01)	9.0
10	ibuprofen (M01AE01)	8.5	levothyroxine sodium (H03AA01)	7.1	low-dose acetylsalicylic acid (B01AC06)	7.7
11	progesterone (G03DA04)	8.4	estriol (G03CC06)	7.1	fosfomycin (J01XX01)	6.2
12	clotrimazole (D01AC01)	7.8	ibuprofen (M01AE01)	5.9	estriol (G03CC06)	5.9
13	azithromycin (J01FA10)	7.3	clotrimazole (D01AC01)	5.9	omeprazole (A02BC01)	5.9
14	fluconazole (J02AC01)	7.2	fluconazole (J02AC01)	5.5	ibuprofen (M01AE01)	5.6
15	clotrimazole (G01AF02)	6.2	omeprazole (A02BC01)	5.3	clotrimazole (D01AC01)	5.4