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ORIGINAL REPORT

Safety profile of medication used during pregnancy: results of a multinational European study†

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ABSTRACT

Purpose The present study describes the safety profile of medications used during pregnancy across European countries and examines maternal factors associated with the use of risky medications during pregnancy.
Methods This study is based on a multinational, web-based study conducted in 15 European countries from October 2011 to February 2012. Information about maternal demographics, illnesses, and medication use during pregnancy was collected via an electronic questionnaire. Pregnant women and new mothers with a child less than 1-year-old could participate. The Swedish, Australian, and U.S. risk classification systems were used to evaluate medication safety. Descriptive statistics and generalized estimating equation models were used.
Results A total of 587 medications were reported by the study sample (n = 6657). Sixty-nine percent of the women used medications classified as safe, 28% used medications classified as risky, and 3% used medications with no classification available. Both socio-demographic and medical factors were associated with the use of risky medications during pregnancy. Having a chronic disorder was the factor with the strongest association with the use of risky medications during pregnancy (adjusted odds ratio = 3.99, 95% confidence interval 3.54–4.49).
Conclusions The majority of women used medications classified as safe to use during pregnancy. However, a considerable proportion of women still used medications classified as risky. Having a chronic disorder was an important driver for using risky medications. Such use may still be appropriate when considering the woman's underlying condition. Pre-pregnancy counselling is important to ensure safe medication use for both mother and child. © 2017 The Authors. *Pharmacoepidemiology & Drug Safety* Published by John Wiley & Sons Ltd.

KEY WORDS—medication; pregnancy; risk classification; multinational; pharmacoepidemiology

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INTRODUCTION

Recent studies have reported that medication use is common among pregnant women.[1–4] Up to 80% of women are estimated to use at least one medication, over-the-counter (OTC) or prescribed, during pregnancy.[4] Taking a medication during pregnancy involves weighing the risk versus benefits for both mother and child. Avoiding required treatment for maternal illnesses, such as diabetes, epilepsy, hypertension, or infections, may endanger both the mother and child. On the other hand, unnecessary medication use during pregnancy can have potential negative consequences for the fetus.[5,6] Different risk classification systems have been established to provide guidance to healthcare professionals when counselling pregnant women on the safety of medications during pregnancy. The most well-known risk classification systems are from Sweden, Australia, and the U.S. and place medications in risk groups according to fetal safety.[7] Although the risk classification systems have limitations,[8–10] they are of great value when describing medication utilization patterns at an aggregated level.

Studies have consistently reported the use of potentially risky medications during pregnancy, with prevalence estimates of 2% in Italy,[11] 19% in Denmark,[12] 21% in the Netherlands,[13] and 59% in France.[14] The variation may be attributed to

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differences in the study methods used to assess medication exposure, the classification system used, and the type of medications assessed, making comparisons of results almost impossible.[1] Uniform collection of data on medication utilization during pregnancy across countries may overcome some of these drawbacks. Moreover, multinational studies of the safety profiles of medications used during pregnancy are lacking. As medication utilization patterns may change over time, such use needs to be continuously monitored in order to identify potentially risky practices during pregnancy and to ensure safe medication use for both mother and child.

To the best of our knowledge, no previous study has uniformly evaluated the safety profile of medications taken by pregnant women across several European countries. The purpose of this study was to describe the safety profile of medications used during pregnancy across European countries and to examine maternal factors associated with the use of potentially risky medications during pregnancy.

METHODS

Study design, population, and data collection

This is a sub-study of "The Multinational Medication Use in Pregnancy Study", a web-based study conducted in countries in Eastern, Northern, and Western Europe, North and South America, and Australia to investigate medication use during pregnancy with a focus on maternal attitudes, perception of risk, and mental well-being.[4] For the present study, we only included women residing in European countries at the time the questionnaire was completed (i.e., Austria, Croatia, Finland, France, Iceland, Italy, Norway, Poland, Russia, Serbia, Slovenia, Sweden, Switzerland, the Netherlands, and UK). Both pregnant women and new mothers with a child less than 1 year of age could participate. The study recruited women through placement of banners (invitations to participate in the study) on national websites and/or social networks commonly visited by pregnant women and new mothers. The survey questionnaire was administered by Questback (http://www.questback.com). The online questionnaire was accessible for a period of 2 months in each participating country between October 1, 2011, and February 29, 2012. The baseline characteristics of the study population were compared on an individual country level with those of the potential general birthing or childbearing population in the same country. Reports from National Statistics Bureaus or previous national studies were utilized for this purpose. The sample was found to be representative with respect to age, parity, and smoking habits.[4] However, the sample comprised a group of women with higher education than the general birthing population in each country. A detailed description of the study was published previously.[4]

Medication use report

The most common short-term/acute illnesses and the most prevalent chronic disorders were listed in the questionnaire, and women were asked if they suffered/had suffered from these conditions during pregnancy. In the case of a positive answer, women could report any medication use according to indication as a free-text entry. The questionnaire also included five questions about the use of OTC medications, with examples of branded product names in the various countries to enhance recall. Timing of exposure was requested when medication use occurred; the options were gestational weeks 0–12 (first trimester), weeks 13–24 (second trimester), and 25 weeks to delivery (third trimester).[4] All medications were then coded into the corresponding Anatomical Therapeutic Chemical (ATC) codes at the fifth (substance) level in accordance with the World Health Organization ATC index.[15] The use of iron, mineral supplements, vitamins, and herbal remedies was excluded from this analysis.

Safety classification of medications

We used internationally recognized risk classification systems to place each medication in risk groups according to fetal safety.

The Swedish classification system (Farmaceutiska Spesialiteter i Sverige [FASS])[16] was used as the primary source because it is relevant for medications on the European market and reflects international text book recommendations better than the U.S. classification system from the Food and Drug Administration (FDA).[7,17] In general, when medications were part of a combination, they were classified according to the main substance (e.g., the medication meclozine and combinations were classified according to meclozine). Medications consisting of components with different risk classifications were classified according to the component with the highest risk. If the medication had no risk classification and was a topical formulation, but the substance had a classification for the oral formulation, the medication was conservatively classified. Whenever the medication risk classification was lacking in FASS, the Australian classification system was used as a

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secondary source.[18] If neither of these classification systems was able to classify the medication, the FDA system was used as a tertiary source.[19,20] The rationale for using two additional risk classification systems was to classify as many medications as possible. Medications that could not be classified by any of these resources were considered as "not classified".

All three risk classification systems place medications in risk groups according to fetal safety. FASS is based on clinical and/or animal data and consists of four different groups (A to D). Group A includes the safest medications; group B includes medications with undetermined risk and classified based on animal data, with allocation to three subgroups (B1, B2, and B3); and groups C and D include medications that may involve risk to the fetus or an increased risk of fetal damage.[8] The FDA categorization also uses letters from A to D, with an additional X category for medications that have been shown to be teratogenic.[8] The Australian classification system is an extrapolation of both of the other systems.[8]

Medications were grouped as "probably safe" or "potentially risky" in order to facilitate the analysis and to make categories of more clinical interest. The "probably safe" group consisted of FASS and Australian categories A, B1, and B2 and FDA categories A and B, and the "potentially risky" group consisted of FASS and Australian categories B3, C, and D, Australian category X, and FDA categories C, D, and X. In a woman-level analysis, women using multiple medications were assigned to the group with the highest risk.

Statistical analysis

Descriptive statistics were used as appropriate. Factors associated with the use of potentially risky medications during pregnancy (dichotomous variable: potentially risky medication user versus probably safe medication user) were examined using the generalized estimating equations (GEE) with a binomial distribution.[21] GEE were used in order to account for any clustering on region of residence. Data are presented as adjusted odds ratios (aOR) with 95% confidence intervals (CI). A two-tailed p-value < 0.05 was considered significant. Candidate variables in a univariate model with $p < 0.25$ were selected for inclusion in the multivariate GEE model. Variables with $p > 0.05$ or $< 20\%$ impact on the beta coefficients of the retained variables were removed from the multivariate model. The final multivariate model included significant independent variables: education level, employment status, parity, folic acid use before and during pregnancy, alcohol consumption, smoking, and chronic disorders.

In a set of sensitivity analyses, women using unclassified medications were grouped together with (i) the probably safe medication users and (ii) the potentially risky medication users. We also restricted the medication pattern analysis to women with an overview of the entire pregnancy (i.e., pregnant women in third trimester and new mothers). A sensitivity analysis excluding all topical formulations was also performed. Country-specific analyses investigating associations between maternal factors and potentially risky medications were performed using logistic regression. We adjusted for the same covariates as in the main analysis. All statistical analyses were performed using STATA/MP 14.1 for Windows (StataCorp LP, TX, USA).

RESULTS

A total of 9615 women replied to the informed consent question after reading the study description, and 9483 (98.6%) confirmed their willingness to participate in the study and completed the online questionnaire. Women with unknown country of residence and women from non-European countries were excluded, leaving 8363 eligible women. We excluded an additional 1576 (18.8%) non-users of medication and 130 (1.6%) women with unspecified medication use, leaving 6657 (79.6%) women with specified medication use as our study sample (Figure 1). The study sample had higher parity and consumed more alcohol after awareness of pregnancy than the non-users of medication. Our study sample included women from Western (n = 2543), Northern (n = 2355), and Eastern Europe (n = 1759). A total of 3455 (51.9%) women were pregnant at the time they completed the questionnaire, and 3202 (48.1%) had delivered their babies within the previous year. The socio-demographic and lifestyle factors of the study sample are summarized in Table 1.

Classification and use of medications during pregnancy

A total of 587 different medications were used by the study sample and classified according to the three risk classification systems (Figure 2).

Using the combined classification method, 223 (38.0%) of the 587 medications were classified

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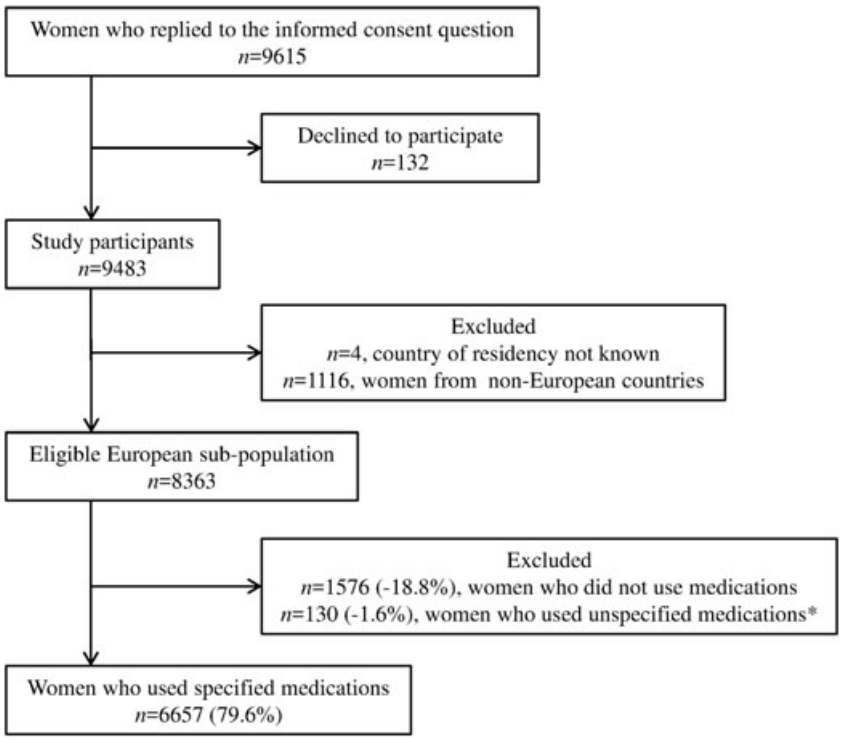

Figure 1. Participant flowchart.*Women with unspecified medication use only provided a general response, such as "antibiotics" or that they could not remember, when asked about medication use and were excluded from the analysis

as probably safe to use during pregnancy. Probably safe medications were used by 4596 (69.0%) women, most commonly paracetamol (acetaminophen), ordinary salt combinations, and alginic acid.

A total of 228 (38.8%) medications were classified as potentially risky to use during pregnancy and were used by 1881 (28.3%) women. The most frequent medications in this group were ibuprofen, metoclopramide, and codeine (combined products excluding neuroleptics).

No classification was available for 136 (23.2%) medications, which were used by 180 (2.7%) of the women. The most frequent medications in this group were drotaverine, hydrotalcite, and combinatory nasal preparations. Table 2 shows the 10 most frequently used medications classified as probably safe, potentially risky, and unclassified, respectively.

Regardless of trimester, the majority of women used medications classified as probably safe (Table S1). A sensitivity analysis including only women with an overview of the entire pregnancy did not find major differences in the percentage of women using medication in the different safety groups according to trimester of use.

Medication use according to country/region of residence

The majority of women across all countries used medications that are safe to use during pregnancy. A higher proportion of women from Northern Europe used medications that are potentially risky during pregnancy compared with women from the other regions. The highest proportion of women using unclassified medications were from Eastern Europe (Figure 3). Table S2 shows the most common potentially risky and unclassified medications according to region.

Factors associated with the use of potentially risky medications during pregnancy

Several factors were associated with the use of potentially risky medications during pregnancy, as summarized in Table 3. Being a student, a housewife, or working as healthcare personnel, having previous children, not using folic acid, consuming alcohol, and smoking were associated with the use of potentially risky medications during pregnancy, and the magnitude of the associations ranged between 10% and 30% increased odds. Having a chronic disorder was the factor with the

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Table 1. Maternal socio-demographic and lifestyle factors among the study sample

Maternal characteristics	Women who used specified medication (n_{total} = 6657) *n* (%)	Women who used probably safe medication (*n* = 4596) *n* (%)	Women who used potentially risky medication (*n* = 1881) *n* (%)	Women who used unclassified medication (*n* = 180) *n* (%)
Region of residence				
Western Europe*	2543 (38.2)	1875 (40.8)	625 (33.2)	43 (23.9)
Northern Europe†	2355 (35.4)	1605 (34.9)	743 (39.5)	7 (3.9)
Eastern Europe‡	1759 (26.4)	1116 (24.3)	513 (27.3)	130 (72.2)
Maternal age (years)				
≤20	195 (2.9)	129 (2.8)	58 (3.1)	8 (10.0)
21–30	3656 (54.9)	2513 (54.7)	1032 (54.9)	111 (61.7)
31–40	2672 (40.2)	1859 (40.4)	752 (40.0)	61 (33.9)
≥41	134 (2.0)	95 (2.1)	39 (2.1)	0 (0.0)
Marital status				
Married/cohabitant	6332 (95.1)	4390 (95.5)	1774 (94.3)	168 (93.3)
Single/divorced/other	325 (4.9)	206 (4.5)	107 (5.7)	12 (6.7)
Education level				
Less than high school	314 (4.7)	201 (4.4)	106 (5.6)	7 (3.9)
High school	1887 (28.4)	1343 (29.2)	505 (26.9)	39 (21.7)
More than high school	3672 (55.2)	2517 (54.8)	1036 (55.1)	119 (66.1)
Other, unspecified	784 (11.7)	535 (11.6)	234 (12.4)	15 (8.3)
Working status				
Student	587 (8.8)	382 (8.3)	191 (10.2)	14 (7.8)
Housewife	538 (8.1)	347 (7.6)	174 (9.3)	17 (9.4)
Healthcare personnel	941 (14.1)	625 (13.6)	303 (16.2)	13 (7.2)
Employed in other sector	3964 (59.5)	2801 (60.9)	1044 (55.5)	119 (66.1)
Job seeker	288 (4.3)	204 (4.4)	74 (3.9)	10 (5.6)
None	331 (5.0)	231 (5.0)	93 (4.9)	7 (3.9)
Previous children				
Yes	3380 (50.8)	2299 (50.0)	1009 (53.6)	72 (40.0)
No	3277 (49.2)	2297 (50.0)	872 (46.4)	108 (60.0)
Planned pregnancy				
Yes, not completely unexpected	6062 (91.1)	4203 (91.4)	1691 (89.9)	168 (93.3)
No, it was not planned	574 (8.6)	380 (8.3)	182 (9.7)	12 (6.7)
Folic acid use				
Yes	6100 (91.6)	4241 (92.3)	1694 (90.1)	165 (91.7)
No	503 (7.6)	324 (7.0)	166 (8.8)	13 (7.2)
Alcohol consumption after known pregnancy				
Yes	1149 (17.3)	750 (16.3)	358 (19.0)	41 (22.8)
No	5457 (82.0)	3816 (83.0)	1506 (80.1)	135 (75.0)
Smoking during pregnancy				
Yes	621 (9.3)	394 (8.6)	205 (10.9)	22 (12.2)
No	6022 (90.5)	4197 (91.3)	1667 (88.6)	158 (87.8)

Numbers may not add up to total number due to missing values. For *folic acid* use and *alcohol consumption during pregnancy*, the response "cannot remember" was treated as a missing value. Missing values are less than 5% of the total.
When a woman used multiple medications, she was assigned to the group with highest risk.
*Western Europe includes Austria, France, Italy, Switzerland, the Netherlands, and UK.
†Northern Europe includes Finland, Iceland, Norway, and Sweden.
‡Eastern Europe includes Croatia, Poland, Russia, Serbia, and Slovenia.

strongest association with the use of potentially risky medications during pregnancy (aOR = 3.99, 95% CI 3.54–4.49).

In the country-specific analyses, maternal chronic disorder was consistently one of the most important factors associated with the use of potentially risky medication during pregnancy. The magnitude of this association across countries was generally similar to that observed in the main analysis, although stronger in the UK (aOR = 7.6, 95% CI 5.2–10.9) and weaker in Russia (aOR = 1.4, 95% CI 1.0–1.9). We observed more common use of potentially risky medications among women using alcohol during pregnancy in some of the Eastern European countries compared with non-drinkers. Similarly, women with previous children (in France, Norway, UK, Sweden, and Russia) or working as healthcare professionals (in Norway, France, Poland, and UK) were more likely to use potentially risky medication than nulliparous women or women employed in a non-health-related sector, respectively.

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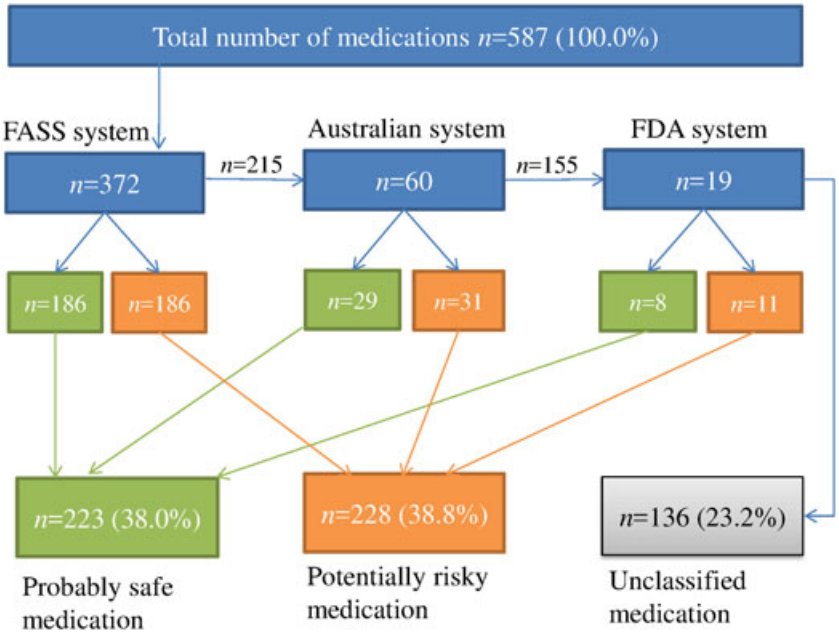

Figure 2. Flowchart of how the medications were evaluated and classified according to three internationally recognized risk classification systems. FASS, Farmaceutiska Spesialiteter i Sverige; FDA, Food and Drug Administration. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 2. Top 10 probably safe, potentially risky, and unclassified medications used during pregnancy

Probably safe medications (ATC code)	*n* (%)	Potentially risky medications (ATC code)	*n* (%)	Unclassified medications (ATC code)	*n* (%)
Paracetamol (acetaminophen) (N02BE01)	4459 (67.0)	Ibuprofen (M01AE01)	309 (4.6)	Drotaverine (A03AD02)	153 (2.3)
Ordinary salt combinations (A02AD01)	1424 (21.4)	Metoclopramide (A03FA01)	230 (3.5)	Hydrotalcite (A02AD04)	93 (1.4)
Alginic acid (A02BX13)	1194 (17.9)	Codeine combinations (N02AA59)	178 (2.7)	Nasal preparations, combinations (R01AX30)	77 (1.2)
Xylometazoline (R01AA07)	787 (11.8)	Acetylsalicylic acid combinations (N02BA51)	96 (1.4)	Glycerol (enema) (A06AG04)	60 (0.9)
Lactulose (A06AD11)	514 (7.7)	Naphazoline (R01AA08)	72 (1.1)	Throat preparations, antiseptics, various (R02AA20)	58 (0.9)
Oxymetazoline (R01AA05)	459 (6.9)	Mometasone (R01AD09)	65 (1.0)	Calcium carbonate (A02AC01)	49 (0.7)
Levothyroxine (H03AA01)	328 (4.9)	Econazole (G01AF05)	54 (0.8)	Phloroglucinol (A03AX12)	47 (0.7)
Meclozine (R06AE05)	257 (3.9)	Formoterol and budesonide (R03AK07)	54 (0.8)	Fusafungine (R02AB03)	47 (0.7)
Amoxicillin (J01CA04)	200 (3.0)	Interferon alpha-2b (L03AB05)	52 (0.8)	Magaldrate (A02AD02)	45 (0.7)
Salbutamol (R03AC02)	166 (2.5)	Sertraline (N06AB06)	48 (0.7)	Glycerol (A06AX01)	42 (0.6)

Women may have used more than one medication.
Study sample, *n* = 6657.

In a sub-analysis of individual chronic disorders (i.e., allergy, asthma, anxiety, depression, cardiovascular disease, hypothyroidism, and rheumatic illness), all except hypothyroidism were significantly associated with the use of potentially risky medications (Table S3).

In sensitivity analyses, we found no difference from the main analysis when unclassified medication

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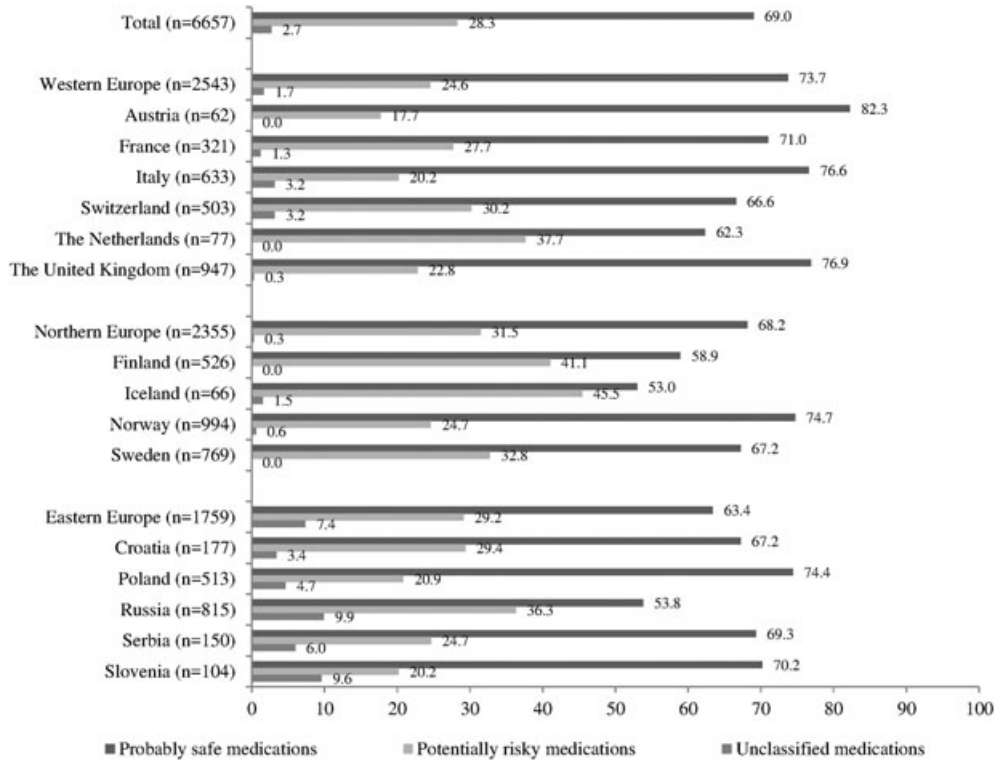

Figure 3. The proportion of women (%) using probably safe, potentially risky, and unclassified medications during pregnancy according to region and country of residence. When a woman used multiple medications, she was assigned to the group with highest risk

users were grouped together with the probably safe medication users. When grouping the unclassified medication users with the potentially risky medication users, smoking and higher parity were not associated with the use of potentially risky medications.

Sensitivity analyses excluding topical formulations did not produce material differences in the results from the main analysis.

DISCUSSION

To the best of our knowledge, this study is the first to examine the safety profile of medications used during pregnancy and maternal factors associated with potentially risky medication use during pregnancy across several European countries. It is reassuring that the majority of women used medications classified as safe to use during pregnancy. However, 28% of the women used potentially risky medications, which is in line with findings from previous studies.[1] In addition, one-fifth of the medications could not be classified, even after using three different risk classification systems. Not surprisingly, the Summary of Product Characteristics for most unclassified medications could not fill this knowledge gap because it had limited or no information available in the pregnancy section. A medication utilization study by Olesen *et al.*[12] was also unable to classify 12% of the prescriptions used by pregnant women in Denmark. Taken together, the findings indicate that many medications used by pregnant women have inadequate safety information available and that studies of medication safety during pregnancy are urgently needed.

Differences in medication use between regions/countries with respect to safety classification may be explained by different health needs of the pregnant population and differences in preconception counselling or pregnancy planning in the individual countries.

The most commonly used medications classified as risky were ibuprofen, metoclopramide, and codeine, which were mainly used among women in Western and Northern Europe. Classification of these medications as potentially risky is related to the risks of premature closure of the *ductus arteriosus* after use in the third trimester,[22] conflicting data on teratogenicity,[23] and perinatal complications after use in the third trimester,[22] respectively. Many of the potentially risky medications are used during pregnancy when safer alternatives are not available

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Table 3. Factors associated with use of potentially risky medications during pregnancy

Maternal characteristics	OR (95% CI)	Adjusted OR (95% CI)
Age (as continuous variable)	1.01 (0.99–1.02)	—
Marital status		
Married or cohabiting	Reference	—
Single/divorced/other	1.29 (1.01–1.63)	—
Education level		
Less than high school	1.40 (1.08–1.81)	1.20 (0.91–1.58)
High school	Reference	Reference
More than high school	1.07 (0.94–1.21)	1.10 (0.96–1.27)
Other	1.19 (0.99–1.43)	1.23 (1.01–1.50)
Working status		
Student	1.25 (1.03–1.51)	1.33 (1.09–1.63)
Housewife	1.40 (1.15–1.70)	1.29 (1.04–1.59)
HCP	1.28 (1.09–1.49)	1.31 (1.11–1.54)
Employed in other sector	Reference	Reference
Job seeker	0.97 (0.74–1.28)	0.92 (0.68–1.23)
None	1.08 (0.84–1.39)	0.93 (0.71–1.21)
Previous children		
Yes	1.13 (1.02–1.26)	1.14 (1.02–1.28)
No	Reference	Reference
Planned pregnancy		
Yes, not completely unexpected	Reference	—
No, it was not planned	1.21 (1.01–1.46)	—
Folic acid use before and/or during pregnancy		
Yes	Reference	Reference
No	1.26 (1.04–1.53)	1.26 (1.02–1.55)
Alcohol use after awareness of pregnancy		
Yes	1.28 (1.11–1.47)	1.29 (1.11–1.50)
No	Reference	Reference
Smoking during pregnancy		
Yes	1.30 (1.09–1.56)	1.30 (1.07–1.59)
No	Reference	Reference
Acute illness		
Yes	0.96 (0.46–1.99)	—
No	Reference	—
Chronic disorder		
Yes	3.93 (3.49–4.42)	3.99 (3.54–4.49)
No	Reference	Reference

The outcome variable is categorized as *using potentially risky medications* (1) and *using probably safe medications* (0). For *folic acid use* and *alcohol consumption*, the response "cannot remember" was treated as a missing value.
OR, odds ratio; CI, confidence interval; HCP, healthcare personnel.

or switching of medications is not recommended. Individual benefit–risk evaluations for mother and child have to be taken into consideration. Avoiding all potentially risky medications during pregnancy is unrealistic because some conditions require treatment, and the woman's medical history and disease severity must be taken into account.[5]

Interestingly, the highest proportion of women using unclassified medications was among women from Russia. This could be due to multiple factors: (i) many of the medications used in Eastern Europe may not be on the market in Northern Europe, U.S., or Australia and may lack a classification in the three reference systems used in the current study; and (ii) medication safety studies during pregnancy have so far focused on common exposures in the Western countries, causing a broader knowledge gap for medications used in other parts of the world. However, our findings at the country level should be interpreted with caution because of the small sample sizes in some of the countries.

Having a chronic disorder was the strongest predictor of the use of potentially risky medications during pregnancy. Women with a chronic disorder had an almost fourfold increased odds of using potentially risky medications compared with women without these conditions. Little information is available on which and to what extent maternal characteristics are associated with exposure to potentially "risky" medications. Previous studies[24,25] have reported that pregnant women with a chronic health condition are more likely to use medications with potential risks than women without these conditions. However, our study provided novel insights into the role of individual chronic disorders on the use of potentially risky medication during pregnancy. Among the individual chronic disorders, we found that anxiety and depression had the strongest association with the use of potentially risky medications during pregnancy.

Chronic conditions often require treatment and, even though safer alternatives may be available, switching medication is not always recommended. Switching medications can cause relapse in well-adjusted patients and increase the risk to the fetus. The importance of pre-pregnancy counselling should be emphasized to optimize antenatal prescribing, especially for conditions in which switching medication is not recommended.

The main strengths of this study include the uniform collection of data regarding medication use during pregnancy across several European countries. The use of a web-based recruitment strategy enabled us to reach a wide segment of the birthing population. An invitation to participate in the study was placed on websites frequently visited by pregnant women in the countries of interest, and an online questionnaire may be appropriate for women of childbearing age residing in countries with high Internet access. However, we cannot rule out the possibility of self-selection bias because respondents were women who had Internet access, happened to visit the actual website(s), and decided to participate in the study. However, recent

epidemiological studies indicate the validity of web-based recruitment methods.[26,27] In addition, women may answer more truthfully in an online questionnaire than in a face-to-face interview. The questionnaire comprised several questions on medication use based on timing and indication for use, and included information on OTC medications.

One limitation of the study was that information about medication use was self-reported and, thus, dependent on the women's reporting and recall. Therefore, an underestimation of medication use cannot be excluded. In addition, a risk of poorer recall cannot be ruled out for new mothers because data were recorded retrospectively. However, as shown previously,[4] this has only deflated the prevalence of short-term medication use, but not the use of chronic medications. Furthermore, our results depend on the classification system used, as they differ with respect to the allocation of drugs to risk categories. Addis *et al.*[8] compared these three classification systems and found that only 26% of the medications common to all three systems were placed in the same risk factor categories. Moreover, the FDA recently ruled to replace the current letter-based classification system with three detailed narrative subsections that provide explanations based on available information about the potential benefits and risks for the mother, fetus, and breastfeeding child.[28] Finally, this study was limited to describing medication utilization patterns during pregnancy and cannot evaluate the appropriateness of the medication use of the individual pregnant women. Our results should be interpreted with these strengths and limitations in mind.

CONCLUSION

It is reassuring that the majority of women across several European countries used medications classified as safe to use during pregnancy. However, a considerable proportion of women still used potentially risky medications. Both socio-demographic and medical conditions were associated with the use of potentially risky medications during pregnancy. However, such use may still be appropriate when considering the woman's underlying condition. Therefore, pre-pregnancy counselling is important to ensure safe medication use for both mother and child.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

KEY POINTS

- The majority of women used medications classified as safe to use during pregnancy.
- Twenty-eight percent of the women used medications classified as potentially risky.
- Regional differences were observed with respect to the use of medications in different risk groups.
- One out of five medications used by the women lacked a classification in the risk classification systems.
- Both socio-demographic and medical factors were associated with the use of potentially risky medications during pregnancy.

ETHICS STATEMENT

All participants provided informed consent by answering "Yes" to the question, "Are you willing to participate in the study?". The South-East Regional Ethics Committee in Norway approved the study. Ethical approval or notification of the relevant national ethics boards was achieved in specific countries as required by national legislation. All data were handled and stored anonymously.

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AUTHOR CONTRIBUTIONS

J. N. T. analyzed the data and drafted the manuscript. J. N. T., A. L., and H. N. planned the study, interpreted

the results, and revised the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript.

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