






## ORIGINAL ARTICLE

# Social media monitoring on the perceived safety of medication use during pregnancy: A case study from the Netherlands

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**Aims:** An increasing number of women trust the Internet for information about medication safety during pregnancy. This study aimed to evaluate the availability and accuracy of social media content on the perceived safety of medication use in pregnancy.

**Methods:** We performed a systematic search of posts related to medication safety during pregnancy in the Dutch language published on social media, blogs and forums between May 2011 and April 2016 using Coosto, a tool for social media monitoring. The perceived safety in the posts was compared with the Dutch Teratology Information Service (TIS) safety classifications.

**Results:** We included 1224 online posts, which described 1441 scenarios about medication safety in pregnancy. A total of 820 (57%) scenarios were in line with the TIS classification. Incorrect perception was higher for prescription medication compared to medication available over-the-counter (60 vs 25%). Furthermore, the safety classification of medications with a TIS classification on strict indication or second-line drugs (93%) and medications with insufficient knowledge on their safety during pregnancy (76%) was more likely to be incorrectly perceived by the public compared to medications with the TIS classification safe (24%).

**Conclusions:** Social media monitoring may be useful for surveillance of potentially unsafe use of medications in pregnancy. Many social posts related to medication safety during pregnancy provide inaccurate information. As this information may affect women's perceptions and decisions, accurate communication between healthcare providers and pregnant women regarding the benefits and risks of medications is vital.

## KEYWORDS

Internet, pharmaceutical preparations, pregnancy, risk perception, social media

## 1 | INTRODUCTION

Medication use during pregnancy is very common, with >80% of Dutch pregnant women using one or more prescription or over-the-

counter (OTC) medications.<sup>1</sup> Pregnant women use a wide variety of medications for pregnancy-related conditions (e.g. nausea and vomiting, gastric reflux, hypertensive disorders) and for conditions unrelated to pregnancy (e.g. asthma, migraine, hay fever), some of

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which cannot be discontinued. Pharmacotherapy during pregnancy involves a benefit–risk assessment, in which there is a trade-off between the potential benefits for the mother and possible risks for the foetus. Although there is insufficient data on the safety during pregnancy for many commonly used medications,<sup>2–4</sup> drug labelling, including the guidelines from the European Medicines Agency and US Food and Drug Administration,<sup>5,6</sup> may assist clinicians and pregnant women in making decisions regarding pharmacotherapy.

The Internet has become an important source of health information to supplement information provided by health care providers.<sup>7</sup> This is also applicable to pregnant women, who increasingly search the Internet for pregnancy-related information for topics such as foetal development, nutrition and medications in pregnancy, pregnancy complications, and prenatal care.<sup>8</sup> More specifically, most pregnant women use the Internet to search for information on a treatment prescribed and over 80% of the women used information from the Internet to influence their decisions about medication use in pregnancy.<sup>9,10</sup>

In a multinational cross-sectional study from 2010, as many as 83% of pregnant and postpartum women considered the quality of online information they retrieved to be *good* or *excellent*.<sup>9</sup> Pregnancy-related information is available on the Internet through many sources, each with a different level of credibility. In addition to information on websites managed by health services or governmental organisations, use of social media sites to search for medication safety information during pregnancy was reported in a 2013 online survey by 85% of a UK sample of women who were pregnant or delivered in the last year.<sup>10</sup> As social media is defined as a collection of websites and applications that enable users to create and share content or to participate in social networking,<sup>11</sup> content is mainly generated by lay people. Consequently, the quality of these unstructured real-world data is generally not clear for the public.

Using social media as a data source for pharmacoepidemiological research or pharmacovigilance is challenging due to technical, regulatory and ethical issues.<sup>12,13</sup> In a 2014 study, a limited number of chats on French forums was analysed to assess the quality and reliability of information on medication use in pregnancy shared by Internet users.<sup>14</sup> Likewise, Hansen et al. reported on YouTube videos as a source of information on medication use during pregnancy in 2016.<sup>15</sup> As both previous studies selected only one source of online information, these do not provide a complete overview of the quality and quantity of social media information available to pregnant women. In the current study, we systematically assessed the availability and accuracy of all social media content in the Dutch language on the safety of medication use during pregnancy using a social media monitoring tool as a novel method of data collection.

## 2 | METHODS

### 2.1 | Search strategy

We performed a systematic search of posts published on social media, which included Facebook, Instagram, Twitter, YouTube, LinkedIn,

#### What is already known about this subject

- Most pregnant women use the Internet to search for information on pharmacological treatment.
- Online pregnancy-related information is available through many sources, each with different levels of credibility.
- A complete overview of the quality and quantity of social media information available to pregnant women is lacking.

#### What this study adds

- There is an abundance of social media posts related to the medication safety during pregnancy.
- Over 40% of posts were not in line with the current knowledge about the medications' risk.
- This inaccuracy of online information may affect women's perception and decisions regarding medication use during pregnancy.

Pinterest, blogs, forums and reviews, between 1 May 2011 and 30 April 2016 related to the safety of medication use during pregnancy using the social media monitoring tool Coosto.<sup>16</sup> This tool enables systematic searches of online content, in different sources and time frames. Furthermore, it keeps an archive of all Dutch posts published on social media and thereby provides the opportunity to extract all posts on a certain topic. Coosto has been used for similar purposes in scientific research before.<sup>17,18</sup> As we used open access Internet sources in which we considered the research as textual representation instead of human subject research,<sup>19</sup> no ethical approval was required. All information included in Coosto datasets is publicly available and does not contain identifiable data besides a nickname and information voluntarily shared by the online contributors.

The search strategy consisted of the following elements: (i) a pregnancy-related term; (ii) commonly used medications during pregnancy; and (iii) a maternal complication related to pregnancy or an adverse outcome for the child, including general statements of safety. The list of commonly used medications ( $n = 127$ , Appendix A), which included both prescription and OTC medications, was compiled using recent data from the PRenancy and Infant DEvelopment (PRIDE) Study.<sup>20</sup> We used both the generic and the brand name of the medications. The complications and adverse outcomes included miscarriage, gestational diabetes, gestational hypertension, preeclampsia, eclampsia, haemolysis, elevated liver enzymes and low platelet (HELLP) syndrome, stillbirth, preterm birth, low birth weight, birth defects, small-for-gestational age, large-for-gestational age, and macrosomia. The complete search strategy is available in Appendix B. All search terms were entered as free text, because Coosto does not contain keywords or subject headings comparable to the common bibliographic databases.

## 2.2 | Inclusion and exclusion criteria

We included posts published in the Dutch language describing a potential association between the use of a specific medication during pregnancy and maternal complications or adverse outcomes for the child, as well as posts implying overall safety or risks of the use of medication during pregnancy. All posts from the web site <https://www.apotheek.nl> were excluded, because these were only described in interactions with other medications, providing no information on the safety or potential risks of the medications selected. Furthermore, duplicate posts were excluded, as well as posts without text.

A random sample of 101 posts was independently assessed for eligibility by 3 reviewers (M.v.G., A.R. and T.v.d.B.), which showed good to excellent agreement between the pairs of reviewers (kappa statistics ranging between 0.79 and 0.83). Therefore, the remaining posts were assessed by a single reviewer. In case of doubt about eligibility, the post was discussed with the other reviewers to accomplish a joint decision.

## 2.3 | Data abstraction

From each post, we extracted the date of publication, URL, text, source, medication mentioned, pregnancy complication or other adverse outcome for the child mentioned, and the perception of safety implied in the post. The latter was classified into 4 mutually exclusive categories: (i) safe; (ii) use on strict indication or second-line drug; (iii) insufficient knowledge on the safety during pregnancy available; or (iv) unsafe or contraindicated. Posts with an unclear perception (e.g. stating that a medication was safe in one part of the post, but also stating unsafe in another part) were discussed among the reviewers to determine the conclusion on the perception of safety implied.

For all medications mentioned in the posts included, we retrieved the safety information as communicated by the Teratology Information Service (TIS) of the Netherlands Pharmacovigilance Centre Lareb.<sup>21</sup> This safety information is grouped into 6 categories; to match the safety classification of the social media posts we combined the categories *pharmacologic effect*, *monitor use* and *teratogenic*, *monitor use* into *use on strict indication* or *second-line drug* and the categories *pharmacologic effect*, *contraindicated* and *teratogenic*, *contraindicated* into *unsafe* or *contraindicated*. If a medication was listed in multiple categories depending on dose or indication for use, we selected the safety application that is most applicable to pregnant women (i.e. OTC medication, most commonly occurring indication).

## 2.4 | Statistical analysis

We used descriptive statistics to characterize the information abstracted from the social media posts. To evaluate the accuracy of the social media content, we compared the perception of safety from the posts with the TIS classification as reference standard. Furthermore, we assessed whether the calendar year of publication, source

of publication, type of medication (OTC vs prescription) and TIS classification were associated with accuracy by determining the risk difference in incorrect perception with its 95% confidence interval (CI). Analyses were conducted using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA).

## 3 | RESULTS

The search yielded 9227 posts published between May 2011 and April 2016, of which 1224 posts related to the safety of medication use were included in this study. Posts were excluded because they were empty ( $n = 92$ ), duplicates ( $n = 933$ ), did not describe the association between medication use and outcomes (e.g. focused on pharmacological treatment for the outcome or mentioned medication use and pregnancy without any connection;  $n = 6780$ ), only included unselected medications or outcomes ( $n = 100$ ) or groups of medication ( $n = 53$ ), or were inconclusive about the association (e.g. asked a question about safety;  $n = 45$ ). The majority of posts included originated from forums (78%), followed by blogs (12%) and Facebook (7%).

The posts described 1441 scenarios on medication safety in pregnancy. These scenarios concerned 111 medications and 30 outcomes; the most frequently mentioned medications and outcomes are listed in Tables 1 and 2, respectively. According to the TIS classification, 57 of these medications (51%) are considered safe during pregnancy, 4 medications (4%) are contraindicated, 21 medications (19%) may only be used on strict indication and, for 29 medications (26%), insufficient knowledge on the safety during pregnancy is available.

In Table 3, the agreement between safety as perceived in the online posts and safety information as communicated by the TIS is shown. A total of 820 (57%) scenarios described in the posts were in line with the TIS classification. The level of agreement was highest for contraindicated medication (80%), followed by medications considered safe during pregnancy (76%), medications with insufficient knowledge (24%), and medications on strict indication or second-line drugs (7%). More specifically, risks of adverse outcomes were overestimated in 24% of posts on medications considered safe, 44% of posts on medications on strict indication or second-line drugs, and 32% of posts on medications with insufficient knowledge. Underestimation of risks was most common for medications on strict indication or second-line drugs (49%), followed by medications with insufficient knowledge (44%) and contraindicated medication (20%). For the individual medications considered safe during pregnancy with at least 10 posts, the percentage of correct online perceptions ranged between 20% (codeine and metronidazole) and 100% (beclomethasone for asthma, lactulose and methyl dopa). These percentages ranged between 54% (acetylsalicylic acid) and 91% (ibuprofen) for contraindicated medication, 0% (fluoxetine, paroxetine, progesterone, and venlafaxine) and 33% (morphine) for medication on strict indication of second-line drugs, and 13% (ondansetron) and 39% (metformin) for medications with insufficient knowledge. In Table 4, examples of correctly and incorrectly perceived risks by TIS classification are shown.

**TABLE 1** Medications mentioned in relation to safety of use during pregnancy in  $\geq 10$  Dutch posts published on social media, blogs, and forums, 2011–2016

Medication	No. posts
Paracetamol <sup>a</sup>	213
Ibuprofen <sup>a</sup>	101
Omeprazole <sup>a</sup>	70
Acetylsalicylic acid <sup>a</sup>	54
Prednisone	52
Progesterone	52
Meclozine/pyridoxine	46
Paroxetine	44
Diclofenac <sup>a</sup>	39
Calcium carbonate/magnesium carbonate <sup>a</sup>	36
Fluoxetine	33
Metoclopramide	32
Ondansetron	32
Salbutamol	32
Citalopram	24
Amoxicilline	22
Xylometazoline <sup>a</sup>	20
Lactulose <sup>a</sup>	19
Melatonine <sup>a</sup>	18
Macrogol/electrolytes <sup>a</sup>	17
Beclometasone (asthma)	16
Cetirizine <sup>a</sup>	16
Lamotrigine	15
Morphine	15
Alginic acid <sup>a</sup>	14
Miconazole (vaginal) <sup>a</sup>	14
Metformin	13
Sumatriptan	13
Tramadol	13
Sulfasalazine	13
Venlafaxine	12
Amoxicillin/clavulanic acid	11
Clotrimazole (vaginal) <sup>a</sup>	11
Methyldopa	11
Codeine <sup>a</sup>	10
Labetalol	10
Metronidazole	10

<sup>a</sup>Available over-the-counter.

The year of publication of the online post and the source of publication were not associated with incorrect perception of the safety of medication use during pregnancy, although posts on Twitter seemed somewhat more likely to be incorrectly perceived compared to forum posts (59% vs 42%; risk difference 17.7, 95% CI 0.0–35.1; Table 5).

**TABLE 2** Outcomes mentioned in relation to safety of use during pregnancy in  $\geq 10$  Dutch posts published on social media, blogs and forums, 2011–2016

Outcome	No. posts
Safety in general	1239
Miscarriage	94
Birth defects	76
Congenital heart defects	15
Cryptorchidism	11
Poor start	11
Preterm birth	10

The safety of medications that are available on prescription only was more often incorrectly perceived than the safety of medications that are available OTC (60% vs 25%; risk difference 35.5, 95% CI 30.7–40.3). Furthermore, medications with the TIS classification on strict indication or second-line drugs (93%, risk difference 69.8, 95% CI 65.7–73.9) and medications with insufficient knowledge (76%; risk difference 52.1, 95% CI 44.9–59.4) were far more likely to receive an incorrect perception of safety compared with medications that are considered safe according to the TIS classification (24%).

## 4 | DISCUSSION

In this study, we reviewed over 9000 social media posts and abstracted information from 1224 posts on forums, blogs, Facebook, Twitter and other social media sources on the safety of medication use during pregnancy. We compared the perceived safety as reported in the posts on 1441 scenarios between selected medication use during pregnancy and safety outcomes with the information from the TIS of the Netherlands Pharmacovigilance Centre Lareb, suggesting that over 40% of posts were not in line with the current knowledge about the medications' risk. This was particularly the case for prescription medication and medications with a TIS classification on strict indication or second-line drugs, and medications with insufficient knowledge on their safety during pregnancy.

This is the first study to systematically review a large number of posts published publicly on multiple social media platforms related to the safety of medication use during pregnancy. Two previous studies focussed on a single social media source only: chats on French forums<sup>14</sup> and English YouTube videos.<sup>15</sup> Similar to those studies, we observed low concordance between the perceived online safety and official ratings. Concordance was lowest for the TIS categories with more subtle interpretations (i.e. on strict indication or second-line and insufficient knowledge), which may resemble the binary treatment decision pregnant women have to make: should I take this medication? Indeed, most medications within these TIS categories were perceived as either safe or contraindicated based on the social media posts. This may particularly be a problem for the commonly used antidepressants, for which an individual-based benefit–risk assessment of pharmacological treatment is vital. To complicate this assessment of medication safety using

**TABLE 3** Perceived safety of medications in  $\geq 10$  Dutch posts published on social media, blogs, and forums, 2011–2016, compared with the classification of the Teratology Information Service (TIS)

Medication	Number of posts				
	Correct perception	Incorrect perception: Perceived as			
		Safe	Contraindicated	Strict indication	Insufficient knowledge
<b>TIS classification: Safe</b>					
All medications	607	NA	108	25	55
Paracetamol <sup>a</sup>	168	NA	37	3	5
Omeprazole <sup>a</sup>	55	NA	8	0	7
Meclozine/pyridoxine	44	NA	1	0	1
Calcium carbonate/magnesium carbonate <sup>a</sup>	32	NA	3	0	1
Salbutamol	26	NA	2	3	1
Metoclopramide	25	NA	4	1	2
Amoxicillin	20	NA	0	2	0
Lactulose <sup>a</sup>	19	NA	0	0	0
Beclometasone (asthma)	16	NA	0	0	0
Alginic acid <sup>a</sup>	13	NA	1	0	0
Miconazole (vaginal)	13	NA	1	0	0
Cetirizine <sup>a</sup>	13	NA	1	0	2
Methyldopa	11	NA	0	0	0
Sulfasalazine	10	NA	1	0	1
Lamotrigine	10	NA	4	0	1
Xylometazoline <sup>a</sup>	10	NA	8	1	1
Clotrimazole (vaginal) <sup>a</sup>	8	NA	0	2	1
Amoxicillin/clavulanic acid	5	NA	0	2	4
Sumatriptan	5	NA	5	0	3
Codeine (short term) <sup>a</sup>	2	NA	1	3	4
Metronidazole	2	NA	3	4	1
<b>TIS classification: Contraindicated</b>					
All medications	155	19	NA	19	2
Ibuprofen <sup>a</sup>	92	3	NA	6	0
Diclofenac <sup>a</sup>	33	0	NA	5	1
Acetylsalicylic acid <sup>a</sup>	29	16	NA	8	1
<b>TIS classification: Strict indication/second-line</b>					
All medications	19	142	111	NA	18
Prednisone	6	19	27	NA	0
Morphine	5	5	4	NA	1
Labetalol	2	5	1	NA	2
Tramadol	1	3	4	NA	5
Citalopram	1	15	7	NA	1
Fluoxetine	0	21	12	NA	0
Paroxetine	0	11	29	NA	4
Progesterone	0	43	9	NA	0
Venlafaxine	0	6	6	NA	0
<b>TIS classification: Insufficient knowledge</b>					
All medications	39	64	51	7	NA

(Continues)

**TABLE 3** (Continued)

Medication	Number of posts				Insufficient knowledge
	Correct perception	Incorrect perception: Perceived as			
		Safe	Contraindicated	Strict indication	
Metformin	5	3	4	1	NA
Melatonin	4	3	10	1	NA
Ondansetron	4	23	5	0	NA
Macrogol/electrolytes	3	8	5	1	NA

<sup>a</sup>Available over-the-counter.

**TABLE 4** Examples of correctly and incorrectly perceived risks on the safety of medication use in Dutch posts published on social media, blogs, and forums, 2011–2016

TIS classification	Correctly perceived	Incorrectly perceived as ...
Safe	What a dumb doctor who does not want to prescribe Emesafene! It has been prescribed to women with nausea during pregnancy for years and it is completely safe!	{... unsafe}: Paracetamol is cheap and available without prescription and can be used during pregnancy. New research results, however, indicate serious side effects, particularly among pregnant women. [...]
Contraindicated	Do not take ibuprofen when you are pregnant, it is harmful for the baby!	{... safe} [...] further in terms you may use Dafalgan and ibuprofen or Brufen. [...]
Strict indication or second-line	In certain dosages, prednisone may be used safely during pregnancy.	{... contraindicated} until October last year, I used paroxetine 30 mg. I was ABSOLUTELY NOT allowed to become pregnant by my GP. [...]
Insufficient knowledge	[...] I quit using it [melatonin] because it is still unknown whether it is harmful. [...]	{... unsafe} [...] I previously used Keppra, but it caused a miscarriage.

TIS, Teratology Information Service.

**TABLE 5** Risk of incorrect perception of safety of medication use during pregnancy according to Dutch posts published on social media, blogs and forums, 2011–2016, by medication characteristics

Characteristic	Total n	Incorrect perception		Risk difference (95% CI)	
		n	(%)		
<b>Year of online publication</b>					
2011 <sup>a</sup>	248	92	(37)	Reference	
2012	392	177	(45)	8.1	(0.0–15.9)
2013	321	143	(45)	7.5	(0.0–15.6)
2014	216	88	(41)	3.6	(–5.3–12.6)
2015	195	86	(44)	7.0	(–2.2–16.3)
2016 <sup>a</sup>	69	35	(51)	13.6	(0.0–27.1)
<b>Post source</b>					
Forum	1,128	470	(42)	Reference	
Blog	179	84	(47)	5.3	(–2.5–13.1)
Facebook	98	46	(47)	5.3	(–4.9–15.5)
Twitter	32	19	(59)	17.7	(0.0–35.1)
<b>Available over-the-counter</b>					
Yes	698	173	(25)	Reference	
No	743	448	(60)	35.5	(30.7–40.3)

(Continues)

TABLE 5 (Continued)

Characteristic	Total n	Incorrect perception		Risk difference (95% CI)
		n	(%)	
<b>TIS classification</b>				
Safe	795	188	(24)	Reference
Contraindicated	195	40	(21)	-3.1 (-9.7-3.5)
Strict indication/second-line	290	271	(93)	69.8 (65.7-73.9)
Insufficient knowledge	161	122	(76)	52.1 (44.9-59.4)

<sup>a</sup>Only part of the year was included.

TIS, Teratology Information Service.

online sources, articles in which harm was associated with antidepressant use during pregnancy receive more tweets than articles with reassuring results,<sup>22</sup> biasing public opinion towards potential risks.

However, for the medications in the more definitive TIS classifications safe and contraindicated, concordance was also suboptimal (approximately 80%). This may have profound impact on clinical practice. For medications that are considered safe during pregnancy, perceived risks associated with use may result in non-adherence, which for some medications, including salbutamol, lamotrigine and different types of antibiotics, may impair maternal and/or infant health. Several studies on women's beliefs and risk perception on medication use in pregnancy confirm that pregnant women tend to overestimate the potential risks and subsequently chose to avoid the use of certain medications.<sup>23-26</sup> By contrast, when contraindicated medication is perceived as safe, pregnant women may decide to take this medication, putting their unborn infants at risk of adverse outcomes.

A recent qualitative study stresses that women lack knowledge about the effects of their medication use on the unborn child and that they use, among others, online sources such as blogs and social media to make decisions about medication use during pregnancy.<sup>27</sup> In light of the inaccuracy of information in online posts, health practitioners involved in care for pregnant women should be aware of this need for information and provide pregnant women with reliable resources to make an evidence-based decision regarding pharmacological treatment. However, we do not have data available on the number of times correct and incorrect posts are actually being read by pregnant women. This information, which may be collected using other study designs and methods of data collection, could shed more light on the actual consequences of inaccurate information in online posts.

The medications most often mentioned in relation to safety of use during pregnancy include relatively many medications that are available OTC, such as paracetamol, ibuprofen and omeprazole. This seems to largely agree with the medications most often used during pregnancy in Europe and North America.<sup>3,28-31</sup> Although valid prevalence estimates of OTC medication use during pregnancy in the Netherlands are not available, ibuprofen use during pregnancy, which is contraindicated, seems far less common in the Netherlands compared to the USA (<2 vs >15%, respectively),<sup>20,32</sup> whereas this medication was often mentioned in the Dutch online posts. Therefore, mentions in

online posts do not imply actual medication use and these results cannot be extrapolated to indicate which medications are most often used during pregnancy in the Netherlands.

In addition to the ability to review posts on multiple social media platforms, other strengths of this study include the predefined selection of prescription and OTC medications based on real-world data and the inclusion of a wide variety of maternal complications and adverse pregnancy outcomes. The latter gives a broader overview of medication safety during pregnancy than the frequent focus on birth defects as the outcome of interest only. However, our study also has some limitations. First, we included online posts in the Dutch language only. Petersen et al. showed that there may be substantial individual and geographical variations in risk perception regarding medication,<sup>25</sup> so our results may not be generalizable to other countries. Second, we may have missed posts due to typos in medication names and pregnancy complications or outcomes, which might be more likely to contain incorrectly perceived safety information. In future studies, including commonly made typos could be included to further improve identification of relevant posts. Additionally, although Coosto claims to find every post that fulfils the search criteria,<sup>16</sup> currently no reference standard is available to confirm its validity and reliability. However, there is no reason to assume that posts with an incorrect perception of risk are more likely to be detected than posts with a correct perception and vice versa, limiting the probability of bias in the accuracy analyses. Third, the posts were hand-coded by a single reviewer as it was too time-consuming to code all posts in duplicate. Although agreement between reviewers was good to excellent in a random sample of posts, this may have led to inaccuracies in the selection and abstraction of data. Natural language processing may overcome this problem as it is capable of generating structured information from unstructured free text,<sup>33</sup> but no algorithms for this task are currently available in the Dutch language. Finally, the identity of the authors of the online posts is unknown, but based on the context of the posts, we may assume that the results reflect the actual knowledge of pregnant women themselves.

In conclusion, there is an abundance of Dutch social media posts on the safety of medication use during pregnancy, but a large proportion of these posts provides inaccurate information. As this information may influence individual treatment decisions during pregnancy, recognition and adequate communication between pregnant women

and healthcare providers may assist women in making evidence-based decisions regarding pharmacotherapy during pregnancy.

## COMPETING INTERESTS

There are no competing interests to declare.

## CONTRIBUTORS

M.M.H.J.v.G. was the lead author, responsible for study design, data collection, statistical analysis, data interpretation and preparation of the draft manuscript. A.R. and T.H.v.d.B. were responsible for study design, data collection, statistical analysis, data interpretation, and critically reviewed the manuscript. S.J.H.B., W.K. and H.N. were responsible for study design, data interpretation and critically reviewed the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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## APPENDIX A

### LIST OF MEDICATIONS SELECTED

Generic name	Brand name(s) /alternative name(s)
Acetic acid	Acid ear drops
Acetylcysteine	Fluimicil
Acetylsalicylic acid	Aspirin
Aciclovir	Zovirax
Adalimumab	Humira
Alprazolam	Xanax
Amitriptyline	
Amoxicillin	
Amoxicillin/clavulanic acid	Augmentin
Antacid	Gaviscon, regla-pH, Rennie*
Azelastine	
Beclometasone	Qvar
Benzoyl peroxide	
Betamethasone	Betnelan, Celestone, Diprosone
Bromhexine	Bisolvon
Brotizolam	

(Continues)

(Continued)

Generic name	Brand name(s) /alternative name(s)
Budesonide	Entocort, Pulmicort, Rhinocort
Calcipotriol/betamethasone	Dovobet
Calcium carbonate	Calcichew
Carbamazepine	Tegretol
Carbasalate calcium	Ascal
Carbomer	Artificial tears, Liposic
Cetirizine	
Chlorhexidine	
Chloroquine	
Ciclesonide	Alvesco
Citalopram	Cipramil
Clemastine	Tavegil
Clobetasol	Dermovate
Clobetasol	Emovate
Clotrimazole	Canesten
Codeine	
Colecalciferol	Devaron, Divisun
Cromoglicic acid	
Dexamethasone	Sofradex
Diazepam	
Diclofenac	
Enoxaparine	Clexane
Escitalopram	Lexapro
Etanercept	Enbrel
Ferrous fumarate	Iron tablets
Fexofenadine	
Fluoxetine	Prozac
Fluticasone	Avamys, Flixonase, Flixotide
Formoterol	Atimos
Formoterol/budesonide	Symbicort
Fusidinic acid	Fucithalmic
Glibenclamide	
Hydrocortisone	
Hydrocortisone acetate	Hydrocortisone Vaseline cream
Hydrocortisone/acetic acid	
Hydroxocobalamin	Vitamin B12
Hydroxychloroquine	Plaquenil
Ibuprofen	
Indometacin	
Insulin	Insulin aspart, Novorapid, insulatart
Ipratropium	Atrovent
Labetalol	

(Continues)

(Continued)

Generic name	Brand name(s) /alternative name(s)
Lacosamide	Vimpat
Lactulose	
Lamotrigine	Lamictal
Levetiracetam	Keppra
Levocetirizine	Xyzal
Levothyroxine	Euthyrox, Thyrax
Lidocaine	
Loperamide	Imodium
Loratadine	Telfast
Losartan	
Macrogol	Forlax
Macrogol/electrolytes	Movicolon
Magnesium hydroxide	
Mebendazole	Antiworm
Meclizine	Emesafene
Melatonin	
Mercaptopurine	Puri-Nethol
Mesalazine	Mezavant, Pentasa, Salofalk
Metformin	
Methyldopa	Aldomet
Metoclopramide	Primperan
Metronidazole	Flagyl
Miconazole	Daktarin, Gyno-daktarin
Midazolam	
Mometasone	Nasonex
Morphine	
Mupirocin	Bactroban
Nadroparine	Fraxiparine
Nifedipine	Adalat
Nitrofurantoin	Furabid
Noscapine	
Nystatin	
Olanzapine	Zyprexa
Olopatadine	Opatanol
Omeprazole	Losec
Ondansetron	Zofran
Oxcarbamazepine	Trileptal
Pantoprazole/claritromycin/ amoxicillin	Pantopac
Paracetamol	
Paroxetine	Seroxat
Penciclovir	Fenistil
Pimecrolimus	Elidel

(Continues)

(Continued)

Generic name	Brand name(s) /alternative name(s)
Pramocaine	Nestosyl
Prednisone	
Progesterone	Proluton
Propranolol	
Psyllium	Metamucil
Rizatriptan	Maxalt
Salbutamol	Airomir, Ventolin
Salicylic acid	
Salmeterol	Serevent
Salmeterol/fluticasone	Seretide
Scopolamine butylbromide	Buscopan
Selenium sulfide	Selsun
Sulfasalazine	
Sumatriptan	Imigran
Temazepam	
Terbutaline	Bricanyl
Thyme sirup	
Tioguanine	Lanvis
Tiotropium	Spiriva
Tramadol	
Triamcinolone	
Trisodium phosphate	Colex
Urea	Calmurid
Valproic acid	Depakine
Venlafaxine	Efexor
Verapamil	
Xylometazoline	Otrivin

## APPENDIX B

### SEARCH STRATEGY

#### (1) a pregnancy-related term

(zwanger\* OR "in verwachting" OR "aanstaande moeder")

#### (2) commonly used medications during pregnancy

(magnesiumhydroxide OR regla-ph OR rennie\* OR gaviscon OR maagtablet OR omeprazol OR losec OR pantopac OR scopolaminebutyl OR buscopan OR metoclopramide OR primperan OR zofran OR ondansetron OR lactulose OR macrogol OR forlax OR movicolon OR psylliumzaad OR psylliumvezels OR metamucil OR klyasma OR colex OR loperamide OR imodium OR nystatine OR miconazol OR daktarin OR budesonide OR entocort OR sulfasalazine OR mesalazine OR mezavant OR salofalk OR pentasa OR metformine OR glibenclamide OR insuline OR novorapid OR insulatard OR

colecalfiferol OR divisun OR devaron OR calciumcarbonaat OR calcichew OR enoxaparine OR clexane OR nadroparine OR fraxiparine OR acetylsalicylzuur OR aspirine OR carbasalaatcalcium OR ascal OR ferrofumaraat OR ijzertabletten OR "vitamine b12 injectie" OR methyldopa OR propranolol OR labetalol OR nifedipine OR verapamil OR losartan OR hydrocortisonacetaat OR lidocaïne OR clotrimazol OR seleensulfide OR hydrocortison OR clobetason OR emovate OR triamcinolon OR betamethason OR betnelan OR diprosone OR clobetasol OR dermovate OR aciclovir OR zovirax OR penciclovir OR fenistil OR mupirocine OR bactroban OR dovobet OR pimecrolimus OR elidel OR nestosylzalf OR chloorhexidine OR benzoylperoxide OR ureum OR calmurid OR metronidazolcreme OR canesten OR "gyno-daktarin" OR progesteron OR proluton OR celestone OR prednison OR levothyroxine OR euthyrox OR thyrax OR amoxicilline OR augmentin OR nitrofurantoïne OR furabid OR mercaptopurine OR "puri-nethol" OR tioguanine OR lanvis OR etanercept OR enbrel OR adalimumab OR humira OR indometacine OR ibuprofen OR diclofenac OR paracetamol OR tramadol OR morfine OR advil OR sarotex OR panadol OR finimal OR citrosan OR antigrippine OR sanalgin OR saridon OR sumatriptan OR imigran OR rizatriptan OR maxalt OR levetiracetam OR keppra OR carbamezepine OR tegretol OR oxcarbazepine OR trileptal OR valproïnezuur OR depakine OR lamotrigine OR lamictal OR lacosemide OR vimpat OR olanzapine OR zyprexa OR alprazolam OR xanax OR midozalam OR brotizolam OR temazepam OR diazepam OR melatonine OR amitriptyline OR fluoxetine OR prozac OR citalopram OR cipramil OR paroxetine OR seroxat OR escitalopram OR lexapro OR venlafaxine OR efexor OR metronidazol OR flagyl OR chloroquine OR hydroxychloroquine OR

plaquenil OR xylometazoline OR otrivin OR azelastine OR beclometason OR rhinocort OR fluticason OR flixonase OR avamys OR mometason OR nasonex OR formoterol OR atimos OR salbutamol OR ventolin OR airomir OR salmeterol OR serevent OR terbutaline OR bricanyl OR seretide OR symbicort OR qvar OR pulmicort OR flixotide OR alvesco OR ipratropium OR atrovent OR tiotropium OR spiriva OR acetylcysteïne OR fluimicil OR broomhexine OR bisolvon OR codeïne OR noscapine OR tijmsiroop OR dropsiroop OR clemastine OR tavegyl OR cetirizine OR levocetirizine OR xyzal OR loratidine OR fexofenadine OR telfast OR emesafene OR meclozine OR fusidinezuur OR fusithalamic OR sofradex OR cromoglicinezuur OR olopatadine OR opatanol OR carbomeer OR "liposic ooggel" OR kunsttranen OR "zure oordruppels" OR "sorradox oordruppels")

(3) **a maternal complication related to pregnancy or an adverse outcome for the (unborn) child, including general statements of safety**

(HELLP OR zwangerschapsvergiftiging OR pre-eclampsie OR zwangerschapshypertensie OR "hoge bloeddruk tijdens de zwangerschap" OR "diabetes gravidarum" OR zwangerschapsdiabetes OR zwangerschapssuiker OR "complicatie tijdens zwangerschap" OR zwangerschapscomplicatie OR miskraam OR misgeboorte OR curettage OR "laag geboortegewicht" OR dysmaturiteit OR dysmatuur OR macrosomie OR macrosoom OR "hoog geboortegewicht" OR "aangeboren afwijking" OR vroeggeboorte OR "te vroeg geboren" OR prematuur OR prematuriteit OR "intra-uteriene vruchtdood" OR "dodgeboren kind" OR (veilig\* zwanger\*) OR (schadelijk\* zwanger\*))