



## The use of risk medication during pregnancy: data from the Dutch Pregnancy Drug Register

Annerose E. van der Mijle<sup>1</sup>, Veronique Y.F. Maas<sup>1\*</sup>,  
Anne-Marie J.M.P. van Gorp<sup>1</sup>, Maartje Conijn<sup>1</sup>

<sup>1</sup>Pharmacovigilance Centre Lareb, 's-Hertogenbosch,  
The Netherlands

\*Presenting author: [v.maas@lareb.nl](mailto:v.maas@lareb.nl)

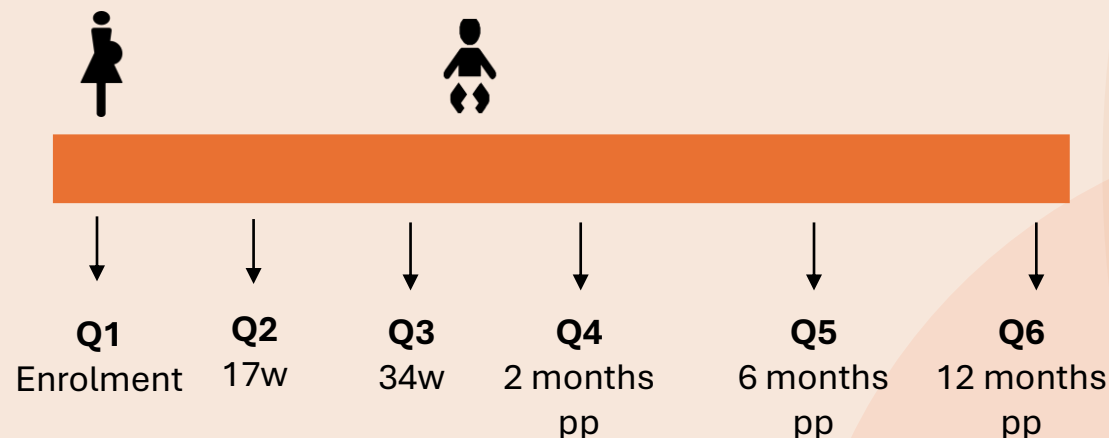
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## Introduction

- Some medication are known to have **teratogenic**- or other harmful effects on the unborn child.
- For medication with a high risk of congenital malformations, a **pregnancy prevention program (PPP)** may be introduced.
- Previous studies have shown that, **despite warnings** on the use of 'risk medication' during pregnancy, it might still be used by women of childbearing age.
- This study aims to gain insight into **the patterns of use of risk medication** during their critical risk windows in the Dutch setting.

## Methods

- Medication classified as '**risk medication**' during a certain period in pregnancy were selected according to the risk classification on the website of the Dutch Teratology Information Service (TIS).
- This may be related to either the high risk of congenital malformations or other severe complications on infant health.
- Data on medication use and pregnancy outcomes was obtained from the **Dutch Pregnancy Drug Register (DPDR)**, an ongoing nationwide prospective cohort study collecting data by web-based questionnaires.
- A maximum of 6 **online questionnaires** are completed by participant, three during the pregnancy and three up until 1 year after birth (**Figure 1**).
- All participants **reporting an exposure** to one of the selected medication were included.
- Exposures outside the **critical period** of development for the congenital malformation or complication associated with the medication were excluded.
- **Primary outcome** was defined as the pattern of medication use during pregnancy
  - Course of medication use during pregnancy
  - Pregnancy- and child outcomes of the exposed pregnancy.
- Descriptive analysis were performed.



**Figure 1. Questionnaire distribution schedule of the DPDR.**

Abbreviations; pp = postpartum, Q = questionnaire, w = weeks of gestation

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## Results (1)

- Based on the risk classifications of the Dutch TIS, a total of 78 medication were classified as **risk medication**.
- At moment of data-extraction, 17.023 participants were enrolled in the DPDR.
- A total of **40 (51,3%) of these risk medication were reported** somewhere in the DPDR (hence, exposure could have taken place prior to, during or after pregnancy).
- A total of **106 exposures were reported to be used during the critical window by 99 women**.
- A total of 14 women used medication within a **PPP**; topiramate (N = 9), valproic acid (N = 2), retinoids N = 2) and mycophenolic acid (N = 1) (**Table 1**).
- The most prevalent exposure of risk medication was **NSAIDs**. A total of 43 participants used an NSAID in the second half of pregnancy (N = 46 exposures).
- The majority of the participants exposed to NSAIDs (N = 23; 53,5%) used **ibuprofen**.
- Sixteen women were exposed to an ACE inhibitor or AT2-antagonist, nine of them started **less than a week before delivery**.

Table 1. Use of risk medication during pregnancy (part 1)

Risk medication groups	Critical period	Exposures in pregnancy <sup>1</sup>	Exposures critical period <sup>1</sup>
<b>PPP</b>			
- Topiramate	<i>Entire pregnancy</i>	9	9
- Valproic acid		2	2
- Retinoids		2	2
- Mycophenolic acid		1	1
<b>NSAID<sup>2</sup></b>			
- Ibuprofen	<i>&gt; 20 weeks of gestations</i>	323	23
- Naproxen		101	8
- Diclofenac		68	6
- Excedrin <sup>®3</sup>		39	4
- Acetylsalicylic acid		30	3
- Flurbiprofen		5	1
- Indomethacin		3	1
<b>ACE inhibitors and AT II antagonists<sup>4</sup></b>			
- Enalapril	<i>2<sup>nd</sup> &amp; 3<sup>rd</sup> trimester</i>	26	14
- Lisinopril		3	2

<sup>1</sup>Unique participants with an exposure to this medicine. Women can have multiple exposures within the same medicine group;

<sup>2</sup>No exposures in the critical period for; meloxicam, carbasalate calcium, metamizole and propyphenazone;

<sup>3</sup>Excedrin = brand name for acetylsalicylic acid with paracetamol and caffeine;

<sup>4</sup>No exposures in the critical period for; perindopril, losartan, irbesartan or candesartan.

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**Table 1. Use of risk medication during pregnancy (part 2)**

Risk medication groups	Critical period	Exposures in pregnancy <sup>1</sup>	Exposures critical period <sup>1</sup>
<b>Vitamin K antagonists</b>			
- Acenocoumarol	<i>Entire pregnancy</i>	9	9
- Phenprocoumon		1	1
<b>Antithyroid medication</b>			
- Propylthiouracil	<i>Entire pregnancy</i>	11	11
- Thiamazole		5	5
<b>Antifungals</b>			
- Fluconazole	<i>Longterm use</i>	36	1
<b>Antibiotics<sup>2</sup></b>			
- Doxycycline	<i>&gt;16 weeks of gestations</i>	20	1
- Minocycline		4	1
- Gentamicin	<i>Entire pregnancy</i>	1	1

<sup>1</sup>Unique participants with an exposure to this medicine. Women can have multiple exposures within the same medicine group;

<sup>2</sup>No exposures in the critical period for; tetracycline or tobramycin.

## Results (2)

- Ten women reported the use of **vitamin K antagonists** during pregnancy (**Table 1**). All of them used it before week 6 or after week 12, not in the most critical period for coumarin embryopathy.
- Antithyroid medication were used by 12 women. All of them used **only one antithyroid medication** at the same time.
- Fluconazole was used long term by one women, two women used tetracyclines after week 16 and one women used gentamycin around the time of delivery.
- One pregnancy exposed to **topiramate** was terminated because of Pentalogy of Cantrell.
- **No other major congenital malformations** or severe infant health complications were reported.

## Conclusion

- The usage of risk medication during pregnancy is still **quite common** in the Dutch setting.
- Although the use of some risk medications during pregnancy may be a conscious consideration, it is important to make women and healthcare professionals **aware of the possible effects** of medication on the unborn child.
- Especially for the use of **NSAIDs** (available over-the-counter) more awareness on its risks in the second half of pregnancy is required.