



IMI2 821520 - ConcePTION

ConcePTION

WP5 - Dissemination and education for HCPs, pregnant and breastfeeding women and general public

D5.4 Report with landscape analysis

<p>Lead contributor</p>	<p>Task 5.1.1: Alison Oliver (27 – ENTIS), Ludivine Douarin (39 – Sanofi)</p> <p>Task 5.1.2: Ulrika Nörby (29 – Region Stockholm), Ludivine Douarin (39 – Sanofi), Chantal El Haddad (39 – Sanofi)</p> <p>Task 5.1.3: Helena Harnik (26 – The Synergist), Maximiliane Rauch (26 – The Synergist), Sashka Hristoskova (38 – NVS), Leàn Rolfes (9 – LAREB)</p>
<p>Other contributors</p>	<p>Benedikte Cuppers (9 – LAREB) Linda Härmark (9 – LAREB) Priya Somar (9 – LAREB) Bonaventure Ikediashi (26 – The Synergist) Judith Cottin (27 – ENTIS) Aurore Gouraud (27 – ENTIS) Feodora Stipoljev (27 – ENTIS) Romana Gjergja (27 – ENTIS) Kristin Rosnes (14 – UOSL) Hedvig Nordeng (14 – UOSL) Ida Niklson (38 – NVS) Michael Steel (38 – NVS) Stéphanie Tcherny-Lessenot (39 – Sanofi) Monali Desai (48 – Abbvie) Rebecca Moore (16 – EIWH) Vanessa Moore (16 – EIWH)</p>

Document History

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Abstract

Deliverable 5.4 is the outcome of task 5.1 which aimed to compile an inventory of key information sources that are available to healthcare professionals (HCPs) and women of child bearing age about the safety of medicines before and during pregnancy and during the breastfeeding period and to explore their preferences in receiving/accessing such information. The task is subdivided in three subtasks:

- Sub-task 5.1.1: Inventory
- Sub-task 5.1.2: Information discrepancies
- Sub-task 5.1.3: End-Users' experiences

Sub-task 5.1.1 provided insights into currently available information resources about the safe use of medicines during pregnancy and breastfeeding, and into the communication methods of organisations that communicate this information. A two-step approach was deployed, the first step involving a general survey from known stakeholders across 25 European countries, then a more in-depth stakeholder communications survey of 23 stakeholders from Sweden, UK, Netherlands and France. An inventory of 78 information resources and their target audiences was created. The main finding regarding communication was that stakeholders communicating about medicine use in pregnancy and breastfeeding use a variety of sources of information and generally have well established processes to collate that information. Target audience consultation was not commonly undertaken however, and this is a key opportunity for the ConcePTION project as a whole and the knowledge bank, specifically.

Previous studies have indicated that information discrepancies are common concerning the safety of medicines in connection with pregnancy and breastfeeding. The aim of sub-task 5.1.2 was to analyse the frequency and nature of discrepancies between different information sources for both health care professionals (HCPs) and patients online in four European languages - Swedish, Dutch, French and English. A selection of six predefined medicines were chosen to explore for information discrepancies because they are commonly used during pregnancy and/or for treating chronic medical conditions in reproductive age. It was concluded that discrepancies in online information sources regarding safety of medicines during pregnancy and breastfeeding are common. These differences are more pronounced for breastfeeding than for pregnancy information. Recommendations from the Teratology Information Service (TIS) centers showed better consistency, indicating that on a scientific level there is more consensus. More work is needed to harmonize information both within and between countries, so that women and HCPs do not encounter conflicting messages. The results support the need for a common European knowledge bank, especially for countries that presently do not have a TIS centre.

The objective of this sub-task 5.1.3 was to explore pregnant and breastfeeding women's and healthcare professionals' (HCPs) information needs regarding the safety of medicines in pregnancy or during breastfeeding, and preferences for receiving such information in the future, both regarding content of the information and how it is delivered/made accessible to them in a knowledge bank. Methods deployed were a literature review, two large scale surveys across 74 countries, and focus group discussions with HCPs and pregnant or breastfeeding women. The surveys confirmed lack of clear and comprehensible information sources and discrepant information sources for women and HCPs. The focus group discussions showed that the pregnant, breastfeeding women and HCPs were positive regarding a European knowledge bank with information about the safe use of medicines during pregnancy and breastfeeding. This study provided insights on the needs and preferences for information. According to these, the information provided on the knowledge bank should be clear and understandable for both HCPs and the general public. The information pages should be easily found and have a clear conclusion. It is also important that the information is available in different native languages. In order to increase the reliability and trust in the knowledge bank, it should be clear on which studies the presented information was based, and the pharmaceutical industry should not be involved. In this way, the knowledge bank will best meet the needs and preferences of the users.

From these studies it was concluded that despite a wide variety of information resources being available for HCPs and the general public about the safety of medicines during pregnancy and breastfeeding, there are significant discrepancies in the available information, and there exists a need for the information to be clear and understandable. There is a general need for a European knowledge bank with clear information about the safe use of medicines during pregnancy and breastfeeding, especially for countries that presently do not have a TIS centre.

Methods

Task 5.1.1

The objective of sub-task 5.1.1 is to collect information on the current methods of communication, and to create an inventory of information resources. This task aims to identify key stakeholders that communicate to women and healthcare professionals (HCPs) and to describe the scope and purpose of information that they provide, the methods they use to disseminate information and the processes used to produce this information.

We utilised ENTIS pan-European contacts and those associated with ConcePTION industry partners to collect information on known stakeholders and information resources through two surveys. This approach gave us broad coverage of 25 European countries and a high level indication of the range of information resources available. Based on the countries represented by 5.1.1 team members, stakeholders in UK, Sweden, Netherlands and France were selected to be analysed more closely using a stakeholder communications survey. The 23 selected stakeholders belonged to one of five categories (National formulary, TIS, organisations that create SmPC/PIL i.e., marketing authorization holders in liaison with health authorities, organisations providing recommendations to HCPs, and organisations providing recommendations/advice to patients) and were considered to produce information that was accessed frequently by women and HCPs (using the results of survey 5.1.3 as a guide).

Task 5.1.2

The aim of task 5.1.2 was to analyse the frequency and nature of discrepancies between different information sources for both health care professionals (HCPs) and patients in online information sources in four European languages.

The study was performed on online data sources in Swedish, Dutch, French and English. The medicines analyzed were ibuprofen, ondansetron, olanzapine, fingolimod, methylphenidate and adalimumab, i.e. medicines commonly used during pregnancy and/or for treating chronic medical conditions in reproductive age. Standardized google search was used in each language. The top search hits with considerable information were collected. For patients, the information sources were classified into the following categories: i) regulatory sources, ii) scientific sources, e.g. Teratology Information Services (TIS) iii) blogs/forums/social media, iv) news articles and v) commercial websites for patients. For HCPs, they were divided into i) regulatory sources, ii) drug formularies, iii) scientific sources (TIS), iv) treatment guidelines and v) main medical journal. The recommendations about medicine use were then categorized as a) Can be used, b) Individual benefit-risk assessment, c) Should not be used, d) Trimester specific information, e) Not classifiable. Thereafter the recommendations about medicine use from each information source category were compared for each drug and each language, in total 24 comparisons for pregnancy and 24 for breastfeeding. Descriptive analysis was used to identify the frequency and nature of the discrepancies.

Task 5.1.3

The objective of task 5.1.3 was to explore pregnant and breastfeeding women's and healthcare professionals' (HCPs) information needs, trust in information and preferences for a knowledge bank about medicine use during pregnancy and breastfeeding. The study included two large scale surveys in women (n=1910) and HCPs (n=665) followed by six targeted focus group discussions with pregnant and breastfeeding women and HCPs.

Results

The summarized results of each task are presented below. Full results are displayed in appendices.

Task 5.1.1

An inventory of 78 information resources and their target audiences was created and represents a reference resource for ConcePTION partners and those undertaking risk communications. Results from the detailed stakeholder analysis provided a number of key insights which may help inform information provision as a deliverable of ConcePTION. While many stakeholders communicate information about medicine use in breastfeeding and pregnancy, this is quite often in the context of a wider scope. There are a small number of resources that are specific to pregnancy and/or breastfeeding but they are available in a very limited number of languages. Of the stakeholders analysed, it was evident that while standard operating procedures were utilised and there was transparency of processes in most cases, there was relatively little target audience consultation in the creation of information materials.

Task 5.1.2

For patients, 11/24 (46%) comparisons of the pregnancy information was consistent between all information sources, while for breastfeeding, only 4/24 (17%) showed consistency. The corresponding figures for HCP data sources were 13/24 (54%) and 5/24 (21%). In 8/24 (33%) of the comparisons for breastfeeding and 3/24 (13%) for pregnancy, the recommendation for patients was completely divergent, i.e. differed from 'Can be used' in one or more sources to 'Should not be used' in other sources. Fingolimod and adalimumab, had the most coherent pregnancy recommendations among the medicines, while there were more inconsistencies for ondansetron and ibuprofen. The regulatory sources were steadily more conservative in their recommendations compared to other sources. Information from five TIS centers in different countries was consistent in 25/27 (93%) of compared recommendations for pregnancy and 15/22 (68%) for breastfeeding.

Task 5.1.3

The results from the survey showed that pregnant and breastfeeding women and HCPs need information about the safe use of drugs during pregnancy. Currently, there is a lack of clear and comprehensible information sources for women in need of this information. HCPs are widely consulted as a source of information, but they are also experiencing difficulties in finding and interpreting information. Discrepancies and often conflicting information in different sources are challenges reported by both women and HCPs. The use of internet has increased and has led to a preference for easily accessible but reliable online resources.

The focus group discussions showed that the pregnant, breastfeeding women and HCPs were positive regarding a European knowledge bank with information about the safe use of drugs during pregnancy and breastfeeding. This study provided insights on the needs and preferences for information. According to these, the information provided on the knowledge bank should be clear and understandable for both HCPs and the general public. The information pages should be easily found and have a clear conclusion. It is also important that the information is available in different native languages. In order to increase the reliability and trust in the knowledge bank, it should be clear on which studies the presented information was based, and the pharmaceutical industry should not be involved in writing recommendations. In this way, the knowledge bank will best meet the needs and preferences of the users.

Conclusion

There is a wide variety of information available for HCPs and the general public about the safety of medicines during pregnancy and breastfeeding. Stakeholders communicating about medicine use in pregnancy and breastfeeding use a variety of sources of information and generally have well established processes to collate that information. Target audience consultation was however not commonly undertaken.

Discrepancies in online information sources regarding safety of medicines during pregnancy and breastfeeding are common. These differences are more pronounced for breastfeeding than for pregnancy information. Recommendations from the teratology information service (TIS) centers showed better consistency, indicating that on a scientific level there is more consensus. More work is needed to harmonize information both within and between countries, so that women and HCPs do not encounter conflicting messages.

There was demonstrated a general need for a European knowledge bank with information about the safe use of medicines during pregnancy and breastfeeding, especially for countries that presently do not have a TIS centre. The focus group discussions showed that the pregnant, breastfeeding women and HCPs were positive regarding a European knowledge bank with information about the safe use of medicines during pregnancy and breastfeeding. This study provided insights on the needs and preferences for information. According to these, the information provided on the knowledge bank should be clear and understandable for both HCPs and the general public. The information pages should be easily found and have a clear conclusion. It is also important that the information is available in different native languages. In order to increase the reliability and trust in the knowledge bank, it should be clear on which studies the presented information was based, and the pharmaceutical industry should not be involved in writing recommendations. In this way, the knowledge bank will best meet the needs and preferences of future users.

Appendices

- **Sub-task 5.1.1 Inventory report**
- **Sub-task 5.1.2 Analysis of information discrepancies report**
- **Sub-task 5.1.3 end-users' experiences report**
- **Appendices of sub-task 5.1.1: Inventory**
 - Appendix 1 – Name of TIS completing table
 - Appendix 2 – Information source in European countries: questionnaire for industry
 - Appendix 3 – Inventory of information resources known to or used by ENTIS members and industry partners
 - Appendix 4 – Description of stakeholders
 - Appendix 5 - IMI ConcePTION Stakeholder communication survey
- **Appendices of sub-task 5.1.2: Information discrepancies**
 - Methods
 - Results – distribution of pregnancy and lactation recommendations
 - Results– detailed discrepancies analysis
- **Appendices of sub-task 5.1.3: End-Users' experiences**
 - Appendix 1 - Literature review results
 - Appendix 2 - Preparatory Survey Results
 - Appendix 3 - Survey Questionnaire HCP
 - Appendix 4 - Survey Questionnaire Women
 - Appendix 5 - Focus group instructions

Sub-task 5.1.1 – Inventory report

Abstract

Background and aim: Numerous stakeholders disseminate different kinds of information about the safety of drug use during pregnancy and lactation and utilise different delivery methods to provide these details. The objective of sub-task 5.1.1 is to collect information on the current methods of communication, and to create an inventory of information resources. This task aims to identify key stakeholders that communicate to women and healthcare professionals (HCPs) and to describe the scope and purpose of information that they provide, the methods they use to disseminate information and the processes used to produce this information.

Materials and methods: We utilised ENTIS pan-European contacts and those associated with ConcePTION industry partners to collect information on known stakeholders and information resources through two surveys. This approach gave us broad coverage of 25 European countries and a high level indication of the range of information resources available.

Based on the countries represented by 5.1.1 team members, stakeholders in UK, Sweden, Netherlands and France were selected to be analysed more closely using a stakeholder communications survey. The 23 selected stakeholders belonged to one of five categories (National formulary, TIS, organisations that create SmPC/PIL i.e., marketing authorization holders in liaison with health authorities, organisations providing recommendations to HCPs, and organisations providing recommendations/advice to patients) and were considered to produce information that was accessed frequently by women and HCPs (using the results of survey 5.1.3 as a guide).

Results are presented descriptively, and so no statistical analysis was applied.

Results: An inventory of 78 information resources and their target audiences was created and represents a reference resource for ConcePTION partners and those undertaking risk communications. Results from the detailed stakeholder analysis provided a number of key insights which may help inform information provision as a deliverable of ConcePTION. While many stakeholders communicate information about medicine use in breastfeeding and pregnancy, this is quite often in the context of a wider scope. There are a small number of resources that are specific to pregnancy and/or breastfeeding but they are available in a very limited number of languages. Of the stakeholders analysed, it was evident that while standard operating procedures were utilised and there was transparency of processes in most cases, there was relatively little target audience consultation in the creation of information materials.

Conclusions: Stakeholders communicating about medicine use in pregnancy and lactation use a variety of sources of information and generally have established processes to collate that information. Target audience consultation was not commonly undertaken however, and this is a key opportunity for the ConcePTION project as a whole and the Knowledge bank, specifically.

Introduction

The majority of women will take at least one medicine during pregnancy and breastfeeding. A number of different stakeholders communicate to women and healthcare professionals (HCPs) regarding the risk associated with medicines in pregnancy and lactation. However, as pregnant women are not included in clinical trials for ethical reasons, there is often a lack of evidence to support these communications. Stakeholders must gather evidence from multiple sources and must make a treatment recommendation based on this variety of information. It is therefore important to understand which stakeholders are communicating to women about medicine use in pregnancy, which information resources are used and how risk is communicated. These learnings will help to highlight gaps and shortcomings in the current information landscape, which will help inform ConcePTION Knowledge Bank development.

Objectives

The objective of sub-task 5.1.1 is to collect information on the current methods of communicating about safety of drug use during pregnancy and lactation. In this sub-task we present an inventory of information resources on medicines in breastfeeding and pregnancy used in Europe and identify key stakeholder groups who undertake risk communications about safety of medicines and drug use during pregnancy and lactation for a selection of countries. We will describe the scope and purpose of the information provided, the methods of information dissemination, and the processes involved in collating data from different sources to produce communication materials.

Overview of methodological approach

A two-step approach was taken to address the objectives of this subtask. First, ENTIS and industry contacts were surveyed to gain a high level and broad understanding of information resources on medicines in pregnancy and/or breastfeeding and their associated stakeholders across Europe (described in Part 1 of this report).

Secondly, selected stakeholders responsible for some of the more highly accessed information resources were analysed in more depth, using a stakeholder communications survey (Part 2). These methods will be described in more detail in subsequent sections.

Part 1. High-level identification of information resources and associated stakeholders: ENTIS and industry surveys

Methods

ENTIS survey

Representatives at 18 European Teratology Information Services (TIS) were contacted to provide details of information resources on medicines in pregnancy and lactation used in their country. A table was provided to gather information on information sources (Appendix I).

Industry survey

A structured survey was created and reviewed by task 5.1.1 team members (Appendix II). The survey was distributed through Sanofi and Novartis networks with local affiliates in most EU countries. The responses were collected from individuals with pharmacovigilance and medical information roles.

Results

Description of participants and countries represented

Responses were received from representatives of 14 TISs in 10 countries. 24 responses to the industry survey were collected (23 responses were from Sanofi pharmacovigilance colleagues from different affiliates and one response from a Medical Information Officer at Novartis).

25 European countries were represented overall (Figure 1).

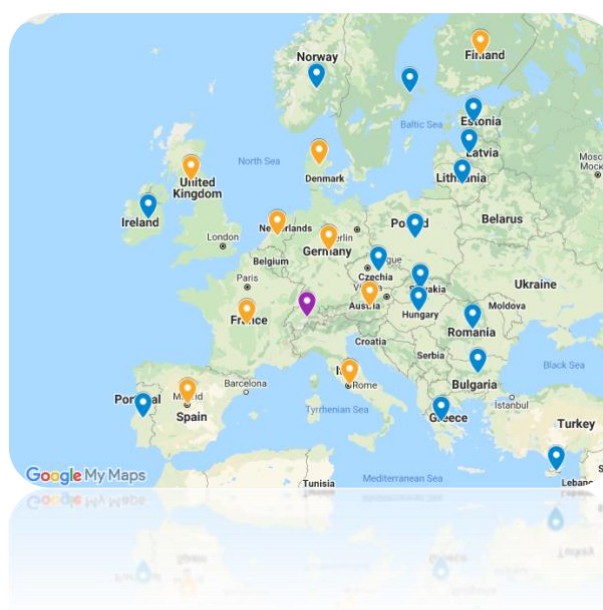


Figure 1. Countries represented in responses from TISs and industry partner contacts
Orange markers show countries that had representation by both industry and TIS. Blue markers show countries that only had industry partners representation. The purple marker shows a country that had representation by TIS only.

Characteristics of the information sources reported

A total of 78 information resources and/or associated stakeholders were reported from ENTIS and industry. These resources were curated and are presented as an inventory in Appendix (Appendix III) which describes the format and scope of each resource. Around half of the resources were aimed at an HCP audience only (Figure 2) and a small number (n=8) were aimed at the general public specifically. More than one third of the resources were aimed at both HCPs and the general public (n=30).

The majority of resources were available in English as well as the local language of the country that the resource originated from. 23 out of the 78 resources were only available in local language.

40 of the resources communicated about medicines in breastfeeding or pregnancy in the context of a more broad medicines information resource. 19 resources were specific to pregnancy, only 6 were specific to breastfeeding while 14 had both pregnancy and breastfeeding in scope.

Just over half (41) of the stakeholders associated with the resources are active on social media.

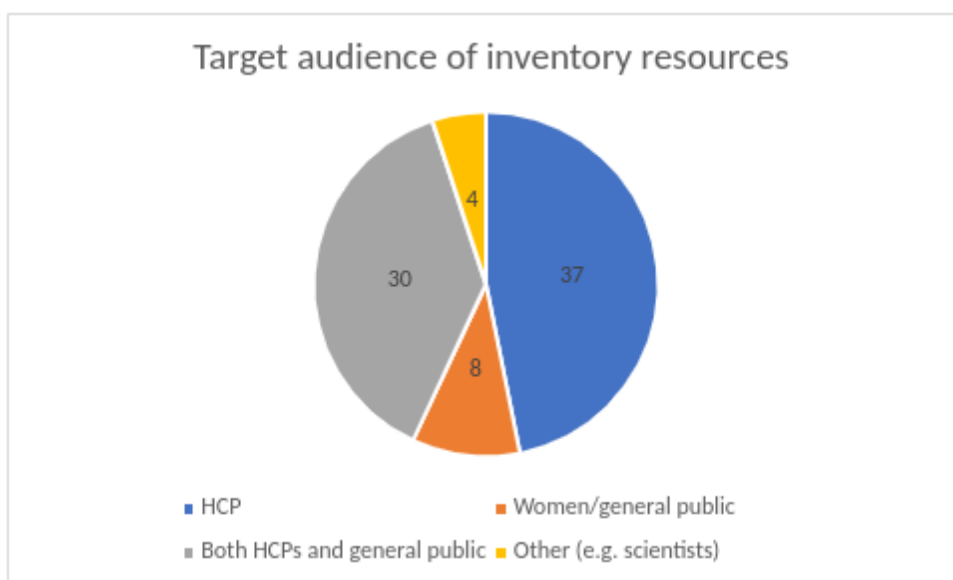


Figure 2. Target audience of inventory resources reported by ENTIS and industry

Note that one resource targets both HCPs and Other.

Part 2. Stakeholder communications survey

Methods

Stakeholder identification by country

The first step was to identify stakeholder groups who produce frequently consulted communications about drug use before/during pregnancy and during the breastfeeding period in a selection of countries. Based on sub-team membership, the Netherlands (NL), Sweden (SW), France (FR) and the United Kingdom (UK) were selected for this more detailed stakeholder analysis. For these selected countries, most frequently consulted stakeholders were identified based on sub-task member local knowledge, the information resources inventory described in Part 1, and on sub-task 5.1.3 survey results regarding the most frequently used internet data sources. Therefore, a first list of stakeholders was built based on sub-task members local knowledge and was cross-checked against data sources cited by women and HCP survey respondents.

Stakeholders belonged to one of five defined categories:

- National formularies where applicable (e.g. UK, Sweden and Netherlands)
- Teratology information service (TIS)
- Organisation providing recommendations to HCPs (e.g. professional guidelines)
- Organisation providing recommendations/advice to patients - most frequently used data source by patients for each country according to local knowledge, 5.1.3 survey, and ENTIS and industry surveys.
- Organisation that creates SmPC/PIL (marketing authorization holders in liaison with Health Authorities) – of note, information about the processes describing SmPC and PIL preparation and update was collected from industry representatives once for all countries (considered as not being country specific).

The 23 stakeholders included in this analysis are listed in Table 1. More detailed information about each of the stakeholders is presented in Appendix IV.

Table 1. List of stakeholders included in the analysis per country

Organisation categories	Country				Other
	FR	SW	NL	UK	
National formularies	-	Fass.se (the texts regarding pregnancy and breastfeeding for the respective drug product)	Farmacotherapeutisch Kompas	BNF	-
TIS	Le Crat	Janusmed*	TIS	UKTIS	-
Recommendations to HCPs	CNGOF	1. Svensk reumatologisk förening 2. Svensk gastroenterologisk förening	Richtlijnen NVOG	1. UKDILAS 2. RCOG	-
Recommendations to Patients	1- La Leche League 2- Doctissimo	1. 1177.se: Subsection: Graviditet och läkemedel 2. Läkemedelsupplysningen	1. Stichting ZEHG 2. borstvoeding.com	1. Tommy's 2. NHS 3. The breastfeeding network	-
Industry and Health Authorities	-	-	-	-	SmPC/PIL preparation and update process
TOTAL by Country	4	6	5	7	1

CNGOF = Collège National des Gynécologues et Obstétriciens Français ; NVOG= Nederlandse Vereniging voor Obstetrie en Gynaecologie ; PIL = Patient Information Leaflet ; RCOG = The Royal College of Obstetricians and Gynaecologists ; SmPC = Summary of Product Characteristics ; TIS = Teratology Information Service ; UKDILAS = UK drugs in lactation advisory service

* Janusmed provides knowledge bases on medicines in connection with pregnancy and lactation but does not handle individual requests. To facilitate, Janusmed has been classified as a TIS.

Data collection

Data on the way each stakeholder communicates and what sources of information and processes they use in the creation of communication materials were collected in a semi-structured way through a word questionnaire, which was gathered in a Google form (Appendix V). The questionnaire was completed via;

- information from the website of the organization (n=14; 60.9%),
- information from the website of the organization and information gathered during a congress presentation (n=1; 4.3%),
- the organisation filling in the form directly (n=7; 30.4%),
- the organisation filling in the form directly and through a phone interview (n=1; 4.3%).

Results

Distribution by organization categories

More than one third of the stakeholders included were providing recommendations to patients as main target audience, one quarter provided recommendations to HCPs as main target audience, 13% corresponded to National Formularies, and 17% to TIS centres. The last stakeholder category was to cover the SmPC/PIL process (involving Marketing Authorization Holder and Health Authorities).

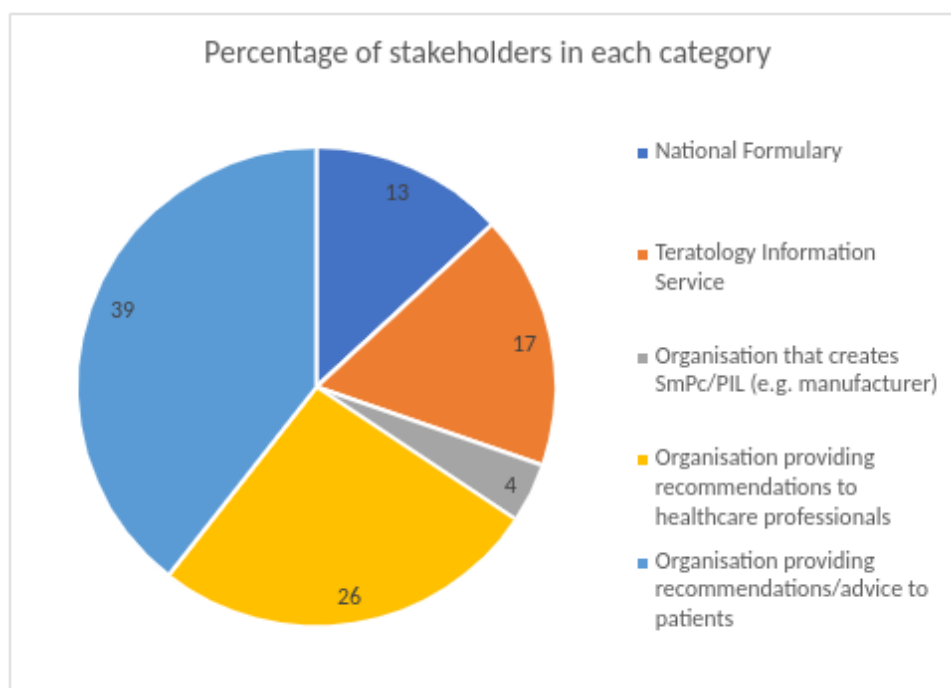


Figure 3. Distribution of stakeholders by category

Stakeholder target audience, scope of communication and topic of communication

The target audiences (main and secondary) for each stakeholder are presented below in Table 2, allowing to see in each country which stakeholder is targeting each category of audience (i.e. HCPs, pregnant women, breastfeeding women, or general public, including pregnant and breastfeeding women). In total, 9 of the 23 stakeholders are targeting both HCPs and patients (pregnant women, breastfeeding women or both), 8 are targeting HCPs only and 6 are targeting patients only (pregnant women, breastfeeding women or both).

It is noteworthy that in France, no website providing specialized information on the safety of drug use during pregnancy and breastfeeding is targeted to patients. However, the French TIS website 'Le CRAT' being an open access website, it can be consulted by everybody, and thus patients can consult it even if they are not its primary target audience, however they cannot directly contact the organization as only HCPs can contact them. And indeed, per 5.1.3 survey, "Le CRAT" website, medical doctors, and the PIL are the most frequently queried sources by women about the safety of medicines use during pregnancy or breastfeeding. It is noteworthy that based on data collected in the French translation of the 5.1.3 survey, "Le CRAT" website was unanimously cited both by HCPs and patients as the most frequently consulted stakeholder, and this may be a reason why there is a limited number of other websites providing updated recommendations on drug use during pregnancy and breastfeeding in France.

In Sweden, only Janusmed offers specialized information regarding medications during pregnancy and breastfeeding for patients. As for 'Le Crat' in France, the information on Janusmed is the same for HCPs and patients. The HCPs have the possibility to contact a Drug information centre for further advice, while a similar service is not available for patients/the public. The other Swedish stakeholders that provide information regarding medicines during pregnancy/lactation for patients (1177 and Läkemedelsupplysningen) only have quite general information regarding these topics as part of a broader scope of information.

Table 2. Presentation of stakeholders' target audiences by country

TARGET AUDIENCE	HCP	Pregnant women	Breastfeeding women	General public, including pregnant and breastfeeding

				women SW
National formularies	UK NL SW			
TIS	UK FR NL SW	UK NL SW	NL SW	
Industry and Health Authorities (SmPC/PIL)	x	x	x	x
Recommendations to HCPs	UKDILAS (UK) RCOG (UK) CNGOF (FR) NVOG (NL) SW (2 websites*)	RCOG (UK)		
Recommendations to Patients	The breastfeeding network (UK) Tommy's (UK) La LLL (FR)	Tommy's (UK) Stichting ZEHG (NL)	The breastfeeding network (UK) La LLL (FR) borstvoeding.com (NL)	NHS (UK) Doctissimo (FR) 1177.se (Subsection: Graviditet och läkemedel AND Läkemedelsupplysningen (SW))

* Svensk reumatologisk förening (Swedish Society of Rheumatology) AND Svensk gastroenterologisk förening (Swedish Society for Gastroenterology).

The target audience for TIS differs from one country to another. They all target HCPs, and all, except the French TIS website Le CRAT, are targeting pregnant women, while breastfeeding women are a target audience only for the Dutch TIS and Janusmed (Sweden).

Depending on the stakeholder, some are providing recommendations regarding only drug use during pregnancy (n=4), others regarding drug use during breastfeeding only (n=4), and both for most of them (n=15), as detailed in Table 3. Among these 15 stakeholders, 4 are specialized on communication regarding drug use during pregnancy or breastfeeding, while the 11 others have a broader scope of communication, such as medicine use in general, or information on health and well-being.

Table 3. Stakeholder's scope of communication

Scope of communication	Counts #	Details
Pregnancy and breastfeeding	15	4 specialized stakeholders: TIS NL, NVOG, Janusmed, Le CRAT 11 stakeholders with a broader scope of communication: BNF, NHS, 2 specialized SW websites, Industry and health authorities via SmPC/PIL, Doctissimo, CNGOF, Fass.se, Farmacotherapeutisch Kompas, 1177.se, Läkemedelsupplysningen
Pregnancy only	4	UKTIS, Tommy's, Stichting ZEHG, RCOG
Breastfeeding only	4	UKDILAS, La LLL, borstvoeding.com, The breastfeeding network

Depending on the stakeholder, information available can be about "products" broadly speaking (medicines, vaccines, cosmetics, chemicals, radiopharmaceuticals, devices) only (n=6), or disease related (gestational or

maternal medical conditions, breastfeeding issues, or medical procedures) only (n=5), or both (n=12) (see details in Table 4).

Table 4. Summary of stakeholders' topics of communication

Topics of communication	Number of stakeholders (%)	Stakeholders list
Product and diseases	12 (52.2%)	TIS NL, UKTIS, 1177, Le CRAT, Doctissimo, Industry and health authorities via SmPC/PIL, Svensk gastroenterologisk förening, Svensk reumatologisk förening, RCOG, NHS, Tommy's, Breastfeeding network
Product only	6 (26.1%)	Farmacotherapeutisch Kompas, UKDILAS, Janusmed, Läkemedelsupplysningen, BNF, Fass.se
Disease (or medical procedure) only	5 (21.7%)	NVOG, CNGOF, La LLL, borstvoeding.com, Stichting ZEHEG

Detailed information regarding the topics of communication covered by the 23 included stakeholders are presented in Figure 4.

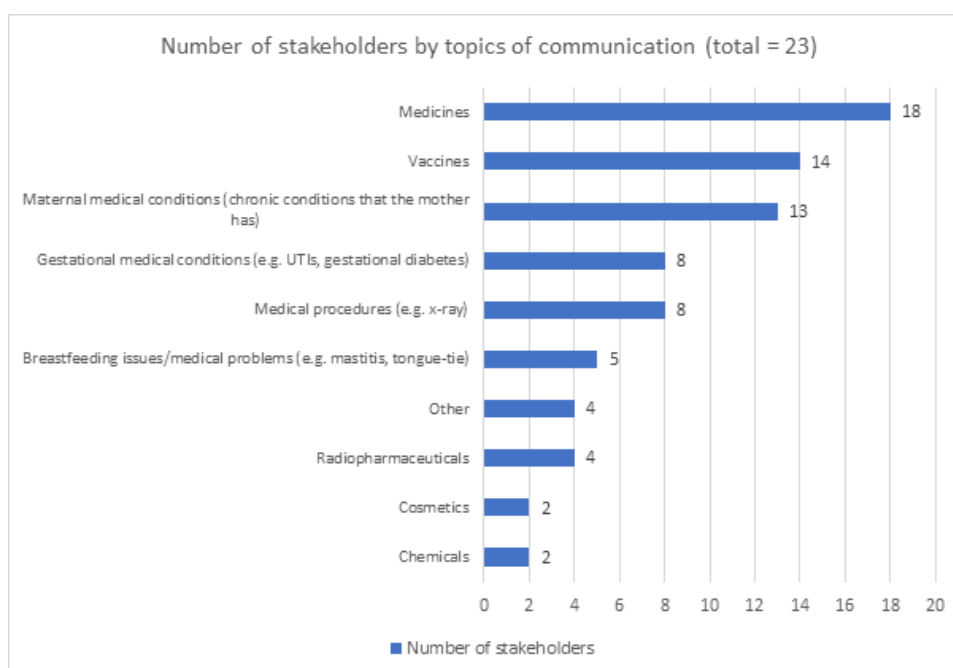


Figure 4. Number of stakeholders communicating about each topic (total stakeholders, n=23)

Most of the included stakeholders that provide information on medical conditions are covering multiple medical conditions, either maternal medical conditions that may pre-exist before pregnancy or medical conditions related to the pregnancy such as gestational diabetes or hyperemesis (NHS, Le CRAT, or 1177.se: Subsection: Graviditet och läkemedel, etc). Fewer stakeholders specialised in specific therapeutic areas covering chronic conditions that are seen in women of childbearing potential, are providing updated therapeutic recommendations on disease management during pregnancy or breastfeeding.

Communications are written in local languages (French, English, Swedish and Dutch), and in plain or specialist language depending on the target audience.

Methods used by stakeholders to disseminate information about safety of drug use during pregnancy and lactation

All stakeholders included have an open access website, that can be complemented by free (n=3) or paid (n=3) subscription access for some sections of the website. One other or several other methods of communications are used by most of the stakeholders including; direct contact (formal and informal phone or email communications, or questions through an internet form) (n=14), training (formal educational programme, conferences, etc.) (n=8), messages in social media (n=10), public forum (n=3), print (i.e. product label/package insert/patient information sheet) (n=5), publications in scientific journals (n=6), and information dispatch through mailing list (n=1), as presented in the graph below (Figure 5). Each stakeholder is using an average of three different methods to disseminate information (going from 1 single method of communication [i.e. website only] up to 6 methods for one stakeholder).

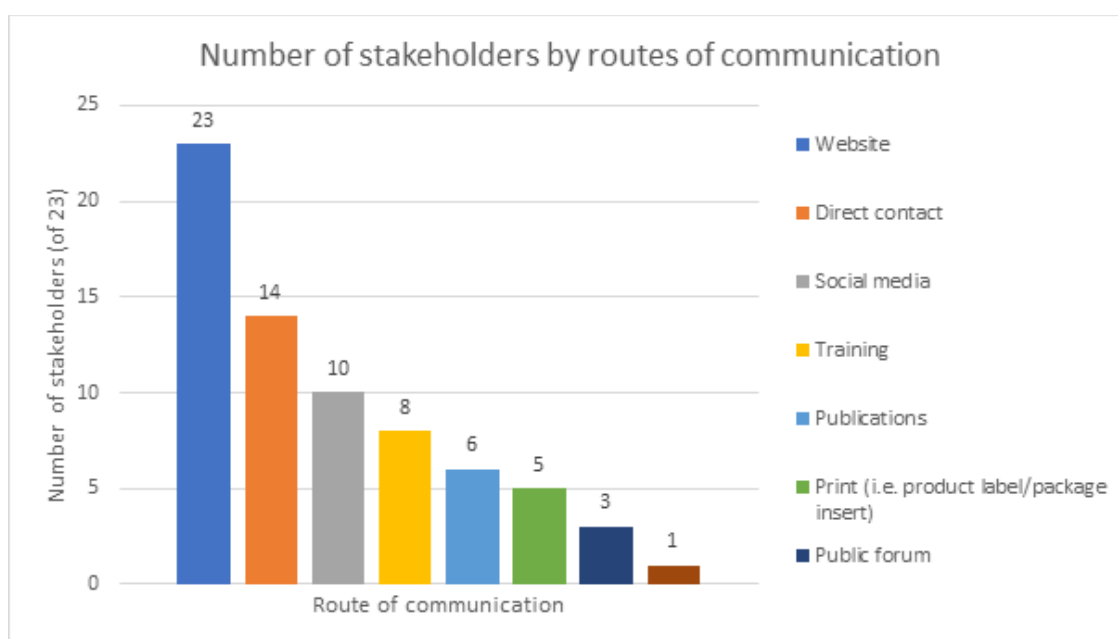


Figure 5. Number of stakeholders using each route of communication (total stakeholders, n=23)

Stakeholder modes of communication depending on audiences

Most stakeholders are using several modes of communication (1 to 7 modes of communication by stakeholders). For those stakeholders targeting both HCPs and women, different modes of communication may be used depending on the target audience. Systematic reviews/short research summaries are done by less than 50% of the stakeholders whatever the target audience.

For HCPs, the most frequently used modes of communication correspond to poster/abstract/public presentations, and lectures/educational materials while for pregnant or breastfeeding women, the most frequently used modes of communication correspond to short social media messages, and systematic reviews/short research summaries (see Figure 6).

Clinical guidelines are a mode of communication used mainly to target HCPs. 42% of the stakeholders are dispatching clinical guidelines on drug use during pregnancy or breastfeeding as part of their mode of communication to HCPs, while only one stakeholder (7% - 1 of 15 stakeholders - communicating with patients) is communicating through clinical guidelines to patients (of note: it is "1177.se"). Also, mode of communications that can be classified as "training or scientific publications" are frequently used to communicate information to HCPs, and less frequently for patients: indeed, conference poster/abstract/presentation are used by 53% of stakeholders to communicate information on drug use during pregnancy or breastfeeding to HCPs vs. 13% for patients, lectures/educational materials are used by 47% of

stakeholders for HCPs vs. 13% for patients, and scientific manuscripts by 42% of stakeholders for HCPs vs. 13% for patients.

Verbal advice is used more frequently by stakeholders to communicate with patients than with HCPs (33% of stakeholders for patients vs. 11% of stakeholders for HCPs), as well as short social media messages (60% of stakeholders for patients vs. 37% of stakeholders for HCPs).

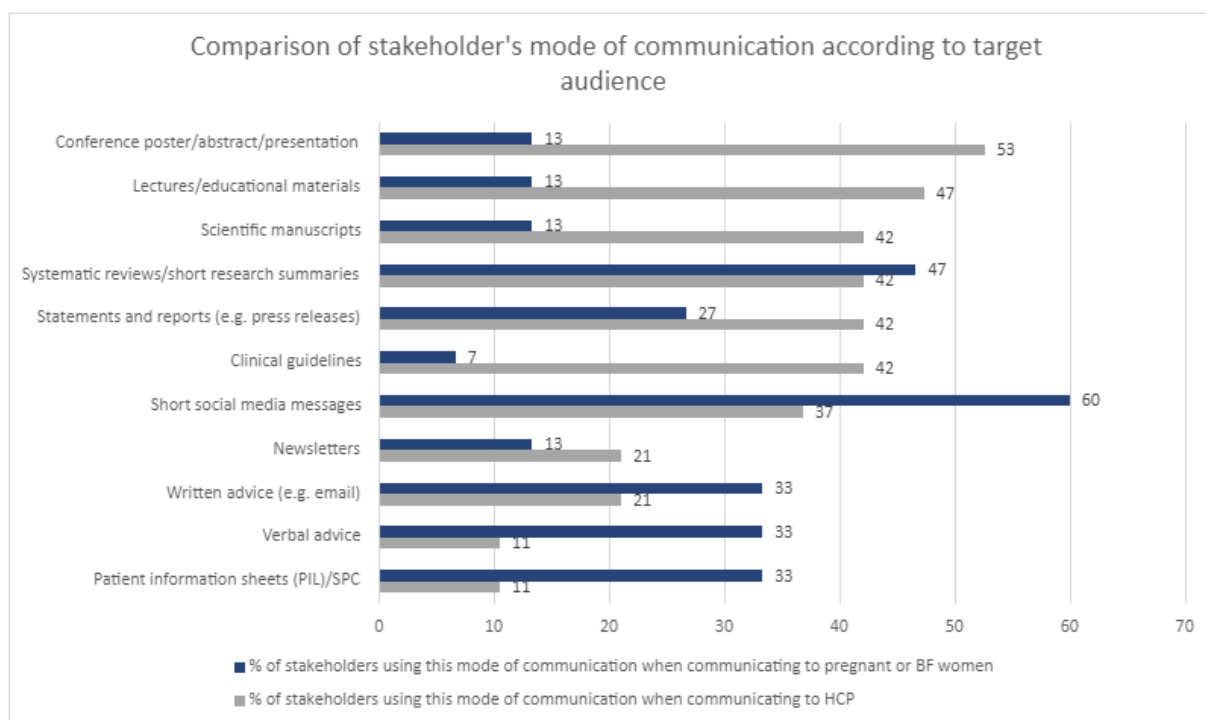


Figure 6. Comparison of modes of communication according to target audience

Processes used to produce communications

- Data sources used by the stakeholders for their primary mode of communication

All except one stakeholder are building their communications based on more than one data source. Indeed, stakeholders are summarizing information from 1 to 12 data sources to deliver their communications, using information from clinical, non-clinical, observational studies, specialised websites, textbook, TIS, SmPC, etc. Percentages of stakeholders by data sources whatever the target audience are detailed in Figure 7a and number of stakeholders by data sources according to their target audience are detailed in Figure 7b. The most frequently used data sources (i.e. data sources used by at least 50% of all stakeholders) are clinical trials, published observational studies, preclinical animal studies data, and information from summary of product characteristics (SPC). These data sources are even more frequently included when the communication is targeting HCPs than when it is targeting patients (see Figure 7b). No major difference is observed regarding data sources used according to the target audience.

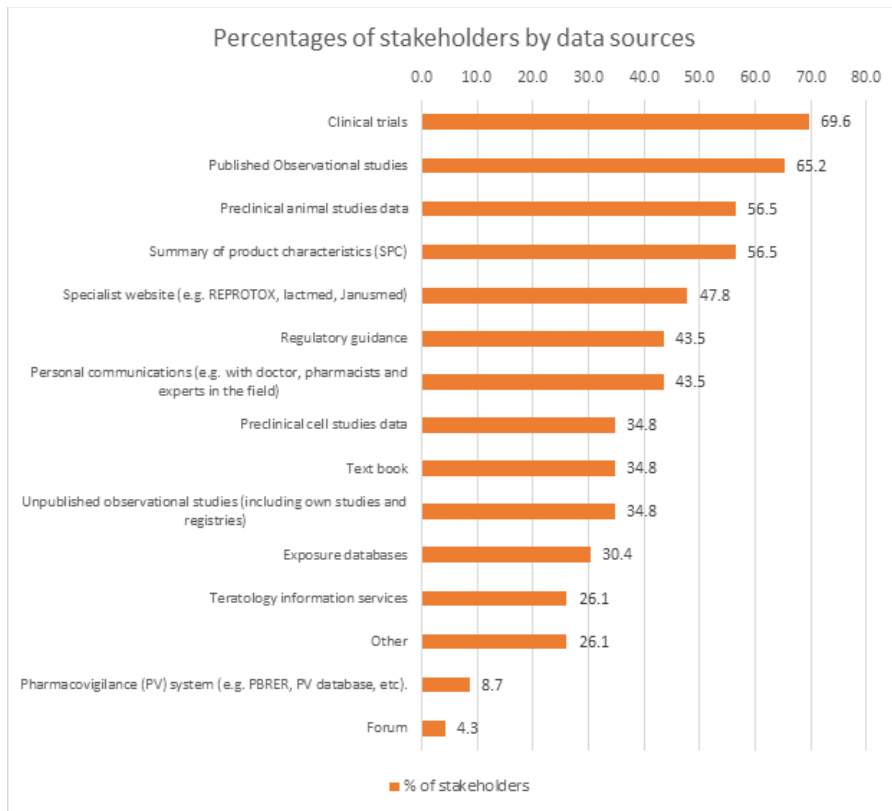


Figure 7a. Numbers of stakeholders using each data source

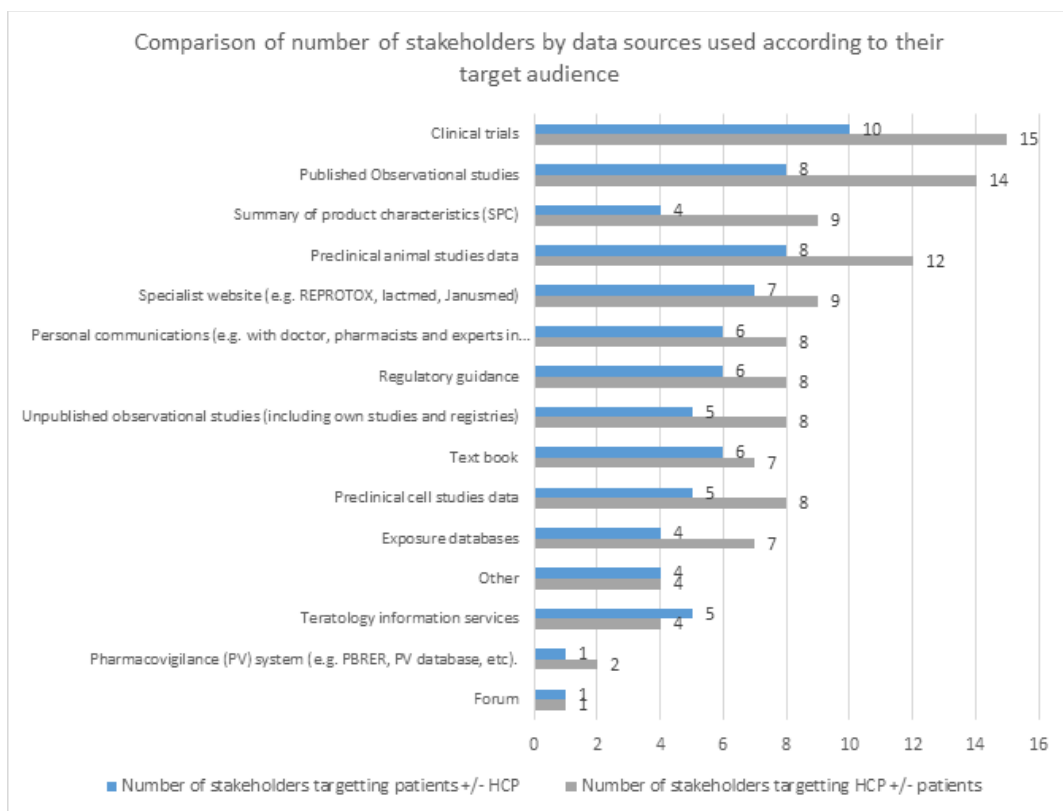


Figure 7b. Comparison of data sources utilisation according to target audience

- Stakeholder processes to develop communications

As detailed in Figure 8, most of the stakeholders have a standard operating procedure in place in the collation of information (n=16; information not available for the 7 remaining stakeholders). Most stakeholders also have an internal peer review before dispatching their communications (n=17 of 23 stakeholders have a mandatory peer review and 1 have an ad hoc peer review, and for 5 stakeholders this information is not available). There is systematic transparency on data sources used to collate information provided for 14 stakeholders, but this is not systematic for 4 stakeholders (and not applicable or unknown for the remaining 5 stakeholders).

It is noteworthy that depending on the organisation, information on processes in place to collate information communicated to HCP or women can be difficult to find or is not available. While the majority of stakeholders have standard processes and transparency of procedures, few consult the target audience during the production of their communications materials (Figure 8).

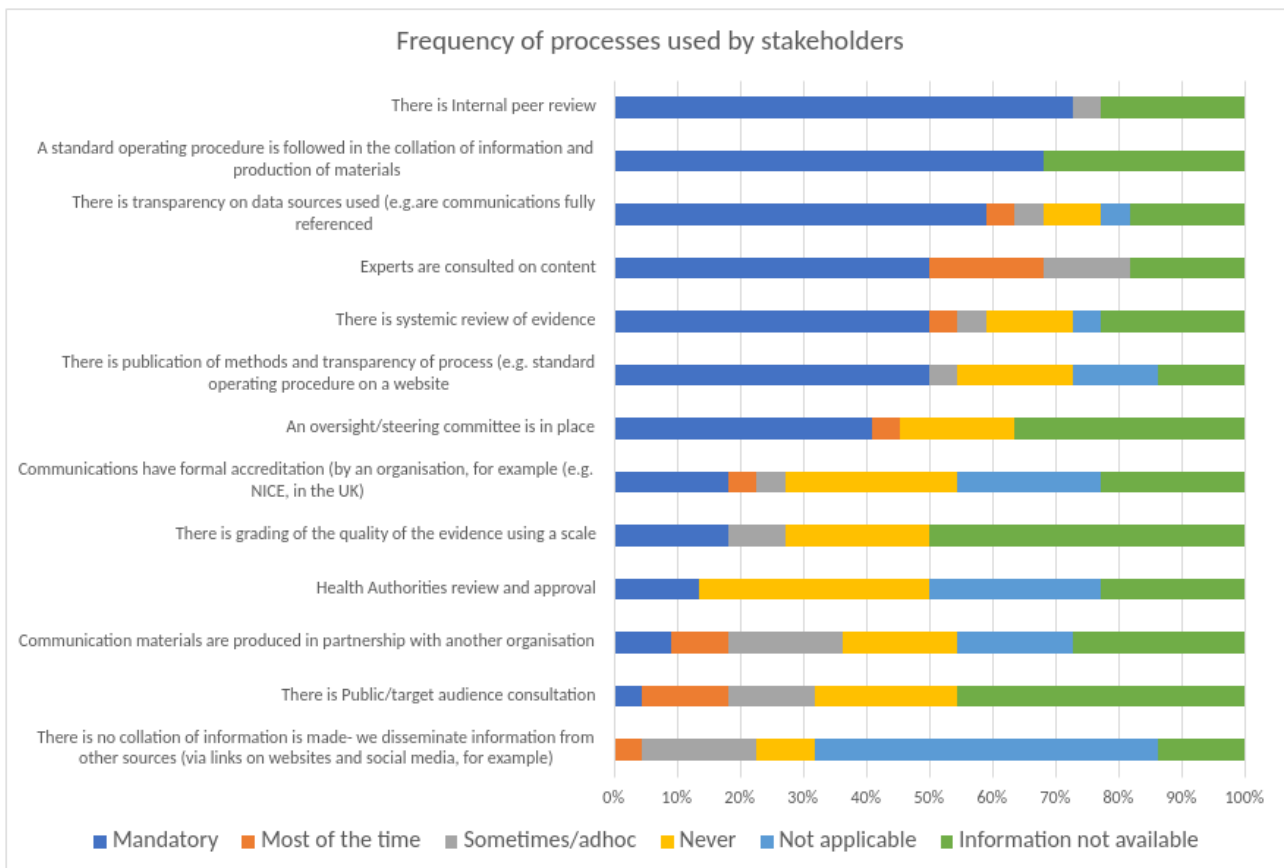


Figure 8. Processes in place to collate information

- Frequency of updates of communications

Information dispatched by stakeholders is updated at different frequencies depending on individual stakeholder’s practice, and sometimes depending on drugs or guidelines (Figure 9). For more than 25% of stakeholders, this information was not available or it was clear that no updates were made on topics on which new information became available in the previous years (n=4 [17%] and n=2 [9%] respectively).

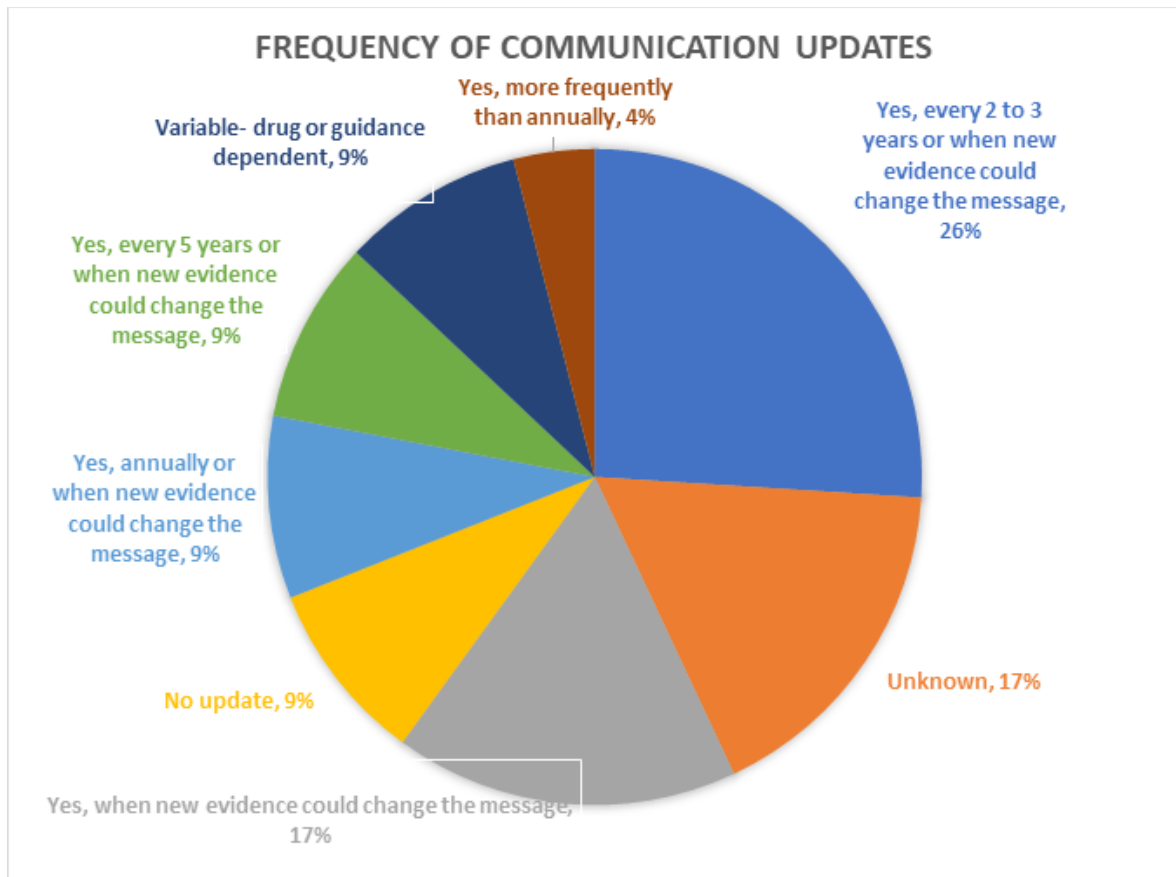


Figure 9. Frequency of updates of primary communication methods

Process of development and updates of SmPC (Summary of Product Characteristics) and PIL (Patient Information Leaflet)

The SmPC is a legal reference document, which provides information on how to use the medicinal product safely and effectively.

SmPC and PIL are prepared by pharmaceutical companies when they submit applications for new drug marketing authorisations or updates to existing marketing authorisations to Health Authorities for their evaluation. Health Authority guidelines exist to define the content, most commonly used standard statements, format, frequency of update. The first version of the SmPC and PIL as well as any update needs to be submitted by the pharmaceutical company to Health Authorities for approval.

The SmPC has to be updated throughout the life of the product as new efficacy or safety data emerge, and at a minimum every 5-years.

Discussion

Key insights from inventory of information resources

We have produced an inventory of information resources which serves to highlight the availability of medicines in pregnancy and breastfeeding information and may serve as a useful tool for those involved in risk communications. This inventory identified key stakeholders that communicate to women and HCPs about the use of medicine during pregnancy and lactation. It examined the scope and purpose of the information provided and the methods that were used to disseminate information.

Whilst a variety of information resources were reported by ENTIS and industry partners, it is evident that relatively few are produced specifically for communicating about medicine use in pregnancy and breastfeeding. This means that often information specific to the needs of a pregnant or breastfeeding woman needs to be searched for within a more broadly focused website. The number of resources specifically targeted at general public are even fewer.

There were a small number of very comprehensive medicines in pregnancy focused websites (Mother to Baby, Best Use of Medicines in Pregnancy (BUMPS) and Pregistry, Bijwerkingencentrum Lareb, Janusmed Stockholm, Le Crat and Embryotox), however they have limited accessibility given that they are only available in English or English and/or a single other language. An even smaller number of websites focused on medicines in breastfeeding were identified (e-lactancia, Breastfeeding Network, Le Crat, Bijwerkingencentrum Lareb, Janusinfo Stockholm and Embryotox). Again, these had limited accessibility due to the information being available only in limited languages. There appears to be no single resource that is available in a broad range of European languages. This may have the potential to generate information inequality, whereby the information available to HCPs and the general public varies depending on first language and country of residence.

These data highlight the need for a resource that is developed specifically for communicating information about medicines in pregnancy and breastfeeding, in a wide range of languages. Resources for translation of the ConcePTION Knowledge Bank should therefore be considered to be a critical consideration to increase impact of the project and should be included in the project sustainability plan.

Approximately half of the stakeholders responsible for resources in the inventory are active on social media. These stakeholders represent potential 3rd party channels to amplify ConcePTION social media messages, increasing audience engagement for project outputs.

Key insights from stakeholder communications survey

All stakeholders are dispatching their information through a website, and most of them are using one or more additional route of communication on top of their website such as verbal or written advice, training, or communication on social media. In the same way, most stakeholders are using several modes of communication, and for those stakeholders targeting both HCPs and women, different modes of communication may be used depending on the target audience.

Whilst most of the stakeholders analysed had well established processes to synthesise information using a wide range of resources, surprisingly few consulted the target audience in the production of their materials. Although, we examined only a small number of stakeholders, this may suggest an opportunity for the ConcePTION Knowledge Bank to create a resource which more closely meets the information needs of the target audience via target audience engagement and consultation. This is particularly important in the dawn of the “Nothing About Us Without Us” movement.

For stakeholders communicating to HCPs or women, the primary literature (clinical trials, observational studies etc.) is the most commonly used resource and secondary sources of information are less commonly used. Very few stakeholders are signposting information produced by other stakeholders. In terms of processes, few of the stakeholders are collaborating with other organisations to produce information. This perhaps suggests that there is opportunity for greater collaboration between stakeholders and potentially less duplication of effort. However, most stakeholders communicate in the local language and this may be a barrier to work sharing.

Communications are written in local languages (French, English, Swedish and Dutch), and in plain or specialist language depending on the target audience.

Limitations

ENTIS centres have knowledge of, and utilise a wide range of resources which provide information about the safety of medicines in lactation and pregnancy, and there is overlap between TISs in the information resources used. Our method did however request known reliable resources only, and therefore did not

provide us with information about other resources which may be deemed less reliable and which may be accessed by the general public (this was however provided by the industry survey). We also did not use a structured survey so relied on individual TIS representatives' recall of resources. TISs are also not present in every European country so our coverage was limited by this.

The industry survey gave us good coverage of European countries and highlighted information resources that the general public access in countries that were potentially not reached by the TIS survey and survey 5.1.3. It should however be noted that this method was indirect with respect to understanding which resources are used by the general public and HCPs. Direct survey of women and HCPs in each country would have potentially yielded different results but would have also duplicated work already undertaken as part of sub task 5.1.3.

The stakeholder survey generated some interesting insights into the processes used by various stakeholders however only a small number of countries and stakeholders were included in the analysis. Systematic collection of data on complex and varying processes was challenging and, in some cases, information was unavailable.

Conclusion

The subtask has provided an overview of the available information resources on medicine use in pregnancy and breastfeeding which are accessed in Europe and has examined the processes of selected stakeholders producing particularly highly accessed material. While the majority of stakeholders have standard processes and transparency of procedures, few consult the target audience during the production of their communications materials. There is also no single resource available in multiple European languages. This represents a significant opportunity for ConcePTION project to engage with the target audience to produce a resource that fits information needs in a number of local languages. This may be particularly important for countries that currently do not have access to local teratology services.

Sub-task 5.1.2 – Information discrepancies

Abstract

Introduction: Previous studies have indicated that information discrepancies are common concerning the safety of medicines in connection with pregnancy and breastfeeding. These inconsistencies might cause confusion, resulting in non-adherence to therapy with subsequent risks for both the mother, foetus or breastfed child. Discrepancies might also lead to increased anxiety and even termination of pregnancies due to fear of having harmed the foetus. The aim of this study was to analyse the frequency and nature of discrepancies between different information sources for both health care professionals (HCPs) and patients in online information sources in four European languages.

Methods: The study was performed on online data sources in Swedish, Dutch, French and English. The medicines analyzed were ibuprofen, ondansetron, olanzapine, fingolimod, methylphenidate and adalimumab, i.e. medicines commonly used during pregnancy and/or for treating chronic medical conditions in reproductive age. Standardized google search was used in each language. The top search hits with considerable information were collected. For patients, the information sources were classified into the following categories: i) regulatory sources, ii) scientific sources, e.g. Teratology Information Services (TIS) iii) blogs/forums/social media, iv) news articles and v) commercial websites for patients. For HCPs, they were divided into i) regulatory sources, ii) drug formularies, iii) scientific sources (TIS), iv) treatment guidelines and v) main medical journal. The recommendations about medicine use were then categorized as a) Can be used, b) Individual benefit-risk assessment, c) Should not be used, d) Trimester specific information, e) Not classifiable. Thereafter the recommendations about medicine use from each information source category were compared for each drug and each language, in total 24 comparisons for pregnancy and 24 for breastfeeding. Descriptive analysis was used to identify the frequency and nature of the discrepancies.

Results: For patients, 11/24 (46%) comparisons of the pregnancy information was consistent between all information sources, while for breastfeeding, only 4/24 (17%) showed consistency. The corresponding figures for HCP data sources were 13/24 (54%) and 5/24 (21%). In 8/24 (33%) of the comparisons for breastfeeding and 3/24 (13%) for pregnancy, the recommendation for patients was completely divergent, i.e. differed from 'Can be used' in one or more sources to 'Should not be used' in other sources. Fingolimod and adalimumab, had the most coherent pregnancy recommendations among the medicines, while there were more inconsistencies for ondansetron and ibuprofen. The regulatory sources were steadily more conservative in their recommendations compared to other sources. Information from five TIS centers in different countries was consistent in 25/27 (93%) of compared recommendations for pregnancy and 15/22 (68%) for breastfeeding.

Conclusion: Discrepancies in online information sources regarding safety of medicines during pregnancy and breastfeeding are common. These differences are more pronounced for breastfeeding than for pregnancy information. Recommendations from the TIS centers showed better consistency, indicating that on a scientific level there is more consensus. More work is needed to harmonize information both within and between countries, so that women and HCPs do not encounter conflicting messages. The results support the need for a common European knowledge bank, especially for countries that presently do not have a TIS center.

Introduction

Availability of consistent, adequate information on the safety of medicines in pregnancy and breastfeeding is important for women's therapeutic decision making. In a multinational study, more than 80 % of pregnant women reported using multiple information sources when seeking information on medicine use during pregnancy. Among these women, 94% used formal information sources (e.g. physicians, pharmacists, patient information leaflets, and drug information centers), 67% used informal information sources (e.g. the internet, family, friends and herbal shop personnel) and 62% used both formal and informal information sources [1].

Being convenient and easily accessible, the internet is routinely used by pregnant women to access information on medicine use during pregnancy. The internet was used by 60% of women using multiple information sources [1] and by 76% of UK women when searching for information about medicine use during pregnancy [2]. Health service sites were most commonly used and deemed to be the most "helpful and trusted" [2].

For healthcare professionals (HCPs), manufacturers labeling information (prescribing information [PI]) appears to be the most frequently used source of information in many countries such as Australia, United States and Canada [3]. In a study from the Netherlands, 87% of general practitioners (GPs) relied on the drug formulary *Farmacotherapeutisch Kompas* [4], which was also frequently used by pharmacists [4]. Internet was used quite often by both groups to search for scientific evidence and reports for consensus groups [4].

Some countries offer specialized Teratology Information Services (TIS). These centers counsel health care professionals and the public on the safety of medicines in connection with pregnancy and breastfeeding, via for example telephone or chat [5-7]. Many also provide written information, sometimes via national knowledge bases [8]. Other ways for HCPs to reach this kind of specialized information is to contact a Pharmacovigilance center or a Drug information center, dependent on the national organization.

With an increasing number of information sources, there is an increased risk that the information will vary or even conflict. Several studies have shown that discrepancies do occur between different sources [1,3,9-13]. For example, evidence suggest that pregnancy and breastfeeding recommendations included in the PI are often conservative [3,9] and that social media sites might provide information that lack evidence to support their conclusion [11-13]. This may cause uncertainty about whether or not to use a medicine which may result in non-adherence to therapy [1], and subsequent risks for both the mother and fetus or breastfed child due to the consequences of untreated disease. It might also lead to unnecessary anxiety and even terminations of pregnancies [14]. Conflicting information for HCPs can potentially result in inappropriate prescribing to pregnant and breastfeeding women. Unjustified warnings regarding breastfeeding may also result in children being unnecessarily weaned from being breastfed [10].

The aim of this study was to analyze the frequency and nature of discrepancies between different online information sources for patients and HCPs in four European languages.

Methods

Selection of data sources and search strategy

Information directed for patients

The study was performed via internet data sources in Swedish, Dutch, French and English. A first investigational step was conducted to identify the top search sites concerning medicines during pregnancy and breastfeeding per country. Based on these preliminary results the following data source defined: i) Regulatory sources, mostly the Patient Information Leaflet (PIL) ii) Scientific sources, e.g. TIS/national knowledge bases and drug formularies, if available iii) Blogs/forums/social media iv) News articles and v) Commercial websites for patients. After that a standardized google search in the respective language was performed. For each medicine four searches were undertaken; i) generic medicine name + pregnancy ii) generic name + breastfeeding iii) most common brand name + pregnancy and iv) most common brand name + breastfeeding. The top search hit within each data source category with considerable information was

thereafter selected, provided that it appeared among the top 10 search hits on google overall. The PIL and the information from TIS and/or national knowledge bases were always included in the analyses, irrespective of whether they appeared among the top searches or not, since they were considered as essential sources for the comparisons. The TIS/national knowledge bases used for patients were: Lareb.nl (NL), Janusmed.sll.se (SE), Lecrat.fr (FR), BUMPS available at medicinesinpregnancy.org (UK) and mothertobaby.org (US). For a detailed overview of the included sources, see Appendix Table 1.

Selection of medicines

The medicines analyzed were ibuprofen, ondansetron, olanzapine, fingolimod, methylphenidate and adalimumab. Selection criteria of the medicines were a) medicines used for common acute illnesses experienced during pregnancy and breastfeeding and b) medicines used for common chronic diseases in reproductive age.

Information directed for HCPs

For HCPs, the following categories of information sources were used in the respective language:

i) Regulatory sources: Summary of Product Characteristics (SmPC) ii) Drug formularies if available, iii) Scientific sources: TIS information/ national knowledge bases iv) Treatment guidelines and v) Main national medical journal. Information from all the above sources were included, if available, irrespective of whether they appeared among the top 10 searches via Google or not. The TIS/national knowledge bases used for HCPs were: Lareb.nl (NL), Janusmed.sll.se (SE), Lecrat.fr (FR), UK Teratology Information Services via Toxbase (UK) for pregnancy and Specialist Pharmacy Services, SPS, for breastfeeding (UK).

See Appendix Table 2 for more details. Several of the data sources for HCPs were not publicly available but accessible for the HCPs using their professional credentials.

Classification of recommendations and discrepancies

From each data source, the recommendation concerning treatment during pregnancy and breastfeeding were collected for the six medicines and classified into six categories, based on previously settled categories by Frost-Widnes [9]. The definitions of each category were adapted by our group for the analysis (Table 1). The classifications were adjudicated by a small team to ensure that the definitions were consistently applied to all medicines and their respective searches.

Table 1. Definition of the recommendation categories

Recommendation category	Definition
Can be used	Medicines that can be used during pregnancy or breastfeeding without any impact on the fetus/newborn infant. Medicines that are compatible with breastfeeding.
Individual benefit-risk assessment	Medicines that might have a negative impact on the fetus/newborn infant but where untreated disease might carry more risks. Medicines that are stated as a second-, third- or fourth-line drug during pregnancy in treatment guidelines. Medicines that probably have a low risk during breastfeeding, and where the advantages with breastfeeding might exceed the potential risks. Surveillance of the infant might be recommended.
Should not be used	Medicines that are clearly contraindicated during pregnancy due to high risks for the fetus/newborn infant. Medicines stated as not compatible with breastfeeding.
Trimester-specific information	Medicines that have different recommendations during different trimesters, e.g. Individual benefit risk assessment during the first trimester, and Should not be used during the second and third trimester.
Not classifiable	Information is available, but is not possible to classify into any of the above

	categories
No available information	No information available at all

The distribution of the pregnancy and breastfeeding recommendations categories were then analyzed for differences between medicines, countries and types of information sources. Medicines with no predominant recommendation – defined as no recommendation category reaching more than 60% of the collected recommendation categories for that medicine were analyzed more in depth.

Classification of discrepancies

To classify the discrepancies, the collected recommendation categories above were compared for each drug and each language. The following discrepancy classes by Brown [3] were used:

1. SmPC/PIL agrees with all other resources, 2. SmPC/PIL has different recommendations from other information resources but those resources are in agreement (2.a. SmPC/ PIL is most conservative, 2.b. SmPC/ PIL is least conservative + which source/s is more conservative in free text), 3. One or more of the non-SmPC/ PIL resources has a recommendation different from the others (+ which resource/s contained the most and the least conservative statement/s in free text), 4. Unclassifiable.

Recommendations that were not classifiable and sources with no available information were excluded from this analysis.

Detailed analyses of discrepancies

To explore discrepancies in more detail, recommendations from selected data sources were compared with each other for the respective medicine. One analysis dealt with medicines with totally divergent recommendations to see whether some resources were more conservative than others. Totally divergent recommendations were defined as recommendations differing from “Can be used” in one source to “Should not be used” in another source, for the same medicine and language.

For the HCP data sources, the SmPC information was compared to the drug formularies, since both sources are frequently used in everyday practice. Therefore, the SmPC in the Netherlands was compared with the two available Dutch drug formularies, one for physicians (Farmacotherapeutisch Kompas) and one for pharmacists (KNMP Informatorium). The British National Formulary (BNF) was compared with the UK approved SmPC. Sweden and France were excluded from these analyses, since the Swedish drug formulary is completely based on the SmPC and no corresponding drug formulary is available in France.

Further, the TIS information for both patients and HCPs were compared between the different languages. The TIS information was also compared with treatment guidelines for HCPs and with the PIL information and the news articles respectively in each language. For these comparisons, the TIS information was considered as the reference, since it is produced by experts within the field and independent from the manufacturer and regulatory procedures. Finally, the PIL recommendations were compared between the different languages.

Statistical analysis

Descriptive analyses were used to identify the frequency and nature of the discrepancies.

Results

In total, the search yielded 249 pregnancy and breastfeeding recommendations from the patient’s resources and 185 recommendations for HCPs. An overview is presented in Table 2. It should be noted that pregnancy and breastfeeding recommendations were not available for each drug in all data sources and all languages.

Table 2 Overall distribution of collected recommendations in data sources for HCPs and patients

	Patients' resources	HCP's resources
Drugs		
Ibuprofen	45	32
Ondansetron	41	31
Methylphenidate	46	31
Adalimumab	43	31
Fingolimod	41	27
Olanzapine	33	33
Languages		
Swedish	65	39
Dutch	69	58
French	53	35
English	62	53
Type of recommendations		
Pregnancy recommendations	137	105
Breastfeeding recommendations	112	80
Internet data sources		
Regulatory data sources	52	48
Scientific data sources	89	44
Social media	27	Not applicable
News articles	24	Not applicable
Commercial websites for patients	57	Not applicable
Drug formularies	Not applicable*	37
Treatment guidelines	Not applicable	36
National Medical Journals	Not applicable	20

*Drug formularies were included in the scientific data sources for patient's analysis

Distribution of pregnancy and breastfeeding recommendations

Patient information resources

For all medicines except ibuprofen, there was more homogeneity between data sources regarding the recommendation of use during pregnancy than regarding use during breastfeeding, see Figure 1 and 2. More information, e.g. number of not classifiable recommendations or no available information is presented in Appendix Table 3.

Furthermore, this analysis showed that there were five drugs with no predominant recommendation: methylphenidate and ibuprofen for pregnancy recommendations, and methylphenidate, olanzapine and ondansetron for breastfeeding recommendations. From the analysis of drugs with no predominant recommendation, it is difficult to state that some types of resources are more conservative than others, especially for breastfeeding recommendations. The regulatory sources (in most cases the PIL) seemed however to be generally more conservative, see details in Appendix Table 4 and 5.

Otherwise, commercial websites for patients, news articles and regulatory data sources tended to provide more conservative pregnancy statements than other data sources. Additional details on the distribution of pregnancy and breastfeeding recommendations by data sources and type of recommendation are available in the Appendix Table 6. It should be noted that a significant part of the information from social media was not classifiable since different posts provided conflicting statements.

Figure 1. Distribution of pregnancy recommendation categories for all languages by type of recommendation and by medicine – patient sources

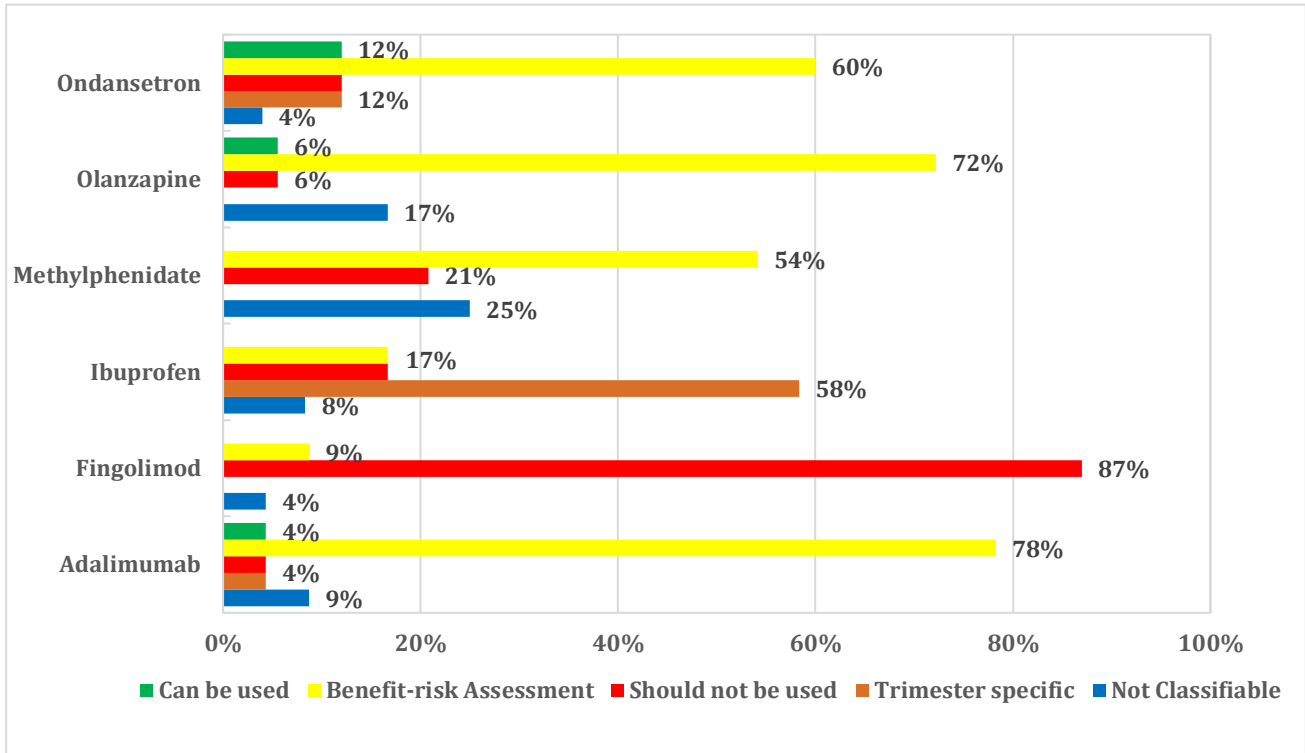
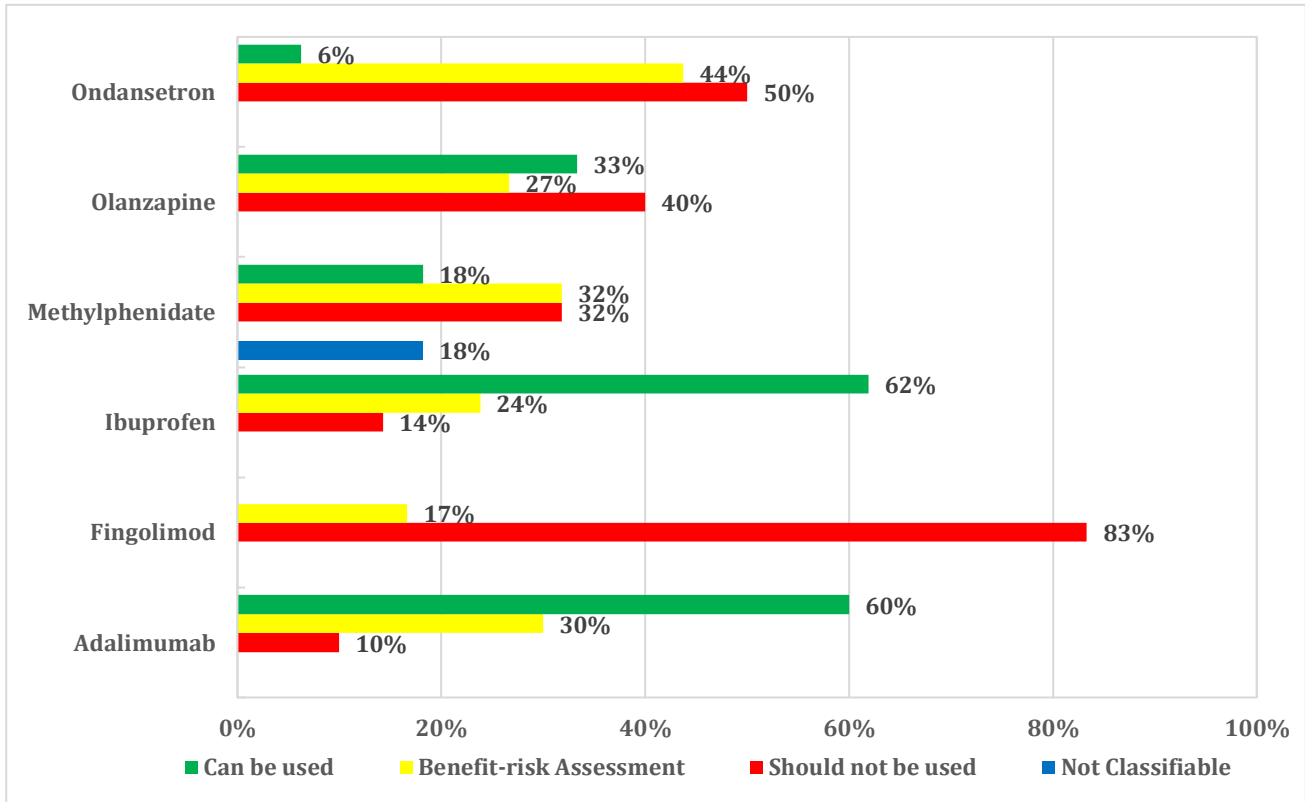


Figure 2. Distribution of breastfeeding recommendation categories for all languages by type of statement recommendation and by medicine – patient sources



HCP information resources

For all medicines except ondansetron, there was more homogeneity between data sources regarding the recommendations about use during pregnancy than regarding use during breastfeeding. Results of this analysis are presented in Figure 3 and Figure 4, and Appendix Table 7. This analysis also showed that there were two drugs with no predominant recommendation: ondansetron in pregnancy and olanzapine in breastfeeding. For both drugs, the discrepancies were partly due to the SmPC being more conservative than information from the TIS (Appendix Table 8). Overall analysis of pregnancy and breastfeeding recommendations by data sources independently of the medicine also indicated that the SmPC tended to be more conservative than other sources (Appendix Table 9).

Figure 3 Distribution of pregnancy recommendation categories for all languages by type of recommendation and by medicine – HCP sources

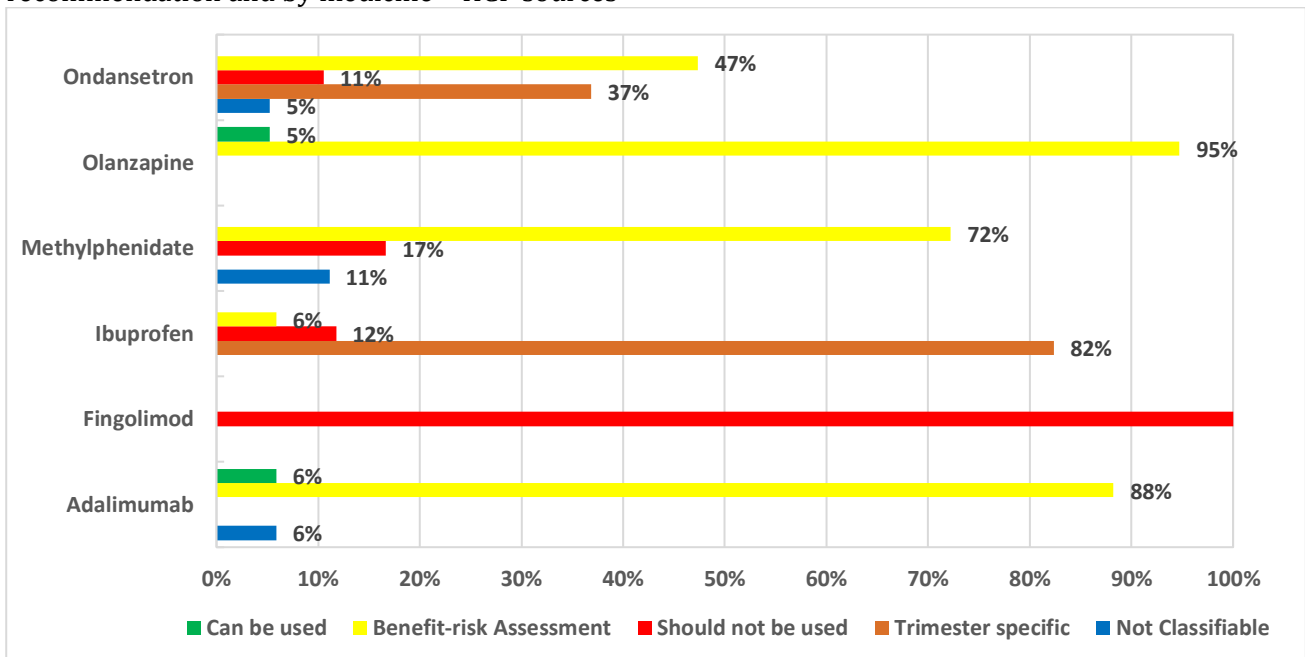
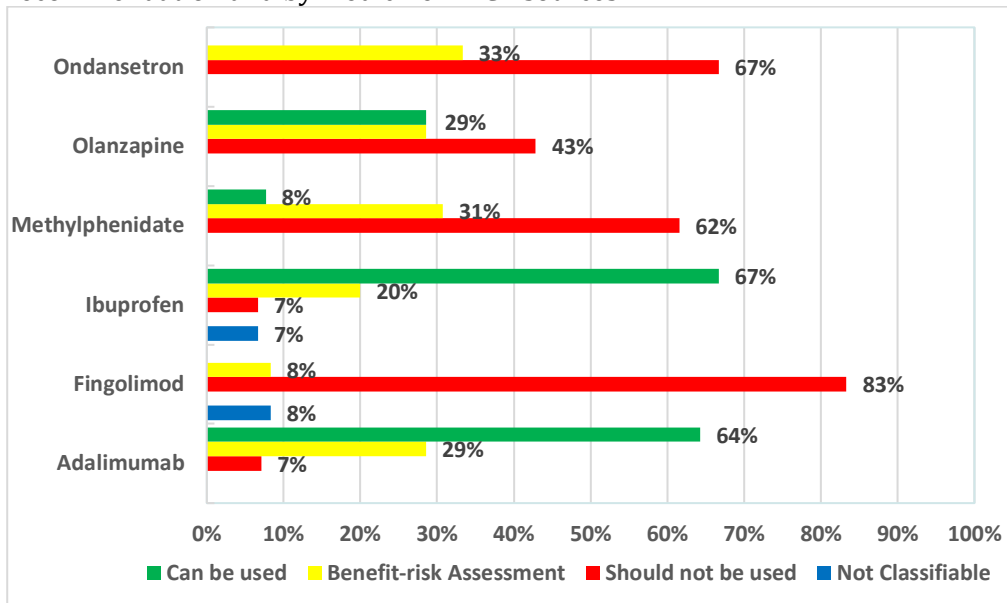


Figure 4 Distribution of breastfeeding recommendation categories for all languages by type of recommendation and by medicine – HCP sources

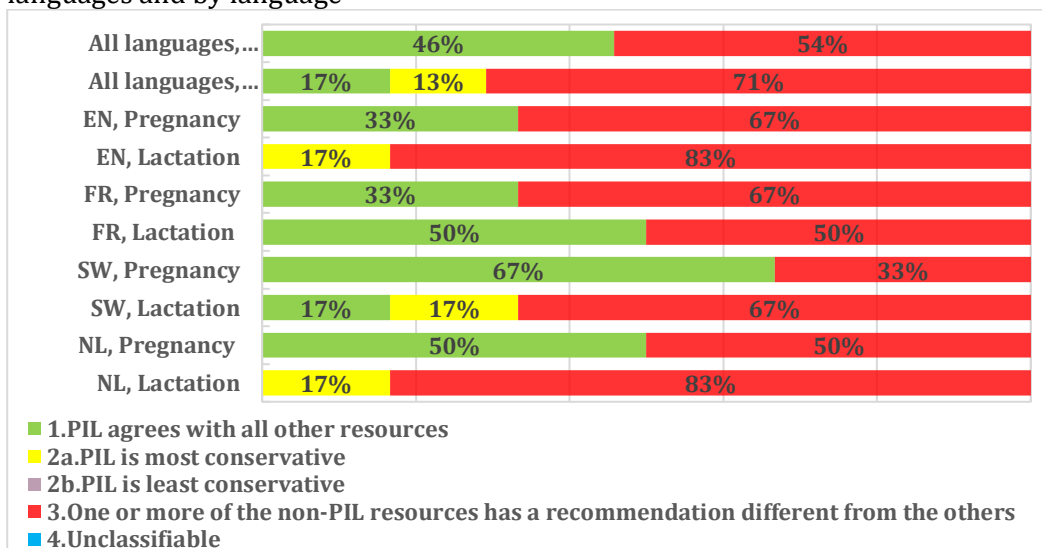


Discrepancies analysis

Patient information resources

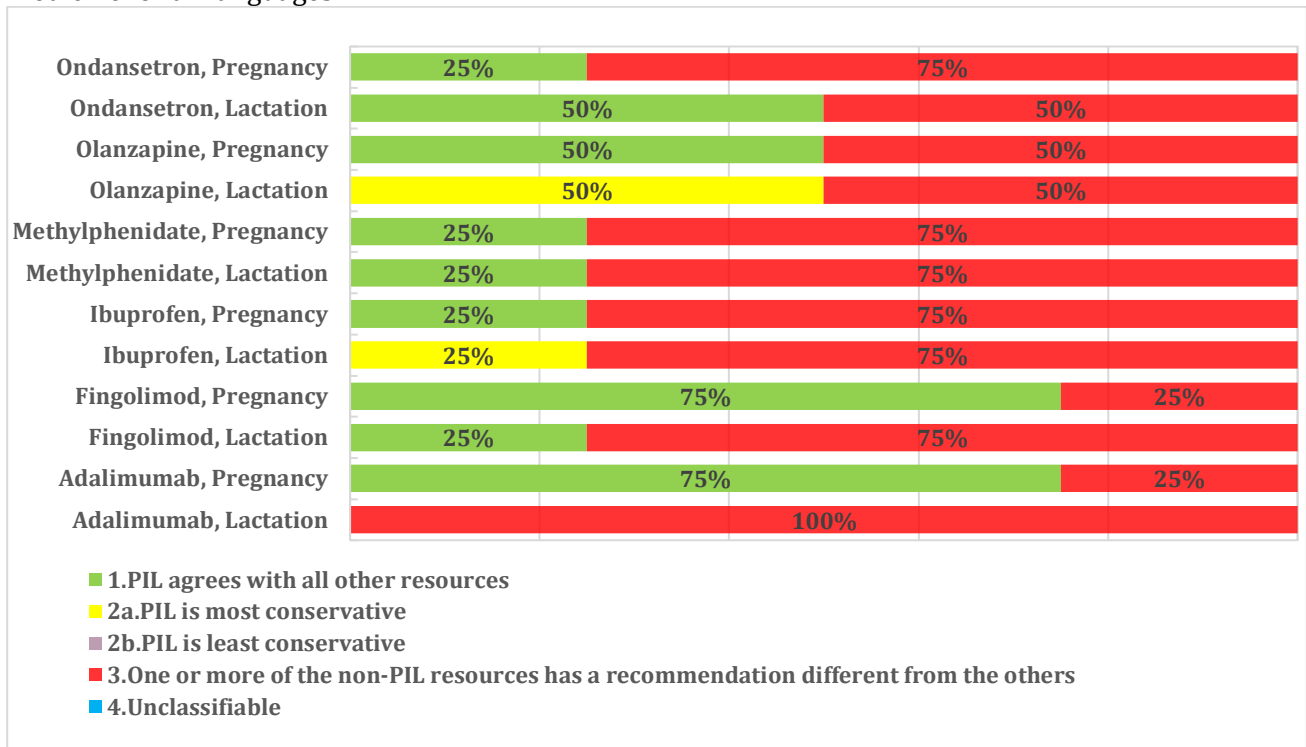
For all languages and medicines, 48 discrepancy comparisons were undertaken, 24 for pregnancy and breastfeeding each. Among the 48 comparisons, 15 (31%) corresponded to consistent recommendations in all data sources (category 1): 46% for pregnancy recommendation and 17% for breastfeeding recommendation comparisons (see Figure 5). The Swedish pregnancy recommendations showed the most consistency between data sources: 4 out of 6 medicines (67%) had consistent recommendations in all data sources (category 1). The least consistent recommendations were found for breastfeeding in English and Dutch, where no medicine had consistent recommendations in all data sources (category 2a and 3).

Figure 5 Discrepancies analysis of patients’ pregnancy and breastfeeding recommendations for all languages and by language



No drug had a unanimous consistent recommendation in all languages and for all data sources regarding their use during pregnancy or breastfeeding, Figure 6. For pregnancy recommendations, adalimumab and fingolimod showed the most consistency between data sources (consistent in all data sources (category 1) in 3/4 languages (75%)), whereas ibuprofen, methylphenidate and ondansetron showed the least consistency between all data sources. For breastfeeding recommendations, ondansetron showed the most consistency between all data sources (consistent in all data sources in half of the languages), whereas recommendations for adalimumab, ibuprofen and olanzapine were inconsistent (category 2a or 3) in all languages.

Figure 6 Discrepancies analysis of patients' pregnancy and breastfeeding recommendations by medicine for all languages

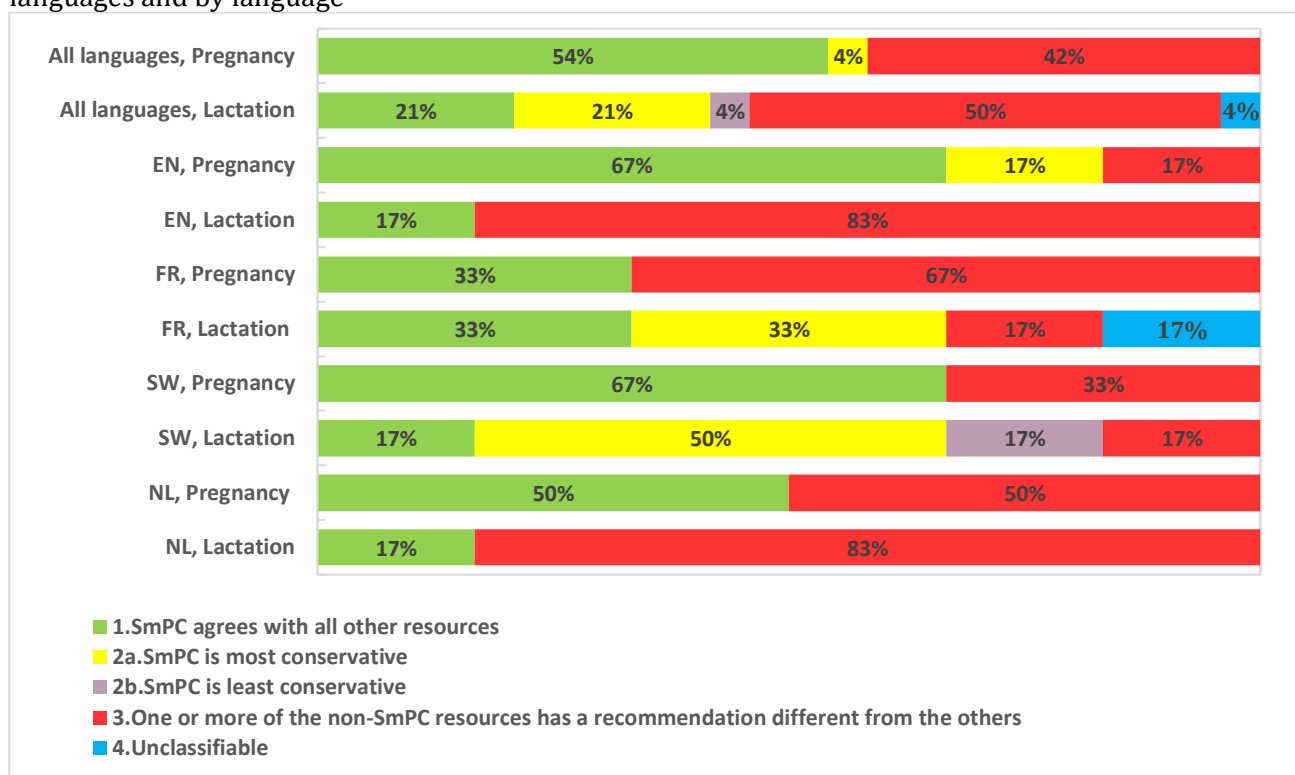


Discrepancies analysis for HCP sources

Among the 48 comparisons, 18 (38%) corresponded to consistent recommendations in all data sources (category 1). For the pregnancy recommendations, 13 out of 24 (54%) recommendations agreed between the data sources for all languages. For the breastfeeding recommendations only 5 recommendations out of 24 (21%) had consistent recommendations in all data sources (Figure 7).

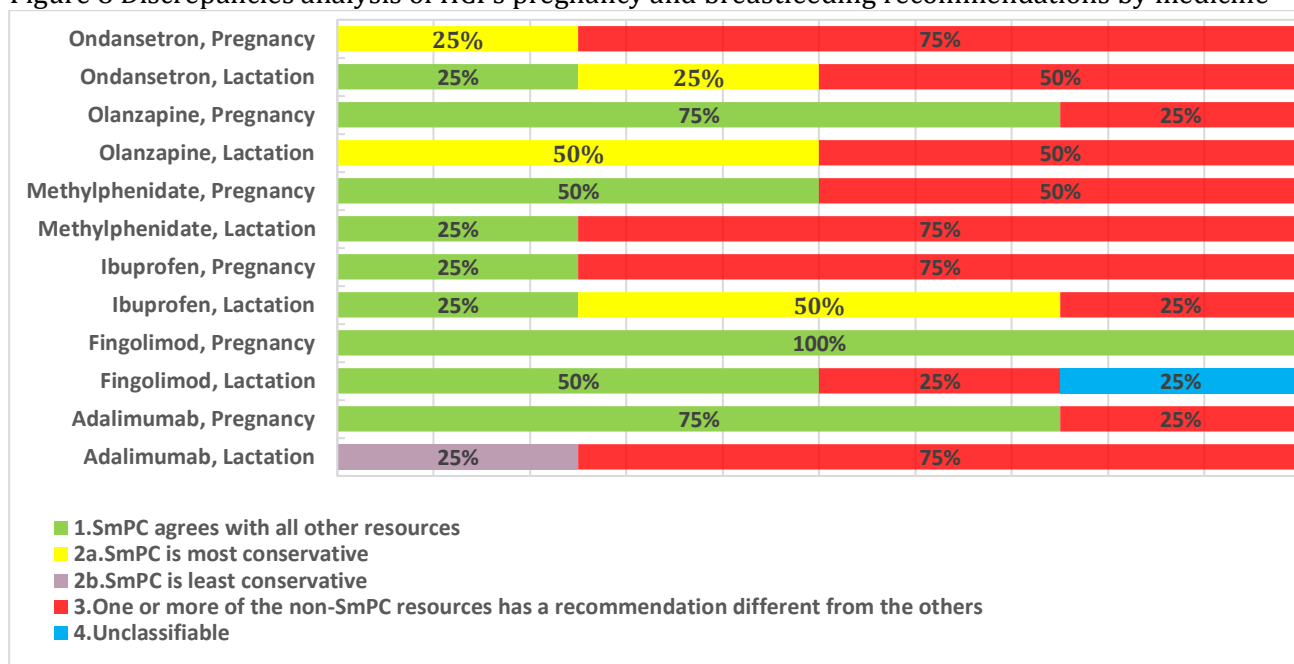
Swedish and English pregnancy recommendations showed the most consistency between data sources: 4 out of 6 (67%) medicines had uniform recommendations in all data sources (category 1). The least consistent recommendations were found for breastfeeding in English, Dutch and Swedish, 5 out of 6 (83%) of the medicines had inconsistent recommendations between the data sources category 2a and 3).

Figure 7. Discrepancies analysis of HCPs pregnancy and breastfeeding recommendations for all languages and by language



Discrepancy analysis by medicine (Figure 8) showed that pregnancy recommendations were consistent between all data sources for fingolimod in all languages (pregnancy recommendations “Should not be used” in all data sources (category 1)) whereas pregnancy recommendations for ondansetron were inconsistent in all languages (category 2a., 2b. or 3). For breastfeeding recommendations, fingolimod showed the most consistency between data sources (breastfeeding recommendations for fingolimod were consistent in all data sources in half of the languages), whereas recommendations for adalimumab and olanzapine were inconsistent (category 2a., 2b. or 3) in all languages.

Figure 8 Discrepancies analysis of HCPs pregnancy and breastfeeding recommendations by medicine



Detailed analysis of discrepancies

Medicines with totally divergent recommendations in patient data sources

Among the 48 comparisons, 11 comparisons (23%) (3 out of 24 (13%) for pregnancy recommendations and 8 out of 24 (33%) for breastfeeding recommendations) included a totally divergent recommendation between different data sources. For pregnancy, totally divergent recommendations were seen for ondansetron in 2 of 4 languages and for adalimumab in 1 of 4 languages (Appendix Table 10). For breastfeeding, totally divergent recommendations were seen in 3 of 4 languages for olanzapine, in 2 of 4 languages for adalimumab, and in 1 of 4 languages for ondansetron, ibuprofen and methylphenidate (Appendix Table 10). Differences between the PIL and a forum discussion (social media) or a scientific data source, were common reasons for the deviations, PIL being more conservative in these cases.

Medicines with totally divergent recommendations in HCP data sources

Among the total 48 comparisons, 6 were totally divergent (13%). All concerned breastfeeding recommendations: for olanzapine in 3 of 4 languages, for ibuprofen, methylphenidate and adalimumab in 1 language (Appendix Table 11). For all medicines except for adalimumab, the discrepancies were partly due to the SmPC being more conservative than information from at least one other data source (frequently the TIS information).

Comparing SmPC with drug formularies

In the UK, the SmPC and the Drug formulary (BNF) were always consistent, while in the Netherlands, the SmPC differed from one of the drug formularies in 6/24 (25%) of the comparisons. There was good consistency for pregnancy recommendations, 16/18 (88%) compared recommendations were consistent. The exception was ondansetron where the Dutch SmPC was more conservative than the Dutch Drug formulary for physicians, and methylphenidate, where the SmPC was less conservative than the Dutch formulary for pharmacists. For breastfeeding recommendations, 14/18 (78%) were consistent. For fingolimod, olanzapine, ondansetron and methylphenidate, the Dutch SmPC was more conservative than the Drug formulary for pharmacists.

Comparison between the Dutch drug formularies for pharmacists and physicians showed that they were similar in 50% of the cases. For pregnancy recommendations, the Drug formulary for pharmacists was more conservative than the Drug formulary for physicians for ondansetron and methylphenidate. For breastfeeding, the Drug formulary for pharmacists was less conservative than the Drug formulary for physicians for fingolimod, olanzapine, ondansetron and methylphenidate.

Comparing TIS recommendations for patients between languages

There was a limited number of discrepancies between the TIS/national knowledge base recommendations for patients. For the pregnancy recommendations, 25/27 (93%) were similar. Of the two discrepant recommendations, none were totally divergent. For breastfeeding, 15/22 (68%) of the recommendations were similar, and 7/22 (32%) were inconsistent. Among the inconsistent recommendations, one was totally divergent, methylphenidate which ranged from Can be used in Swedish and English (US Mother to baby) to Should not be used in French. Detailed results of this analysis are available in Appendix Table 12.

Comparing TIS recommendations for HCPs between languages

For pregnancy recommendations, the TIS/national knowledgebase information for HCPs was consistent for 20/22 (91%) of the recommendations. Only for ibuprofen, there was a slight difference. Two languages (NL, FR) had slightly stricter recommendations during the third trimester than the others (SW, UK).

For breastfeeding recommendations, 14/23 (61%) of recommendations were consistent, 8/23 (35%) were slightly different and one (4%) was totally divergent. Methylphenidate ranged from Can be used (SW) to Should not be used (FR). Detailed analyses for each medicine are available in the Appendix Table 12.

Comparing TIS recommendations with treatment guidelines

There were some discrepancies between TIS and treatment guidelines, especially for breastfeeding. However, no one was totally divergent. For pregnancy, they were consistent in 12/18 (67%) of the recommendations, treatment guidelines were more conservative in 4/18 (22%) and TIS was more conservative than the treatment guidelines in 2/18 (11%). For breastfeeding, TIS and treatment guidelines were consistent in 6/11 (55%) of the recommendations, treatment guidelines more conservative in 4/11 (36%) and TIS more conservative than treatment guidelines in 1/11 (9%) of the recommendations.

Comparing PIL with TIS recommendations

The PIL pregnancy recommendations were frequently consistent with those of the TIS 18/22 (82%) while there was significant inconsistency between the PIL and TIS breastfeeding recommendations, only 7/14 (41%) were in agreement. When discrepancies were found, PIL was more conservative in all cases, except one. Additional results of this analysis are detailed in Appendix Table 13 and 14.

Comparing news articles with TIS recommendations

For pregnancy recommendations, in 7/11 (64%) of the recommendations, the news article and the TIS were equally conservative, in 2/11 (18%), the news article was more conservative and in 2/11 (18%), TIS was more conservative. For breastfeeding recommendations, only 4 statements were comparable. Of these, 3/4 (75%) were equally conservative, and in 1 out of 4 cases (25%) the TIS was more conservative.

Comparing PIL recommendations between languages

When comparing the PIL recommendations between languages, as expected for the 3 EU-centrally approved products, i.e. adalimumab, fingolimod, and olanzapine, both pregnancy and breastfeeding recommendations were consistent in all languages. Discrepancies were noted across languages between the PILs for other products:

Methylphenidate and ibuprofen: Pregnancy recommendations were consistent, but breastfeeding recommendations were not consistent (“Should not be used” in one language versus “Benefit Risk Assessment” in all other languages for both drugs)

Ondansetron: For pregnancy, the PIL differed between Should not be used, Trimester specific and Individual Benefit Risk Assessment in different languages. For breastfeeding it varied between Should not be used and Individual Benefit Risk assessment.

Discussion

This analysis aimed to describe the frequency and nature of discrepancies between different online information sources for patients and HCPs in four European languages: Swedish, Dutch, French and English. The analysis was done for selected medicines which are used for common acute illnesses experienced during pregnancy and breastfeeding and medicines used for common chronic diseases in reproductive age.

The study showed that inconsistencies regarding pregnancy and breastfeeding recommendations are common both in online data sources for patients and for HCPs. These discrepancies were slightly more pronounced in patients’ information sources than in the ones for HCPs. For patients, 31% of the pregnancy and breastfeeding recommendations were consistent between the selected data sources compared to 38% of consistency between HCPs’ data sources. The significant discrepancies between data sources for HCPs is especially noteworthy, since this analysis only included highly credential data sources. The discrepancies between the drug formularies for pharmacists and physicians are for example unfortunate, since different categories of health care professionals might rely on contradictory information when counselling the women.

It was also seen that for the majority of selected medicines there was more homogeneity between data sources regarding pregnancy recommendations than regarding recommendations on medicine use during breastfeeding. For patients, 46% of pregnancy recommendations were consistent between data sources versus 17% for breastfeeding recommendations. This is also applicable for HCPs information sources where 54% of pregnancy recommendations were consistent between data sources versus 21% of consistency for breastfeeding recommendations. One reason for the wide spectrum of recommendations during breastfeeding, could be that different countries have different breastfeeding cultures and practices. National plans for breastfeeding promotion, protection and support are not available in all countries and recommendations from these plans, when available, might vary between countries [15]. Even though these national plans and general breastfeeding culture do not address safety of medication use during breastfeeding, they might have an impact on medicine breastfeeding recommendations. Another explanation could be that overall, there is less evidence to rely on for risk assessment of medicines during breastfeeding. Further, medicine exposure during breastfeeding is avoidable to a higher extent than during pregnancy which might contribute to that some countries are more conservative regarding medicine use breastfeeding. Online information concerning medicines and breastfeeding was also overall sparser and more difficult to find than for pregnancy.

The discrepancies varied moreover by languages and by selected medicines in the analysis. Even though it is probably most common to search in a local language, some women might also search for information in other languages. Therefore, discrepancies between different languages and countries may cause further confusion.

Concerning the different medicines, there was good consistency for fingolimod and adalimumab during pregnancy, in data sources both for patients and for HCPs. Both are centrally authorized medicines by the EMA, and thereby the regulatory information was consistent between the countries, which might promote more consistent information also in other data sources. Compared to the other medicines in our study, fingolimod was more recently introduced to the market and is clearly contraindicated in pregnancy and breastfeeding from the manufacturer, which probably adds to that most data sources correspond to the labelled information. In addition, the EMA had issued updated restrictions for the use of the medicine in pregnancy a few months before the present study [16].

At the time of the study, the EMA had announced a warning for using ondansetron during early pregnancy due to a potential link to orofacial clefts [17]. This was probably a reason to the inconsistencies in pregnancy recommendations for ondansetron, since some recommendations were published before this announcement. Secondly, this warning was debated and scientific sources like the TIS-centers did not agree with the EMA recommendation and had consistently less conservative recommendations for ondansetron than the PIL/SmPC.

Comparison of TIS/national knowledgebase information for HCPs and patients showed that there was good consistency between languages regarding pregnancy recommendations (93% and 91% of consistency between patients and HCPs data sources, respectively) with no medicine having totally divergent recommendations. There is still though room for improvement when it comes to breastfeeding recommendations (68% and 61% of breastfeeding recommendations were consistent between patients' and HCPs' data sources, respectively). Again, this might be dependent on the 'breastfeeding culture' in a country. Even though there are some discrepancies for breastfeeding recommendations between the TIS centres, the information from these specialists are quite in agreement. A closer collaboration between TIS centres might further improve the consistency.

In general, regulatory sources tended to be more conservative than other data sources. For example, there was good consistency between TIS and PIL pregnancy recommendations, but worse for breastfeeding recommendations, with PIL being generally more conservative. The same tendency was seen in the analysis of medicines with totally divergent recommendations where the regulatory recommendations were generally more conservative. This is in accordance with the Australian study by Brown et al [3], which showed that discrepancies frequently occur between the Australian Prescribing Information (PI) and credible Australian and international clinical sources. The same was demonstrated in the Norwegian study by Frost Widnes et al, where the Norwegian Pharmaceutical Product Compendium (Felleskatalogen) was frequently more restrictive than advice from the drug information centres [9].

While a conservative approach may be necessary based on available data, it can leave the HCP and patient without the most needed information on what to do in the given situation. The possibility of users resorting to single case reports/blogs/social media cannot be ruled out. In addition, it has been shown in a previous study that many posts on social media provide inaccurate evidence, especially for drugs that should only be used on a strict or second line indication [11]. A French study found that approximately 20% of the advice given in online forum conversations regarding medication use during pregnancy lacked sufficient evidence to support their conclusions [13]. Another study also found that 42% of medicines classified as safe on different internet sites, were not safe according to the Teratogen Information System (TERIS) classification [18]. This emphasizes the need to have reliable, scientifically based and up-to-date information in data sources.

This study has some limitations. First, pregnancy and breastfeeding recommendations were not available in every data sources category for every medicine, resulting in potential bias in the analysis where all data sources for all medicines were compared. Some data sources might have focused more on medicines that have been linked to negative impact on the fetus or breastfed child. This bias was however addressed in the detailed analysis where recommendations were compared between different data sources for the same medicine in the same language. Second, in social media, most of the time, no clear recommendation could be concluded from the discussions, and therefore, their recommendations were frequently categorized as "Not classifiable". This was one reason that some medicines did not have a predominant recommendation. Third, selected medicines for the analysis were partly medicines for which risk assessment are complicated which limits the representativeness and generalization of the study results.

To our knowledge, our study is one of the few published studies [1,10] analysing information discrepancies between different languages and data sources. Most of the available studies focused on discrepancy analysis between data source within one country or language. Overall, our results with significant discrepancies regarding recommendations on medicines during pregnancy and breastfeeding between different online data sources, are in line with previous research. It is important to increase the availability of reliable, consistent information to endorse that women will receive as safe medicine treatment as possible, during this special period of life.

Conclusion

There are significant discrepancies between online information sources concerning medicines during pregnancy and breastfeeding. This applies both to information sources intended for patients and for health care professionals. The differences in recommendations are seen within as well as between languages. To ensure the health of the mother, foetus and breastfed child, it is crucial to provide women in reproductive age with consistent and evidence-based information. A working procedure where TIS centres collaborate would probably save resources and time and reduce the risk of conflicting messages. The TIS centres should preferably work together with national stakeholders to harmonise information also within the respective countries.

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Sub-task 5.1.3 – End-Users' experiences

Abstract

The objective of this study was to explore pregnant and breastfeeding women's and healthcare professionals' (HCPs) information needs, trust in information and preferences for a knowledge bank about medicine use during pregnancy and breastfeeding. The study included two large scale surveys in women (n=1910) and HCPs (n=665) followed by six targeted focus group discussions with pregnant and breastfeeding women and HCPs.

The results from the survey showed that pregnant and breastfeeding women and HCPs need information about the safe use of drugs during pregnancy. Currently, there is a lack of clear and comprehensible information sources for women in need of this information. HCPs are widely consulted as a source of information, but they are also experiencing difficulties in finding and interpreting information. Discrepancies and often conflicting information in different sources are challenges reported by both women and HCPs. The use of internet has increased and has led to a preference for easily accessible but reliable online resources.

The focus group discussions showed that the pregnant, breastfeeding women and HCPs were positive regarding a European knowledge bank with information about the safe use of drugs during pregnancy and breastfeeding. This study provided insights on the needs and preferences for information. According to these, the information provided on the knowledge bank should be clear and understandable for both HCPs and the general public. The information pages should be easily found and have a clear conclusion. It is also important that the information is available in different native languages. In order to increase the reliability and trust in the knowledge bank, it should be clear on which studies the presented information was based, and the pharmaceutical industry should not be involved in writing recommendations. In this way, the knowledge bank will best meet the needs and preferences of the users.

Introduction

Women and healthcare professionals (HCPs) have the right to make informed decisions on the safety of medicines use during pregnancy and breastfeeding. While a pregnant woman takes on average three medicines during her pregnancy and four medicines during breastfeeding, there is almost no evidence-based information available on most medicines to guide a woman's fully informed decision (1).

A huge information gap exists and this is due to several factors, including but not limited to non-existent and inadequate data, lack of awareness of the information gap and of the rights of women and HCPs to be able to make informed decisions.

One of the key aims of ConcePTION is to improve the value, quality and harmonisation of the dissemination of information on available evidence related to the safety of medicines during pregnancy and breastfeeding. To ensure that the information needs of women and HCPs are met, it is first necessary to understand the information needs and preferences of these women and HCPs. This includes understanding how they search for and interpret existing information, and assessing what their preferences would be in receiving such information in the future, both regarding content of the information and how it is delivered/made accessible to them.

Used sources by HCPs and women

A literature review (for methods and detailed findings see Appendix 1) demonstrated that HCPs use different sources of information that they considered reliable on safety of medicines during

pregnancy and breastfeeding. These sources vary per type of HCP and country, there are no well-established and unified sources of information. The use of the internet as the preferred source of information to get access to up to date information is widespread. Physicians often search for the information before contacting specialised services for information (such as drug information or teratology information services). When evaluating HCPs' needs for information, it was noted that HCPs require sources that provide more specific and detailed information that they could use when explaining medicines risk and teratogenic side effects in a way that would be meaningful to their patients.

Only limited data exist regarding HCP information needs related to medicines use and safety during breastfeeding, however this literature search confirmed the need for evidence-based information to support GPs and pharmacists in managing the risk of medicines and preventing unnecessary cessation of breastfeeding.

Most of the studies reviewed show that pregnant women rely on their health care practitioners (Physicians, Pharmacists and Midwives) for information about medicine use during pregnancy, followed by information accessible on the internet. It was reported that a high percentage of women are using the internet as a resource during pregnancy, often via Google or other search engines, and the use of pregnancy-related applications is increasing. Women express interest in personal communications and resources that facilitate connections to other women and their experience such as video chat tools or social media groups.

Conflicting information

The literature review also identified that difficulties finding the information as well as encountering conflicting information in different sources are common issues for both HCPs and pregnant women. Another challenge is inaccurate perception of risk, either overestimated or underestimated by both HCPs and pregnant women. This may be an indication of unmet information needs during pregnancy. It is thus important that HCPs are equipped with the relevant information to enable them to provide accurate information and counselling to women about teratogenic effects of drugs and safe use in breastfeeding, thus helping to create a more accurate perception of the risks. Teratology information services can play an important role in ensuring HCPs have the required information by providing education materials that can be used by these HCPs, however many countries do not have national teratology information services. More information is needed to understand current information sources and needs of HCPs about the use of medicines during pregnancy and especially in breastfeeding.

The increase in internet use has been accelerated by the global expansion of smartphones and other devices in the last decades. It is therefore important that good quality information is accessible through the internet and should be easily visible, searchable and provided with appropriate details and content for end users. More research is needed to understand internet use, such as the specific sites visited and also women's perception of how reliable they find information from the internet.

Background survey

Building on the findings from the literature review, a background survey of women was conducted from September - November 2019 (577 respondents, disseminated by ConcePTION members) to inform the design of the main survey and focus groups, to enable the consortium to begin communicating about ConcePTION, and to begin building an engaged supporter network to retarget for the main survey. The survey was conducted in English, French and Dutch.

The results (see Appendix 2) broadly represent how women from the general public find information they are looking for about medicine use before, during and after pregnancy and breastfeeding, who directed them to that source, to what extent it was easy to find and understand, and if they trusted it.

It was notable that a large proportion of European respondents (around 44%) came from Eastern Europe - Albania, Bulgaria, Romania, Serbia and Macedonia - despite the fact that the ConcePTION consortium does not have a big representation in this area. It was decided to translate the main survey into at least one Eastern European language (Romanian and Czech were chosen) to be able to explore better the needs from this region.

While 60% of non-English natives did state that it was adequate to only have information in English and of those 50% did say the information was easy to understand, it might still mean that a proportion of women may not have understood crucial details for safe use of medicines in pregnancy and breastfeeding or gave up their search completely. Results from the pilot survey suggested to explore this further in the main survey.

In terms of information sources, medical doctors (approx. 67%) were still a major source of information for the pilot survey respondents. While approximately only 29% of all respondents believed that information coming from a drug manufacturer is trustworthy, it was still the third most cited source of information. Many respondents (approx. 18%) used social media groups or specific websites but most women just used search engines such as Google (approx. 55%). It was suggested to explore the use of the internet in more detail as a follow up. Nearly a third (approx. 30%) said that part of the information was different when coming from different sources, supporting the need for this project.

In terms of information needs, the most important information (ranked) that women look for in medicine packaging was information concerning birth issues, the possibility of birth defects (96.5%) and miscarriages (96.4%) when taking the medicine as well as effects on child development (95%). Nearly 90% of respondents also needed information on dosages of medicine during pregnancy or breastfeeding. In terms of trustworthiness of sources, respondents clearly favoured information from scientific or clinical studies (approx. 88%) or information collected through organisations that have an official role to follow-up and record pregnancies of women who have taken medicines (approx. 61%).

Overall, based on the pilot survey results we hypothesise that there is misinformation among women when it comes to the availability of accurate information on pregnancy and breastfeeding. Although the majority of women said they could find needed information on the safety of medicine use during pregnancy and breastfeeding, the fact that nearly 30% of women claimed to have found differing wording and answers for the same questions, arguably indicates that there are important gaps in available information and research within this field.

Further research needed

Despite all information that was found in the literature and previously described survey, more research is needed in order to more deeply investigate the possibility that HCPs and women are not aware of the information gap on medicine use during pregnancy and breastfeeding, and to better understand language preferences for tools and resources. Also, more information is needed on women with chronic medical conditions, who may have different needs or experiences from other women, and from HCPs, who may have access to different sources of information and a different level of health literacy.

Aim

The overall objective of this study was to explore pregnant and breastfeeding women's and HCPs' information needs, trust in information and preferences for a knowledge bank about medicine use during pregnancy and breastfeeding.

More specifically, the aims of this study were:

- To describe the information needs of pregnant and breastfeeding women and HCPs regarding drug use during pregnancy and breastfeeding.
- To describe the information sources pregnant and breastfeeding women and HCPs are currently using for information regarding drug use during pregnancy and breastfeeding and their reasons for their choice.
- To describe factors influencing pregnant and breastfeeding women's and HCPs' trust in information sources providing information about drug use during pregnancy and breastfeeding.
- To describe pregnant and breastfeeding women's and HCPs' needs and preferences for a knowledge bank about drug use during pregnancy and breastfeeding, available to all European citizens.

Methods

To achieve the aims of the study, it was decided to 1) conduct a large scale survey in women with the aim to collect data from large groups of women and HCPs across several countries and 2) to conduct targeted focus group discussions with women and HCPs in order to verify and obtain more detailed information on findings from the study, further evaluate information needs and preferences in women and HCPs and specifically obtain preferences and test design assumptions for the European knowledge bank.

Survey methodology

Study overview

Two multinational, cross-sectional, web-based surveys were conducted. One survey was open to women, including mothers to be, pregnant, breastfeeding women and mothers, and the second survey was aimed at HCPs. The members of IMI ConcePTION supported the creation and dissemination of the surveys, with The Synergist leading the overall coordination of the surveys.

Study population

Respondents from 74 countries, participated in the women's survey (UK, BE, NL, SE, FR, RO, ES, IE, US, IL, MK, RS, BG, PL, AT, IT, AL, CA, MT, XK, AU, IN, PT, DE, MX, CH, NG, BA, HR, ZA, GR, ME, MD, AM, NZ, UA, FI, EE, LV, NO, SK, CM, HU, JP, KE, PK, PH, RU, ZW, BZ, BJ, BN, CL, EG, GH, GD, JM, KI, KP, LB, LU, MV, SO, LK, UG, VN, MG, PE, SN, BH, BR, UY, LT, CZ)

Respondents from 46 countries, participated in the HCP survey (SE, IL, BE, UK, FR, IL, IE, AT, IN, NL, MK, ES, AL, PL, RS, RO, CH, NG, EE, XK, BG, HR, US, AU, MT, PT, TZ, DK, IR, SK, GR, DE, MY, GD, AR, CA, NO, MD, KE, PK, GY, PH, BR, AF).

Data collection

Data was collected through an anonymous online questionnaire hosted by Survey Monkey (<https://www.surveymonkey.com/>) and accessible for four months in each participating country within the period 27.01.2020 to 30.04.2020. The questionnaires were open to the public via utilization of banners (invitations to participate in the study) on national websites and/or social networks commonly visited and consulted by pregnant women and/or new mothers. The relevant sections of the questionnaires are presented in Appendix 3 and 4.

Study design

The questionnaires were both first developed in English and then translated into French, German, Italian, Czech, Romanian, Spanish, Dutch and Swedish. These languages were chosen to ensure a good spread by geography and by GDP/ level of health system maturity and the majority being ENTIS representative countries, for better dissemination. Czech and Romanian were added since there were many respondents from these countries in a preliminary survey conducted in 2019. The translations were provided by native speakers of these languages in the ConcePTION consortium. The GDPR privacy notices were all translated by a professional translation office. The translations of the responses back to English were carried out by the same translation office, except Dutch and German which was by done by native Conception partners.

A questionnaire was piloted in December 2019 (11 pilot participants) and elicited no major change to the questionnaire. Although no IP addresses were collected, the survey tool only allows one submission per device, limiting the possibility of potential duplicates.

Dissemination

In order to disseminate the surveys, several tactics were used. A survey landing page was created on the ConcePTION website (including 8 translated landing pages) and a toolkit for communicating to women on social media was shared with ConcePTION consortium partners. There was an internal campaign to ask all consortium partners to cascade the surveys to their networks. The survey was also shared on partner websites and channels, including the EFPIA network and ENTIS network services/websites and the Bumps website, taking advantage of related campaigns and platforms such as Safe Motherhood Week. The survey was also shared in social media groups where pregnant and nursing mothers meet to discuss pregnancy and breastfeeding. Additionally, several important external stakeholders were asked for their support in sharing the survey. This includes the European Midwives Association, Multipharma, International Confederation of Midwives, La Leche League International, IMI, UNFPA, FIGO, the International Pediatric Association, EBCOG, the European Association of Perinatal Medicine and the health system in Montenegro.

Analysis

Results regarding socio-demographics, health-related characteristics (only women), their informational needs, commonly used sources for information, the type of information they are usually looking for and who they trust as a sender of information were analysed using descriptive statistics for women and HCPs respectively, as appropriate. In addition, results on Internet usage as well as what elements are important for women and HCPs regarding a future existing knowledge bank on medicines use during pregnancy and breastfeeding, were analysed descriptively.

The women were grouped according to current situation (pregnant, breastfeeding, other women) and descriptive data were presented both for the total study population and for subpopulations based on current situation. The HCPs were grouped according to profession (general practitioner (GP), specialist physician, nurse, pharmacist, other) and descriptive data were presented both for the total study population and for subpopulations based on profession.

Both univariate and multivariate logistic regressions were performed to:

- Investigate the association between sociodemographic factors/health-related characteristics of women and their need for information during pregnancy and breastfeeding among women
- Investigate the association between sociodemographic factors/health-related characteristics and women who are having difficulties understanding information on medicines use during pregnancy and breastfeeding
- Investigate the association between sociodemographic factors and type of HCPs who are often being asked about medicines use during pregnancy and breastfeeding
- Investigate the association between sociodemographic factors and HCPs who are having difficulties understanding information on medicines use during pregnancy and breastfeeding

Multivariable analyses were presented as both full and reduced models for the women, while for the HCPs we only made full models (due to fewer variables for the latter group). Variables were entered simultaneously into the model, and non-significant variables removed (Full model). Collinearity between variables was assessed. When two variables correlated, the variable with the largest effect estimates in the full model and the largest number of participants was selected (Final model). Results from the logistic regressions were presented as OR (95% CI). The Hosmer and Lemeshow test were used to assess goodness-of-fit of the final multivariable models. SPSS (IBM SPSS Statistic) was used for statistical analysis.

Ethics

Anonymous – no formal ethical approval required. All data were handled and stored anonymously. At the end of the questionnaires, they were able to give their email address if they wanted to participate in further studies – but this was fully optional.

Focus groups methodology

Study design

A qualitative, multi-country study was used to explore pregnant and breastfeeding women's and HCPs information needs, trust in information and preferences for a knowledge bank about medicine use during pregnancy and breastfeeding. The qualitative method that was used was focus group discussions.

Study population

As the knowledge bank will be designed for European usage, the focus groups in this study took place in three different European countries: Croatia (Zagreb), France (Lyon) and the Netherlands ('s-Hertogenbosch). These three countries represent Northern, Western and Eastern Europe. In each of these countries the Teratology Information Service (TIS) located in these cities were responsible for running the focus groups. In total six focus groups were held, two in each country, one with pregnant and breastfeeding women and one with HCPs.

Inclusion and exclusion criteria

For the focus groups with the women, we included pregnant women or non-pregnant women with a child no older than 6 months. Both women with as well as those without chronic disease were eligible for inclusion. For the focus groups with HCPs, we included general practitioners, obstetrician/gynaecologists, community pharmacists and midwives, practicing in either Croatia, France or the Netherlands.

Participants were excluded for participation in the focus group when they could not speak, read, or write the language of the country in which the focus group is held (i.e. Croatian in Croatia, French in France and Dutch in the Netherlands), had not reached the age of eighteen, or were not competent to make informed decisions or do not give informed consent.

Recruitment and enrolment of participants

It is generally recommended that focus groups should not have more than six to nine people, as this allows for a range of opinions and interaction while still being manageable. Anything more than nine people can lead to issues such as higher likelihood of the group fragmenting with splinter groups talking amongst themselves, the discussion becoming unruly, less confident people feeling inhibited and therefore not contributing or making themselves heard, and the risk that the loudest persons will dominate (2). We aimed for each focus group to have eight participants. To reach this number, more participants (about 10) were invited than were eventually needed to be sure that all groups had at least eight participants.

Each country used a tailored approach for recruiting participants. Examples of channels for recruiting participants were the national Teratology Information Service, hospitals, people who filled in the previous ConcePTION survey, and social media channels. Possible participants were invited

for the focus groups by e-mail, including an information sheet in which the aim of the focus group was explained. After showing initial interest, the participant was sent a short form (either on paper or electronic) where they could provide some baseline information regarding their demographics, pregnancy, breastfeeding and medicines use. Participants recruited via social media and other forums did not receive an e-mail, but were asked to fill in the form with baseline information directly on-line. When participants had filled in the form, they were checked for eligibility for the study based on the baseline information provided. After selection, the participants filled in an informed consent before the start of the focus group. Participants did not receive any reimbursement for participation.

Focus group topics

The focus groups discussed topics related to:

- What kind of information women and HCPs need around medicine use during pregnancy and breast feeding, and why
- What information sources they use and trust, and why
- Their needs and preferences for a knowledge bank

The focus group instructions can be found in Appendix 5. Concerning discussion around the needs and preferences for a knowledge bank, for the Croatian and French women and HCPs, it was asked what kind of knowledge bank they would prefer in relation to drug use during pregnancy and breastfeeding. In the Netherlands, the prototype of the knowledge bank was shown to the participants.

The questions used for the focus groups were pre-tested for readability by the one person in each target group. Thereafter a pilot discussion was organised in which the moderator and the assistant could see if they were prepared well enough and if their questions needed to be revised.

Data collection and analysis

All focus groups were held in the local language. The focus groups were audio-recorded and transcribed verbatim. The potential for the identification information was removed from the transcripts. The transcripts in Croatian and French were translated into English before analysis. The transcript in Dutch was analysed in Dutch.

Data analysis was performed by the two researchers at the Netherlands Pharmacovigilance Centre Lareb. The transcripts were coded by one researcher using directed content analysis. In this analysis, specific codes were identified using a deductive (top/down) theoretical approach. After coding of the first transcript, the codes were discussed with the second researcher and adapted were needed. This led to a structured coding template that was used to code the other transcripts. During analysis, new codes could be added.

Survey Results

Women - Population characteristics

A total of 2118 women accessed the online questionnaire, whereof 1910 (90.2%) responded to it. Of these, 39.5% were pregnant, 32.0% were breastfeeding and 28.5% were in other situations, e.g. trying to get pregnant or thinking about getting pregnant.

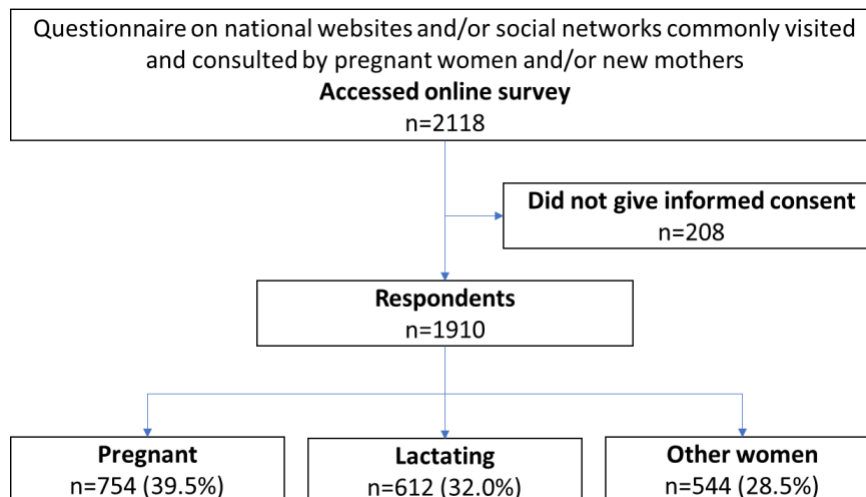


Figure 1. Participant Flow Chart Women

Almost 90% of the women had been pregnant before and most of the women were between 26 and 40 years old (table 1). Three quarters of the women had a university education. Approximately 60% of the study population were living in West-European countries, and in total 90% of the women were living in European countries. The most frequent native languages were English, Dutch, Swedish and French (38.7%, 13.8%, 8.0% and 7.2%, respectively).

Approximately one third of the women reported having a pre-existing or chronic medical condition, and 36% reported taking medicines regularly (table 1).

Table 1. Characteristics of study population, women, n=1910.

	Total (n=1910)	Pregnant (n=754)	Lactating (n=612)	Other women (n=544)
Previous pregnancies (≥1) (n=1910)				
No	228 (11.9)	106 (14.1)	0 (0.0)	122 (22.4)
Yes	1682 (88.1)	648 (85.9)	612 (100.0)	422 (77.6)
Age (years) (n=1896)				
≤25	132 (7.0)	69 (9.3)	24 (3.9)	39 (7.2)
26-30	468 (24.7)	225 (30.2)	150 (24.6)	93 (17.2)
31-35	735 (38.8)	304 (40.8)	257 (42.2)	174 (32.1)
36-40	398 (21.0)	134 (18.0)	142 (23.3)	122 (22.5)
≥41	163 (8.6)	13 (1.7)	36 (5.9)	114 (21.0)
Education level (n=1894)				
High school or professional degree	441 (23.3)	199 (26.7)	113 (18.6)	129 (23.9)
University	1392 (73.5)	518 (69.5)	478 (78.5)	396 (73.3)
Other education	61 (3.2)	28 (3.8)	18 (3.0)	15 (2.8)
Region of residence (n=1910)				
Northern Europe	176 (9.2)	25 (3.3)	109 (17.8)	42 (7.7)
Western Europe	1162 (60.8)	434 (57.6)	363 (59.3)	365 (67.1)
Eastern Europe	269 (14.1)	160 (21.2)	61 (10.0)	48 (8.8)
Southern Europe	113 (5.9)	51 (6.8)	34 (5.6)	28 (5.1)
Other regions	190 (9.9)	84 (11.1)	45 (7.4)	61 (11.2)
Healthcare professionals (n=1896)^a				
Medical doctor	76 (4.0)	31 (4.2)	25 (4.1)	20 (3.7)
Nurse	116 (6.1)	38 (5.1)	39 (6.4)	39 (7.2)
Pharmacist	73 (3.9)	25 (3.4)	20 (3.3)	28 (5.2)
Other HCPs	201 (10.6)	63 (8.5)	71 (11.7)	67 (12.4)
Non-HCPs	1430 (75.4)	588 (78.9)	454 (74.5)	388 (71.6)
Pre-existing/chronic medical conditions (n=1883)				
No	1275 (67.7)	497 (67.0)	448 (73.9)	330 (61.7)
Yes	608 (32.3)	245 (33.0)	158 (26.1)	205 (38.3)
Medical condition (n=1898)				
Asthma or allergy	118 (6.2)	50 (6.7)	38 (6.3)	30 (5.6)
Mental health problem	115 (6.1)	57 (7.7)	20 (3.3)	38 (7.1)
Hypothyroidism	97 (5.1)	37 (5.0)	29 (4.8)	31 (5.8)
Inflammatory disorder	54 (2.8)	20 (2.7)	14 (2.3)	20 (3.7)
Cardiovascular/blood disease	41 (2.2)	8 (1.1)	12 (2.0)	21 (3.9)
Diabetes	17 (0.9)	6 (0.8)	8 (1.3)	3 (0.6)
Epilepsy	15 (0.8)	5 (0.7)	4 (0.7)	6 (1.1)
Migraine / headache	13 (0.7)	3 (0.4)	3 (0.5)	7 (1.3)
Pain condition	10 (0.5)	5 (0.7)	1 (1.7)	4 (0.7)
Other/multiple disorders	116 (6.1)	47 (6.3)	27 (4.5)	42 (7.9)
Take medication regularly (n=1866)				
No	1191 (63.8)	440 (60.1)	436 (72.3)	315 (59.3)
Yes	675 (36.2)	292 (39.9)	167 (27.7)	216 (40.7)
Taking medication for ... (n=661)^b				
Chronic medical condition	434 (65.7)	173 (60.3)	110 (67.9)	151 (71.2)
Pregnancy related condition	116 (17.5)	90 (31.4)	17 (10.5)	9 (4.2)
Other conditions	207 (31.3)	87 (30.3)	55 (34.0)	65 (30.7)

*Data presented as percentage of total (n=1910), pregnant (n=754), lactating (n=612), other women (n=544) in the first, second, third and fourth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100): Previous pregnancies n=0, age n=14, education level n=16, region of residence n=0, healthcare professionals n=14, pre-existing/chronic medical conditions n=27, medical condition n=12, take medication regularly n=44, taking medication for n=14.

Abbreviations: HCP, Healthcare Professional.

^a The question was only accessible for those who replied that they were a HCP, n=466.

^b The question was only accessible for those who replied that they take medication regularly, n=675.

Information about medicines during pregnancy and breastfeeding

Approximately 85% of the women said they had had the need for information about medicines during pregnancy/breastfeeding. As the first information source, medical doctor and Internet were most used (table 2). Pregnant women searched for information at the Internet first more often than the other groups of women. When looking for information online, search engines (45.0%) were the most common to use, followed by scientific articles (33.4%), patient information leaflet (31.7%), discussion forums (24.6%) and birth defect information service (22.2%). More than half of the women discussed the information they had found online with an HCP and approximately 75% went online in retrospect to check for information received by an HCP (table 2). The most common information to look for regarding medicines use during pregnancy and breastfeeding was: “Is it safe for the baby if I take this medicine when I am pregnant?”.

Table 2. Need for information about medications during pregnancy and lactation.

	Total (n=1910)	Pregnant (n=754)	Lactating (n=612)	Other women (n=544)
Need for information about medicines during pregnancy/lactation (n=1846)				
No	280 (15.2)	95 (13.1)	52 (8.7)	133 (25.4)
Yes	1566 (84.8)	631 (86.9)	545 (91.3)	390 (74.6)
When in need for information^{ab} (n=1557)*				
When thinking about/trying to get pregnant	652 (41.9)	198 (31.5)	186 (34.2)	268 (69.6)
When pregnant	1340 (86.1)	581 (92.5)	480 (88.2)	279 (72.5)
When lactation	857 (55.0)	144 (22.9)	510 (93.8)	203 (52.7)
First medicine information source^b (n=1544)*				
Medical doctor	511 (33.1)	197 (31.5)	153 (28.4)	161 (42.3)
Internet	510 (33.0)	252 (40.3)	158 (29.4)	100 (26.2)
Medicine packaging	197 (12.8)	72 (11.5)	80 (14.9)	45 (11.8)
Midwife/nurse	92 (6.0)	30 (4.8)	39 (7.2)	23 (6.0)
Pharmacy personnel	87 (5.6)	31 (5.0)	35 (6.5)	21 (5.5)
Information leaflet about medicine use during pregnancy or lactation from your doctor's office	26 (1.7)	9 (1.4)	7 (1.3)	10 (2.6)
Family/friends	24 (1.6)	10 (1.6)	10 (1.9)	4 (1.0)
Other sources	92 (6.0)	23 (3.7)	54 (10.0)	15 (3.9)
Online information sources^{ab} (n=464)				
Search engines	209 (45.0)	106 (46.7)	52 (35.9)	51 (55.4)
Scientific articles	155 (33.4)	90 (39.6)	41 (28.3)	24 (26.1)
Patient information leaflet	147 (31.7)	72 (31.7)	44 (30.3)	31 (33.7)
Discussion forums	114 (24.6)	58 (25.6)	35 (24.1)	21 (22.8)
Birth defect information service	103 (22.2)	51 (22.5)	31 (21.4)	21 (22.8)
Patient organization websites	68 (14.7)	32 (14.1)	19 (13.1)	17 (18.5)
Social media	48 (10.3)	17 (7.5)	25 (17.2)	6 (6.5)
National medical services	25 (5.4)	6 (2.6)	12 (8.3)	7 (7.6)
Online magazines	18 (3.9)	8 (3.5)	3 (2.1)	7 (7.6)
Other online sources	73 (15.7)	21 (9.3)	39 (26.9)	13 (14.1)
Discussion about online information with HCP^b (n=465)				
No	212 (45.6)	105 (46.3)	56 (38.6)	51 (54.8)
Yes	253 (54.4)	122 (53.7)	89 (61.4)	42 (45.2)
Went online in retrospect to check for information received by HCP^b (n=1460)				
No	354 (24.2)	145 (24.8)	116 (22.7)	93 (25.4)
Yes	1106 (75.8)	439 (75.2)	394 (77.3)	273 (74.6)
Type of information looking for^{ab} (n=1460)				
Safe for the baby if I take this medicine when pregnant?	1332 (91.2)	557 (95.4)	447 (87.6)	328 (89.6)
Safe for the baby if I take this medicine when lactating?	910 (62.3)	193 (33.0)	483 (94.7)	234 (63.9)
How much of this medicine can I take when pregnant?	621 (42.5)	296 (50.7)	177 (34.7)	148 (40.4)
How to treat a disease when pregnant or lactating	501 (34.3)	203 (34.8)	183 (42.2)	115 (31.4)
How much of this medicine can I take when lactating?	411 (28.2)	85 (14.6)	215 (42.2)	111 (30.3)
Experiences or advice from women who have used the same medicine in pregnancy/lactation	409 (28.0)	187 (32.0)	127 (24.9)	95 (26.0)
Can the medicine make it difficult to become pregnant?	153 (10.5)	51 (8.7)	29 (5.7)	73 (19.9)
Other types of information	42 (2.9)	13 (2.2)	13 (2.5)	16 (4.4)

*Data presented as percentage of total (n=1910), pregnant (n=754), lactating (n=612), other women (n=544) in the first, second, third and fourth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100): medicines information need during pregnancy or lactation n=64, when in need for information n=9, first medicine information source n=22, online information sources n=46, discussion about online information with HCP n=45, went online in retrospect to check for information received by HCP n=106, type of information looking for n=106.
 Abbreviations: HCP, Healthcare Professional.

Fifty-two percent of the women have experienced discrepancies between different sources and approximately 20% have experienced not finding a useful answer about medicine use during pregnancy/breastfeeding (table 3). The most frequent consequences of not finding a useful answer were “I discussed with my doctor, midwife or pharmacist” and “I decided not to take the medicine”. In addition, many women reported becoming anxious.

There were 40.3% of the women who reported having difficulties understanding information about medicines use during pregnancy/breastfeeding and the main reasons for difficulties understanding the information were that the information was not precise enough and that the information did not include scientific results.

Almost half of the women selected their medical doctor as their preferred source of information in an ideal world, while more than 25% reported their midwife or nurse. One third of the women knew of organisations that specialise in providing information about how safe it is to use medicines during pregnancy and breastfeeding.

Table 3. Difficulties interpreting information about medication use during pregnancy and lactation.

	Total (n=1910)	Pregnant (n=754)	Lactating (n=612)	Other women (n=544)
Experienced discrepancies between different information sources^b (n=1459)				
No	525 (36.0)	175 (30.0)	230 (45.1)	120 (32.8)
Yes	759 (52.0)	345 (59.2)	219 (42.9)	195 (53.3)
Experienced not finding a useful answer^{abc} (n=1460)				
No	726 (49.7)	284 (48.6)	283 (55.5)	159 (43.4)
Yes	295 (20.2)	128 (21.9)	83 (16.3)	84 (23.0)
Consequences of not finding a useful answer^{ab} (n=391)				
I discussed with my doctor, midwife or pharmacist	149 (38.1)	73 (40.1)	33 (33.7)	43 (38.7)
I decided not to take the medicine	144 (36.8)	71 (39.0)	51 (52.0)	22 (19.8)
I became anxious	87 (22.3)	38 (20.9)	22 (22.4)	27 (24.3)
I looked for a new information source	53 (13.6)	24 (13.2)	11 (11.2)	18 (16.2)
I decided to take the medicine anyway	52 (13.3)	14 (7.7)	13 (13.3)	25 (22.5)
Other consequences	52 (13.3)	18 (9.9)	15 (15.3)	19 (17.1)
Difficulties understanding information^{bc} (n=1423)				
No	788 (55.4)	320 (56.8)	286 (57.0)	182 (50.8)
Yes	574 (40.3)	219 (38.9)	201 (40.0)	154 (43.0)
Reasons for difficulties understanding information^{ab} (n=519)				
Information was not precise enough	329 (63.4)	125 (63.8)	112 (61.2)	92 (65.7)
Information did not include scientific results	247 (47.6)	96 (49.0)	93 (50.8)	58 (41.4)
The presentation was not clear	97 (18.7)	28 (14.3)	37 (20.2)	32 (22.9)
Information was too detailed	53 (10.2)	18 (9.2)	15 (8.2)	20 (14.3)
I did not understand the words they used	40 (7.7)	12 (6.1)	15 (8.2)	13 (9.3)
Other reasons	87 (16.8)	31 (15.8)	31 (16.9)	25 (17.9)
Preferred source in an ideal world (n=1447)				
My medical doctor	655 (45.3)	265 (47.7)	175 (36.4)	215 (52.3)
My midwife or nurse	414 (28.6)	174 (31.4)	139 (28.9)	101 (24.6)
My pharmacist	85 (5.9)	29 (5.2)	33 (6.9)	23 (5.6)
Birth defect information service	82 (5.7)	21 (3.8)	42 (8.7)	19 (4.6)
The companies that develop medicines	58 (4.0)	22 (4.0)	19 (4.0)	17 (4.1)
Patient organisations	19 (1.3)	8 (1.4)	7 (1.5)	4 (1.0)
Print media	7 (0.5)	2 (0.4)	1 (0.2)	4 (1.0)
Other sources	127 (8.8)	34 (6.1)	65 (13.5)	28 (6.8)
Know of organisations that specialise in providing information (n=1439)				
No	955 (66.4)	402 (72.7)	242 (50.7)	311 (76.0)
Yes	484 (33.6)	151 (27.3)	235 (49.3)	98 (24.0)

*Data presented as percentage of total (n=1910), pregnant (n=754), lactating (n=612), other women (n=544) in the first, second, third and fourth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100): experienced discrepancies between different information sources n=107, experienced not finding a useful answer n=106, consequences of not finding a useful answer n=2, reasons for difficulties understanding information n=56, preferred source in an ideal world n=463, know of organisations that specialise in providing information n=471.

^a Respondents could choose more than 1 answer (percentages may consequently exceed 100%).

^b The question was only accessible for those who replied that they needed information, n=1566 (see table 2).

^c Data for the answer option "Don't know" are not shown.

The women in this study reported the Internet as the source easiest to access, followed by medical doctor and medicine packaging (figure 2, appendix 1). The sources easiest to understand were medical doctor, Internet and midwife/nurse. The most trustworthy source was medical doctor,

followed by scientific articles written by researchers and midwife/nurse. According to the women, medical doctor was the source best tailored to their needs. In total, approximately 50% of the women found it essential or important that the information was based on women’s own experiences.

Half of the women found it essential that the information was written or verified by a medical doctor and based on results from clinical studies (figure 3, appendix 2). In addition, many women required recent information (less than 5 years) and wanted the information to come from an official source and be written or verified by an HCP. Information based on woman’s own experience was of less importance, but still significant to many women.

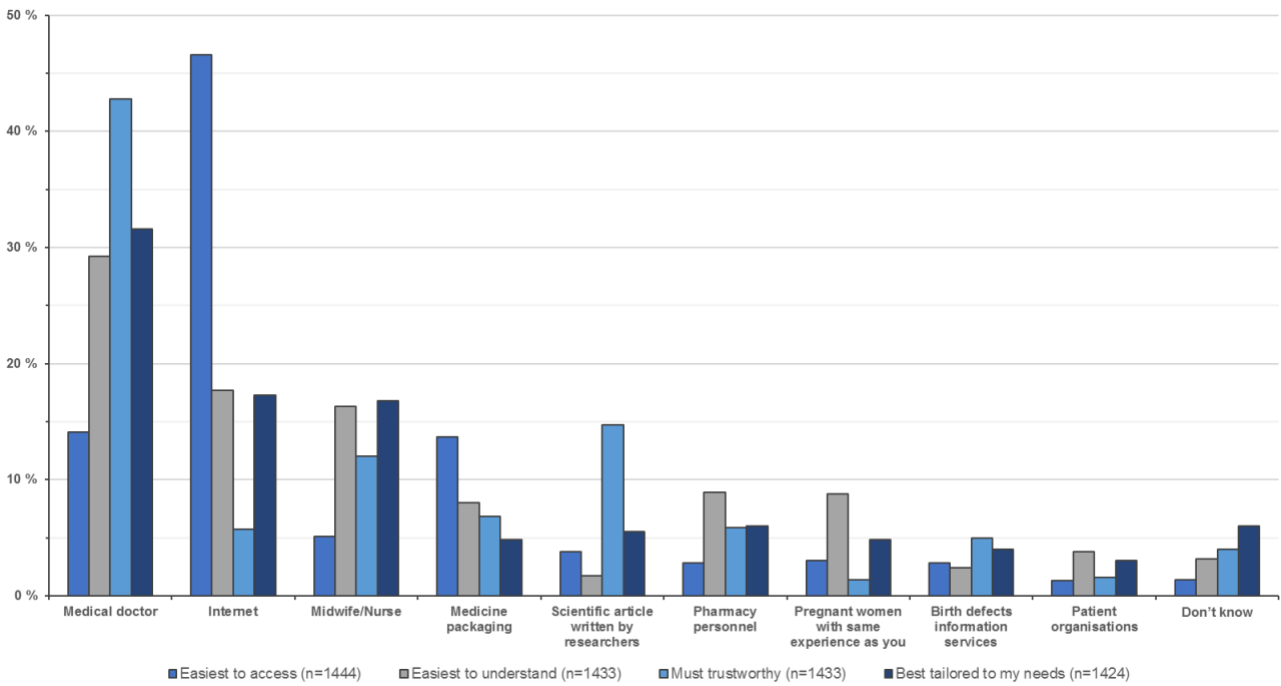


Figure 2. The sources easiest to access, easiest to understand, most trustworthy and best tailored to the women’s needs.

Data presented as percentages. Data do not always add up due to missing numbers: easiest to access n=466, easiest to understand n=477, most trustworthy n=477, best tailored to my needs n=486.

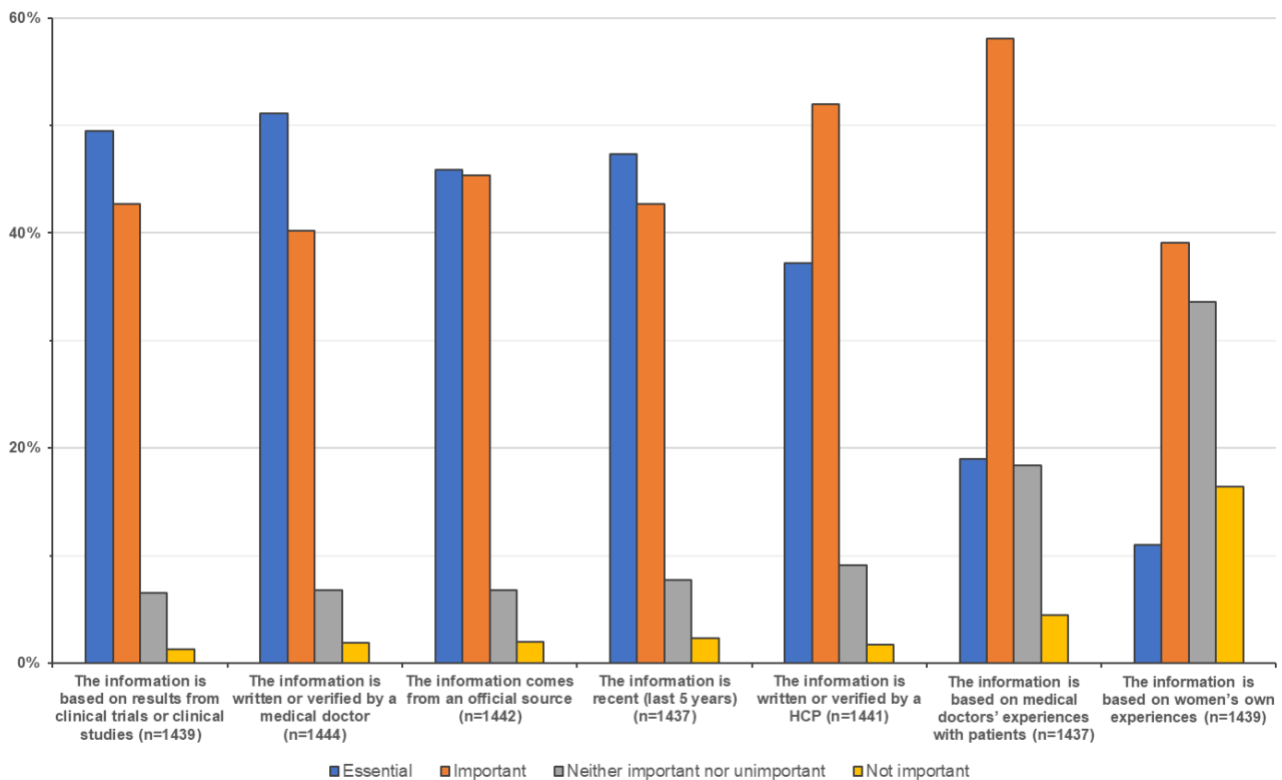


Figure 3. Degree of importance of different factors for women to trust a source of information. Data presented as percentages.

Data do not always add up due to missing numbers: the information is based on results from clinical trials or clinical studies n=471, the information is written or verified by a medical doctor n=466, the information comes from an official source n=468, the information is recent (last 5 years) n=473, the information is written or verified by a HCP n=469, the information is based on medical doctors' experiences with patients n=473, the information is based on women's own experiences with patients n=471. Abbreviations: HCP, Healthcare professional.

Factors associated with women's need for information

Factors associated with women needing information about medicines use during pregnancy or breastfeeding are shown in table 4. Multiparity and having a pre-existing/chronic medicines condition was associated with an increased need for information, while having a lower than University educational degree, being a medical doctor by profession or belonging to the group of women neither pregnant or breastfeeding was associated with a lower need for information compared to their counterparts. Due to multicollinearity, the variables "Medical condition", "Take medicines regularly" and "Taking medicines for" were removed from the final regression model.

Table 4. Factors associated with women needing information about medication use during pregnancy and lactation.

Variable	n	WOMEN NEEDING INFORMATION		
		Univariable logistic regression OR (95% CI)	Full model: Multivariable logistic regression (n=1423) OR (95% CI)	Final model: Multivariable logistic regression (n=1839) OR (95% CI)
Status of the woman (n=1846)				
Pregnant	726	1.00	1.00	1.00
Lactating	597	1.58 (1.10-2.26)	1.37 (0.93-2.01)	1.32 (0.90-1.93)
Other women	523	0.44 (0.33-0.59)	0.43 (0.31-0.60)	0.44 (0.32-0.60)
Previous pregnancies (≥1) (n=1846)				
No	1626	1.00	1.00	1.00
Yes	220	3.15 (2.29-4.33)	2.48 (1.71-3.61)	2.47 (1.74-3.51)
Age (years) (n=1846)				
≤25	127	0.57 (0.36-0.91)	0.80 (0.47-1.36)	-
26-30	455	0.79 (0.57-1.10)	0.85 (0.60-1.20)	-
31-35	713	1.00	1.00	-
36-40	391	1.18 (0.81-1.71)	1.13 (0.76-1.67)	-
≥41	160	0.73 (0.46-1.15)	0.98 (0.59-1.61)	-
Education level (n=1839)				
High school/ professional degree	418	0.58 (0.44-0.77)	0.56 (0.41-0.77)	0.57 (0.42-0.78)
University	1360	1.00	1.00	1.00
Other education	61	0.46 (0.26-0.85)	0.44 (0.23-0.85)	0.46 (0.24-0.88)
Region of residence (n=1846)				
Northern Europe	166	2.33 (1.29-4.19)	1.83 (0.99-3.38)	1.81 (0.98-3.33)
Western Europe	1127	1.00	1.00	1.00
Eastern Europe	261	1.37 (0.92-2.03)	1.40 (0.91-2.15)	1.31 (0.86-2.01)
Southern Europe	111	0.96 (0.57-1.61)	1.02 (0.59-1.77)	0.98 (0.57-1.69)
Other regions	181	1.04 (0.68-1.59)	1.07 (0.67-1.70)	1.06 (0.67-1.67)
Healthcare professionals (n=1846)				
Medical doctor	75	0.57 (0.33-1.01)	0.58 (0.31-1.07)	0.51 (0.28-0.94)
Nurse	112	0.62 (0.38-0.99)	0.67 (0.40-1.13)	0.65 (0.39-1.09)
Pharmacist	72	1.56 (0.71-3.45)	2.02 (0.88-4.64)	1.96 (0.86-4.48)
Other HCPs	190	0.86 (0.57-1.30)	0.96 (0.61-1.49)	0.94 (0.61-1.47)
Non-HCPs ^a	1397	1.00	1.00	1.00
Chronic conditions (n=1846)				
No	1256	1.00	1.00	1.00
Yes	590	1.97 (1.45-2.68)	1.61 (0.78-3.34)	2.36 (1.71-3.26)
Medical condition (n=1846)				
Asthma or allergy	117	1.00	1.00	-
Hypothyroidism	97	0.68 (0.30-1.54)	0.59 (0.25-1.40)	-
Mental health problem	114	1.75 (0.66-4.61)	2.59 (0.95-7.06)	-
Take medication regularly (n=1846)				
No	1185	1.00	1.00	-
Yes	661	1.48 (1.12-1.95)	0.83 (0.30-2.29)	-
Taking medication for^a (n=1856)				
Chronic medical condition	432	1.76 (1.25-2.48)	1.56 (0.55-4.43)	-
Pregnancy related condition	116	1.45 (0.80-2.61)	1.41 (0.57-3.49)	-
Other conditions	205	1.09 (0.72-1.66)	1.53 (0.57-4.14)	-

^a Includes the women answering no to the question “Are you a HCP?”.

Factors associated with difficulties understanding information

Factors associated with difficulties understanding information about medicines use during pregnancy or breastfeeding are shown in table 5. Living in Southern Europe and being an HCP was associated with having less difficulties understanding information on medicines use during pregnancy or breastfeeding. Again, due to multicollinearity, the variables “Medical condition”, “Take medicines regularly” and “Taking medicines for” were removed from the final regression model.

Table 5. Factors associated with women experiencing difficulties understanding information about medication use during pregnancy or lactation.

Variable	n	DIFFICULTIES UNDERSTANDING INFORMATION		
		Univariable logistic regression	Full model: Multivariable logistic regression (n=1395)	Final model: Multivariable logistic regression (n=1417)
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Status of the woman (n=1423)				
Pregnant	563	1.00	1.00	-
Lactating	502	1.05 (0.82-1.34)	1.09 (0.83-1.43)	-
Other women	358	1.19 (0.91-1.55)	1.27 (0.94-1.72)	-
Previous pregnancies (≥1) (n=1423)				
No	1286	1.00	1.00	-
Yes	137	0.91 (0.64-1.30)	0.96 (0.64-1.43)	-
Age (years) (n=1423)				
≤25	83	1.12 (0.70-1.79)	0.91 (0.55-1.51)	-
26-30	342	1.05 (0.80-1.38)	0.96 (0.72-1.28)	-
31-35	559	1.00	1.00	-
36-40	323	0.90 (0.68-1.19)	0.84 (0.62-1.12)	-
≥41	116	0.93 (0.62-1.40)	0.83 (0.53-1.29)	-
Education level (n=1417)				
High school or professional degree	289	1.12 (0.86-1.46)	1.09 (0.82-1.46)	1.11 (0.84-1.45)
University	1085	1.00	1.00	1.00
Other education	43	0.90 (0.48-1.69)	0.89 (0.46-1.71)	0.88 (0.46-1.68)
Region of residence (n=1423)				
Northern Europe	143	1.29 (0.90-1.84)	1.25 (0.86-1.82)	1.26 (0.87-1.81)
Western Europe	865	1.00	1.00	1.00
Eastern Europe	193	0.75 (0.54-1.04)	0.80 (0.56-1.12)	0.75 (0.54-1.05)
Southern Europe	86	0.37 (0.21-0.63)	0.33 (0.19-0.58)	0.33 (0.19-0.57)
Other regions	136	0.97 (0.67-1.40)	1.08 (0.73-1.59)	1.09 (0.75-1.60)
Healthcare professionals (n=1423)				
Medical doctor	54	0.25 (0.12-0.51)	0.24 (0.11-0.50)	0.25 (0.12-0.51)
Nurse	79	0.84 (0.53-1.34)	0.76 (0.47-1.23)	0.78 (0.49-1.26)
Pharmacist	60	0.25 (0.12-0.49)	0.23 (0.12-0.47)	0.24 (0.12-0.48)
Other HCPs	152	0.44 (0.30-0.64)	0.42 (0.28-0.62)	0.43 (0.29-0.63)
Non-HCPs ^a	1078	1.00	1.00	1.00
Chronic conditions (n=1423)				
No	930	1.00	1.00	1.00
Yes	493	1.25 (1.00-1.56)	1.10 (0.66-1.84)	1.15 (0.91-1.44)
Medical condition (n=1423)				
Asthma or allergy	96	1.00	1.00	-
Hypothyroidism	77	0.90 (0.49-1.66)	1.06 (0.56-2.02)	-
Mental health problem	101	1.48 (0.84-2.60)	1.40 (0.78-2.51)	-
Take medication regularly (n=1423)				
No	893	1.00	1.00	-
Yes	530	1.22 (0.98-1.52)	0.92 (0.46-1.77)	-
Taking medication for^a (n=1856)				
Chronic medical condition	357	1.22 (0.96-1.56)	1.02 (0.52-1.97)	-
Pregnancy related condition	95	1.08 (0.71-1.65)	1.20 (0.70-2.06)	-
Other conditions	163	4.23 (0.89-1.71)	1.31 (0.72-2.40)	-

^a Includes the women answering no to the question “Are you a HCP?”.

Abbreviations: HCP, Healthcare professional.

HCPs - Population characteristics

A total of 665 HCPs accessed and completed the online questionnaire. Of these, 8.9% were general practitioners (GPs), 21.5% were specialists, 35.5% were nurses, 24.1% were pharmacists and 10.1% were in other professions.

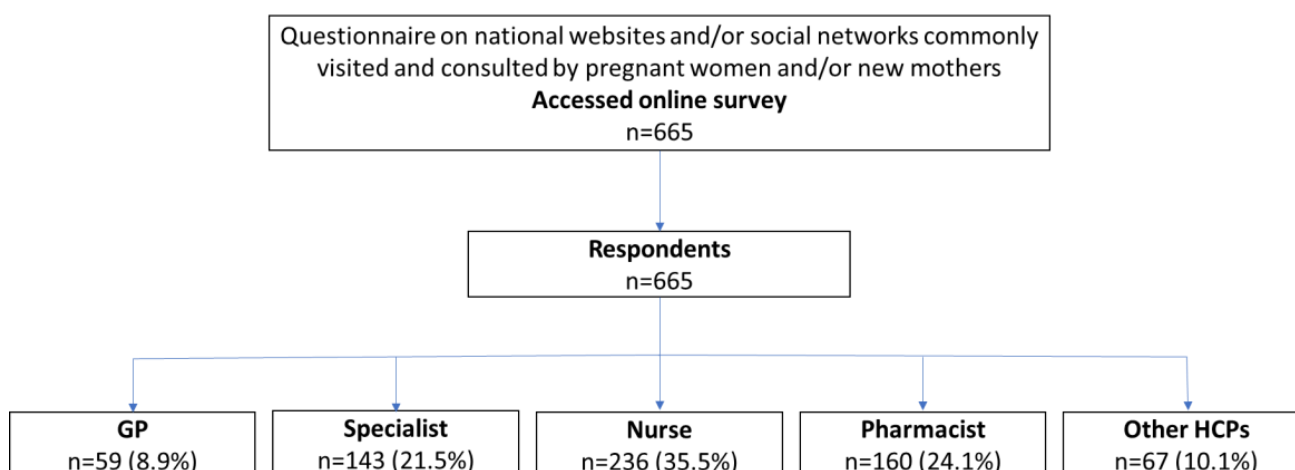


Figure 4. Participant flow chart, HCPs.

Table 6. Characteristics of the HCPs, n=665.

	Total (n=665)	GP (n=59)	Specialist (n=143)	Nurse (n=236)	Pharmacist (n=160)	Other HCPs (n=67)
Age (years) (n=665)						
≤30	146 (22.0)	12 (20.3)	6 (4.2)	62 (26.3)	50 (31.3)	16 (23.9)
31-40	242 (36.4)	29 (49.2)	52 (36.4)	74 (31.4)	57 (35.6)	30 (44.8)
41-50	128 (19.2)	7 (11.9)	35 (24.5)	48 (20.3)	30 (18.8)	8 (11.9)
>51	149 (22.4)	11 (18.6)	50 (35.0)	52 (22.0)	23 (14.4)	13 (19.4)
Region of practice (n=665)						
Northern Europe	136 (20.5)	4 (6.8)	16 (11.2)	101 (42.8)	8 (5.0)	7 (10.4)
Western Europe	324 (48.7)	30 (50.8)	47 (32.9)	120 (50.8)	88 (55.0)	39 (58.2)
Eastern Europe	37 (5.6)	7 (11.9)	7 (4.9)	4 (1.7)	13 (8.1)	6 (9.0)
Southern Europe	28 (4.2)	2 (3.4)	18 (12.6)	3 (1.3)	4 (2.5)	1 (1.5)
Israel	112 (16.8)	15 (25.4)	49 (34.3)	4 (1.7)	35 (21.9)	9 (13.4)
Other regions	28 (4.2)	1 (1.7)	6 (4.2)	4 (1.7)	12 (7.5)	5 (7.5)

*Data presented as percentage of total (n=665), GP (n=59), specialist (n=143), nurse (n=236), pharmacist (n=160), other HCPs (n=67) in the first, second, third, fourth, fifth and sixth column, respectively.

Abbreviations: HCP, Healthcare Professional; GP, General Practitioner.

Information about medicines usage during pregnancy and breastfeeding

More than 60% of the HCPs reported being asked about medicines use during pregnancy daily or weekly (table 7). The most frequently used medicines information source was online databases, followed by websites, medical specialists and desk references or textbooks. Fifty percent of the participating HCPs reported that they found it easy to find the needed information, while 12% reported that they found it difficult. Their patients are often looking for information during their

pregnancy and when breastfeeding, and the information they are looking for is most often about foetal safety/potential effects on the child and dose excreted to breastmilk/safety during breastfeeding. More than 70% of the HCPs have experienced finding contradictory information about medicines use during pregnancy/breastfeeding. Most of the HCPs reported of occasionally having difficulty interpreting information about medicines use during pregnancy/breastfeeding and main reasons for this were reported as the information was not precise enough, the information did not fulfil their information needs, the information was not sufficiently evidence based and the information did not present the risks adequately (table 7).

Table 7. HCPs and information about medication use during pregnancy and lactation.

	Total (n=665)	GP (n=59)	Specialist (n=143)	Nurse (n=236)	Pharmacist (n=160)	Other HCPs (n=67)
Asked about medicine use during pregnancy (n=647)						
Daily	149 (23.0)	6 (10.3)	37 (26.2)	43 (18.7)	52 (33.3)	11 (17.7)
Weekly	258 (39.9)	29 (50.0)	54 (38.3)	97 (42.2)	60 (38.5)	18 (29.0)
Monthly	124 (19.2)	14 (24.1)	25 (17.7)	41 (17.8)	28 (17.9)	16 (25.8)
Seldom	116 (17.9)	9 (15.5)	25 (17.7)	49 (21.3)	16 (10.3)	17 (27.4)
Medication information sources^{ab} (n=540)						
Online databases	310 (57.4)	33 (61.1)	80 (61.5)	80 (43.0)	95 (72.5)	22 (56.4)
Websites	210 (38.9)	30 (55.6)	47 (36.2)	50 (26.9)	65 (49.6)	18 (46.2)
Medical specialists	199 (36.9)	15 (27.8)	32 (24.6)	119 (64.0)	19 (14.5)	14 (35.9)
Desk references or textbooks	181 (33.5)	10 (18.5)	36 (27.7)	76 (40.9)	46 (35.1)	13 (33.3)
Medicine packaging	169 (31.3)	6 (11.1)	21 (16.2)	47 (25.3)	77 (58.8)	18 (46.2)
Teratology information services or registries	167 (30.9)	20 (37.0)	57 (43.8)	28 (15.1)	51 (38.9)	11 (28.2)
National or local hospital guidance	141 (26.1)	13 (24.1)	39 (30.0)	61 (32.8)	21 (16.0)	7 (17.9)
Other sources	82 (15.2)	7 (13.0)	19 (14.6)	34 (18.3)	14 (10.7)	8 (20.5)
To find the needed information^b (n=540)						
Easy	270 (50.0)	25 (46.3)	64 (49.2)	118 (63.4)	50 (38.2)	13 (33.3)
Neither easy nor difficult	148 (27.4)	15 (27.8)	46 (35.4)	39 (21.0)	38 (29.0)	10 (25.6)
Difficult	65 (12.0)	7 (13.0)	11 (8.5)	15 (8.1)	25 (19.1)	7 (17.9)
Varies from case to case	57 (10.6)	7 (13.0)	9 (6.9)	14 (7.5)	18 (13.7)	9 (23.1)
When patients usually look for information^{ab} (n=540)						
During their pregnancy	431 (79.8)	46 (85.2)	96 (73.8)	145 (78.0)	117 (89.3)	27 (69.2)
When lactation	336 (62.2)	36 (66.7)	81 (62.3)	102 (54.8)	96 (73.2)	21 (53.8)
Other situations	215 (39.8)	14 (25.9)	75 (57.7)	98 (52.7)	59 (45.0)	27 (69.2)
Type of information usually looking for^{ab} (n=540)						
Foetal safety / potential effects on the child	504 (93.3)	52 (96.3)	124 (95.4)	172 (92.5)	124 (94.7)	32 (82.1)
Dose excreted to breastmilk / safety during Lactation	425 (78.7)	49 (90.7)	99 (76.2)	142 (76.3)	103 (78.6)	32 (82.1)
Optimal dosage for treatment	107 (19.8)	9 (16.7)	27 (20.8)	29 (15.6)	34 (26.0)	8 (20.5)
Information on the medical condition the medication is used for	79 (14.6)	4 (7.4)	9 (6.9)	33 (17.7)	25 (19.1)	8 (20.5)
Other types of information	12 (2.2)	1 (1.9)	3 (2.3)	2 (1.1)	2 (1.5)	5 (12.8)
Type of information compared^{ab} (n=540)						
Safety for the child during pregnancy	454 (84.1)	45 (83.3)	104 (80.0)	155 (83.3)	120 (91.6)	30 (76.9)
Dose excreted to breastmilk / safety during lactation	352 (65.2)	32 (59.3)	83 (63.8)	118 (63.4)	91 (69.5)	28 (71.8)

The majority of HCPs with a Teratology Information Service (TIS) centre available reported it as being sufficient to meet their needs always or occasionally (table 8). Almost 70% of the participating HCPs used an information service or database for questions about medicines use before or during pregnancy and breastfeeding daily, weekly or monthly. There were no major differences in the percentages who reported experiencing difficulties finding the needed information between those who have and do not have a TIS centre (data not shown).

Table 8. HCPs and TIS centre.

	Total (n=665)	GP (n=59)	Specialist (n=143)	Nurse (n=236)	Pharmacist (n=160)	Other HCPs (n=67)
Do you have a TIS centre or similar available in your country or region? (n=547)						
Yes	263 (48.1)	31 (58.5)	88 (68.8)	72 (36.9)	54 (41.5)	18 (43.9)
No	55 (10.1)	7 (13.2)	10 (7.8)	14 (7.2)	20 (15.4)	4 (9.8)
Don't know	229 (41.9)	15 (28.3)	30 (23.4)	109 (55.9)	56 (43.1)	19 (46.3)
Is the information from the TIS sufficient to meet your needs?^a n=249)						
Yes, always	109 (43.8)	12 (42.9)	36 (41.4)	32 (47.8)	26 (52.0)	3 (17.6)
Yes, occasionally	92 (36.9)	10 (35.7)	31 (35.6)	29 (43.3)	15 (30.0)	7 (41.2)
Often not	17 (6.8)	3 (10.7)	7 (8.0)	0 (0.0)	5 (10.0)	2 (11.8)
Don't know	31 (12.4)	3 (10.7)	13 (14.9)	6 (9.0)	4 (8.0)	5 (29.4)
How often do you use an information service or database for questions about medicine use before or during pregnancy and lactation?^a (n=530)						
Daily	43 (8.1)	2 (4.1)	5 (3.9)	14 (7.5)	15 (11.8)	7 (17.5)
Weekly	178 (33.6)	20 (40.8)	41 (32.3)	63 (33.7)	47 (37.0)	7 (17.5)
Monthly	141 (26.6)	16 (32.7)	37 (29.1)	52 (27.8)	27 (21.3)	9 (22.5)
More seldom	145 (27.4)	10 (20.4)	40 (31.5)	51 (27.3)	31 (24.4)	13 (32.5)
Never	23 (4.3)	1 (2.0)	4 (3.1)	7 (3.7)	7 (5.5)	4 (10.0)

*Data presented as percentage of total (n=665), GP (n=59), specialist (n=143), nurse (n=236), pharmacist (n=160), other HCPs (n=67) in the first, second, third, fourth, fifth and sixth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100): do you have a TIS centre or similar available in your country or region? n=118, is the information from the TIS sufficient to meet your needs? n=14, how often do you use an information service or database for questions about medicine use before or during pregnancy and lactation? n=125.

Abbreviations: HCP, Healthcare Professional; TIS, Teratology Information Service; GP, General Practitioner.

^a Percentages were calculated based on those that replied that they had a TIS centre available, n=263.

Factors associated with being asked about medicines use during pregnancy or breastfeeding are shown in table 9. Practicing as an HCP in Northern Europe or being a pharmacist, specialist physician or GP was associated with more often being asked about medicines use during pregnancy or breastfeeding.

Table 9. Factors associated with HCPs often being asked about medication use during pregnancy or lactation.

Variable	n	Asked about medication use during pregnancy or lactation, n (%)		Univariable logistic regression OR (95% CI)	Multivariable logistic regression (n=647) OR (95% CI)
		Often ^a	Seldom ^b		
Profession					
GP	58	49 (84.5)	9 (15.5)	0.98 (0.54-1.76)	1.50 (0.79-2.84)
Specialist physician	141	116 (82.3)	25 (17.7)	1.17 (0.76-1.81)	1.69 (1.01-2.83)
Nurse	230	181 (78.7)	49 (21.3)	1.00	1.00
Pharmacist	156	140 (89.7)	16 (10.3)	1.64 (1.06-2.54)	2.39 (1.47-3.90)
Other HCPs	62	45 (72.6)	17 (27.4)	0.57 (0.32-0.99)	0.81 (0.44-1.47)
Age (years)					
≤30	141	118 (83.7)	23 (16.3)	1.45 (0.94-2.22)	1.60 (1.02-2.53)
31-40	235	181 (77.0)	54 (23.0)	1.00	1.00
41-50	125	110 (88.0)	15 (12.0)	2.13 (1.33-3.40)	1.93 (1.19-3.15)
>51	146	122 (83.6)	24 (16.4)	1.44 (0.94-2.20)	1.21 (0.77-1.92)
Region of practice					
Northern Europe	134	117 (87.3)	17 (12.7)	2.20 (1.40-3.46)	2.77 (1.67-4.60)
Western Europe	313	243 (77.6)	70 (22.4)	1.00	1.00
Eastern Europe	35	25 (71.4)	10 (28.6)	1.08 (0.53-2.20)	1.03 (0.49-2.18)
Southern Europe	28	24 (85.7)	4 (14.3)	0.83 (0.38-1.80)	0.74 (0.32-1.69)
Israel	111	100 (90.1)	11 (9.9)	1.38 (0.88-2.17)	1.12 (0.68-1.86)
Other region	26	22 (84.6)	4 (15.4)	0.98 (0.44-2.21)	0.84 (0.36-1.96)

Abbreviations: HCP, Healthcare Professional; GP, General Practitioner;

^a A grouping of the answer options “Daily” and “Weekly”.

^b A grouping of the answer options Monthly”, “Less than once a month” and “Never”.

Factors associated with most frequent difficulties interpreting information

Factors associated with most frequent difficulties interpreting information about medicines use during pregnancy or breastfeeding are shown in table 10. Practicing as an HCP in Southern Europe or Israel was associated with more often having difficulties interpreting information about medicines use during pregnancy or breastfeeding, while being >40 years old was associated with less often having difficulties interpreting information

Table 10. Factors associated with HCPs often having difficulties interpreting information about medication use during pregnancy or lactation.

Variable	n	Having difficulties interpreting information about medication use during pregnancy or lactation, n (%)		Often having difficulties interpreting information about medication use during pregnancy or lactation	
		Often ^a	Seldom ^b	Univariable logistic regression OR (95% CI)	Multivariable logistic regression (n=540) OR (95% CI)
Profession					
GP	54	13 (24.1)	41 (75.9)	2.36 (1.10-5.09)	1.72 (0.75-3.98)
Specialist physician	130	17 (13.1)	113 (86.9)	1.12 (0.57-2.21)	0.83 (0.38-1.82)
Nurse	186	22 (11.8)	164 (88.2)	1.00	1.00
Pharmacist	131	29 (22.1)	102 (77.9)	2.12 (1.16-3.89)	1.51 (0.76-2.99)
Other HCP	39	11 (28.2)	28 (71.8)	2.93 (1.28-6.70)	2.65 (1.11-6.33)
Age (years)					
≤30	110	25 (22.7)	85 (77.3)	1.15 (0.65-2.04)	1.30 (0.71-2.39)
31-40	187	38 (19.3)	149 (75.6)	1.00	1.00
41-50	113	13 (11.5)	100 (88.5)	0.51 (0.26-1.01)	0.53 (0.26-1.08)
>51	130	16 (12.3)	114 (87.7)	0.55 (0.29-1.04)	0.56 (0.29-1.09)
Region of practice					
Northern Europe	121	13 (10.7)	108 (89.3)	0.63 (0.32-1.22)	0.96 (0.46-2.01)
Western Europe	254	41 (16.1)	213 (83.9)	1.00	1.00
Eastern Europe	24	3 (12.5)	21 (87.5)	0.74 (0.21-2.60)	0.60 (0.17-2.17)
Southern Europe	25	6 (24.0)	19 (76.0)	1.64 (0.62-4.36)	2.67 (0.93-7.67)
Israel	96	25 (26.0)	71 (74.0)	1.83 (1.04-3.22)	2.53 (1.35-4.77)
Other regions	20	4 (20.0)	16 (80.0)	1.30 (0.41-4.08)	1.20 (0.37-3.90)

Abbreviations: HCP, Healthcare Professional; GP, General Practitioner;

^a A grouping of the answer options “Always” and “Often”.

^b A grouping of the answer options “Sometimes”, “Occasionally” and “Never”.

Preferences regarding a European knowledge bank - Women

Approximately 80% of the women perceived a European knowledge bank on the safety of medicines during pregnancy/breastfeeding as very useful and less than 1% thought it would not be useful (table 11a). The most common situation where the women could imagine using the knowledge bank was “to decide if I should use a medicine while pregnant or breastfeeding”. In total, 87.4% reported a website to be their preferred access to knowledge bank, while approximately 50% reported the mobile app as their preferred way to access knowledge bank.

Only 22.4% preferred to get access through their HCP. In total, 83% of the women were native English speakers or thought English would be sufficient for them to be able to use the knowledge bank (table 11a). However, in Northern and Southern Europe, the percentages reporting they were able to use an English knowledge bank was lower than in the other regions. Here, 36.6% from

Northern Europe and 35.5% from Southern Europe reported that they preferred at least a short summary in their own language or needed all information in their own language.

Table 11a. The Knowledge bank: Women's preferences for information about the safety of medication use during pregnancy and lactation.

	Total (n=1910)	Pregnant (n=754)	Lactation (n=612)	Other women (n=544)
Perceived usefulness of European knowledge bank on the safety of medications during pregnancy and lactation (n=1374)				
Very useful	1098 (79.9)	417 (79.9)	378 (82.0)	303 (77.5)
Somewhat useful	205 (14.9)	72 (13.8)	70 (15.2)	63 (16.1)
Neither useful nor not useful	29 (2.1)	11 (2.1)	6 (1.3)	12 (3.1)
Not that useful	9 (0.7)	4 (0.8)	1 (0.2)	4 (1.0)
Not useful at all	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Don't know	33 (2.4)	18 (3.4)	6 (1.3)	9 (2.3)
Type of situations imagining using such a knowledge bank^a (n=1376)				
To decide if I should use a medication while pregnant or lactation	1046 (76.0)	385 (73.6)	393 (85.1)	268 (68.5)
To double check information I found somewhere else	926 (67.3)	338 (64.6)	327 (70.8)	261 (66.8)
To get a second opinion on recommendations made by my doctor, midwife, pharmacist, or healthcare professionals	844 (61.3)	305 (58.3)	305 (66.0)	234 (59.8)
To prepare for a visit to see my doctor, midwife, pharmacist, or other HCP	712 (51.7)	263 (50.3)	243 (52.6)	206 (52.7)
Other situations	45 (3.3)	16 (3.1)	5 (1.1)	24 (6.1)
Preferred access to knowledge^a bank (n=1379)				
Website	1205 (87.4)	454 (86.3)	420 (91.1)	331 (84.4)
Mobile app	727 (52.7)	280 (53.2)	255 (55.3)	192 (49.0)
Through my healthcare provider (e.g. doctor, midwife, pharmacist)	309 (22.4)	98 (18.6)	122 (26.5)	89 (22.7)
Able to use information from the knowledge bank if it is only available in English (n=1376)				
Yes, English is my native language	558 (40.6)	277 (53.0)	120 (26.0)	161 (41.1)
Yes, English would be adequate	584 (42.4)	190 (36.3)	238 (51.6)	156 (39.8)
No, I would prefer at least a short summary in my own language	180 (13.1)	49 (9.4)	77 (16.7)	54 (13.8)
No, I would need all information in my own language	54 (3.9)	7 (1.3)	26 (5.6)	21 (5.4)

*Data presented as percentage of total (n=1910), pregnant (n=754), lactating (n=612), other women (n=544) in the first, second, third and fourth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100); perceived usefulness of European knowledge bank on the safety of medications during pregnancy and lactation n=536, type of situations imagining using such a knowledge bank n=534, Preferred access to knowledge bank n=531, able to use information from the knowledge bank if it is only available in English n=534.

^a Respondents could choose more than 1 answer.

Table 11b. The Knowledge bank. Women's preferences for information about the safety of medication use during pregnancy and lactation.

	Total (n=1910)	Northern Europe (n=176)	Western Europe (n=1162)	Eastern Europe (n=269)	Southern Europe (n=113)	Other regions (n=190)
Perceived usefulness of European knowledge bank on the safety of medications during pregnancy and lactation (n=1374)						
Very useful	1098 (79.9)	85 (64.9)	726 (83.4)	133 (80.6)	71 (89.9)	83 (64.3)
Somewhat useful	205 (14.9)	36 (27.5)	112 (12.9)	20 (12.1)	5 (6.3)	32 (24.8)
Neither useful nor not useful	29 (2.1)	7 (5.3)	14 (1.6)	1 (0.6)	1 (1.3)	6 (4.7)
Not that useful	9 (0.7)	0 (0.0)	5 (0.6)	1 (0.6)	1 (1.3)	2 (1.6)
Not useful at all	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Don't know	33 (2.4)	3 (2.3)	13 (1.5)	10 (6.1)	1 (1.3)	6 (4.7)
Situations imagining using such a knowledge bank^a (n=1376)						
To decide if I should use a medicine while pregnant or lactation	1046 (76.0)	116 (87.9)	688 (79.0)	95 (57.6)	56 (70.9)	91 (70.5)
To double check information I found somewhere else	926 (67.3)	108 (81.8)	591 (67.9)	97 (58.8)	40 (50.6)	90 (69.8)
To get a second opinion on recommendations made by my doctor, midwife, pharmacist, or healthcare professionals	844 (61.3)	104 (78.8)	508 (58.3)	108 (65.5)	52 (65.8)	72 (55.8)
To prepare for a visit to see my doctor, midwife, pharmacist, or other healthcare professionals	712 (51.7)	83 (62.9)	470 (54.0)	65 (39.4)	30 (38.0)	64 (49.6)
Other situation	45 (3.3)	2 (1.5)	34 (3.9)	2 (1.2)	2 (2.5)	5 (3.9)
Preferred access to knowledge bank^a (n=1379)						
Website	1205 (87.4)	123 (93.9)	775 (88.6)	138 (83.6)	56 (70.9)	113 (87.6)
Mobile app	727 (52.7)	72 (55.0)	465 (53.1)	88 (53.3)	47 (59.5)	55 (42.6)
Through my healthcare provider	309 (22.4)	46 (35.1)	207 (23.7)	17 (10.3)	19 (24.1)	20 (15.5)
Able to use information from the knowledge bank if it is only available in English (n=1376)						
Yes, English is my native language	558 (40.6)	3 (2.3)	461 (52.9)	8 (4.8)	5 (6.3)	81 (62.8)
Yes, English would be adequate	584 (42.4)	80 (61.1)	287 (32.9)	129 (78.2)	46 (58.2)	42 (32.6)
No, I would prefer at least a short summary in my own language	180 (13.1)	41 (31.3)	92 (10.6)	23 (13.9)	18 (22.8)	6 (4.7)
No, I would need all information in my own language	54 (3.9)	7 (5.3)	32 (3.7)	5 (3.0)	10 (12.7)	0 (0.0)

*Data presented as percentage of total (n=1910), Northern Europe (n=176), Western Europe (n=1162), Eastern Europe (n=269), Southern Europe (n=113), other regions (n=190) in the first, second, third, fourth, fifth and sixth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100); perceived usefulness of European knowledge bank on the safety of medications during pregnancy and lactation n=536, type of situations imagining using such a knowledge bank n=534, Preferred access to knowledge bank n=531, able to use information from the knowledge bank if it is only available in English n=534.

Abbreviations:

^a Respondents could choose more than 1 answer.

Preferences regarding a European knowledge bank - HCPs

Approximately 85% of the HCPs gave a score between 8 and 10 (on a scale from 0-10 in regard to usefulness, 0 being not valuable and 10 being most valuable) to the idea of having a European knowledge bank on the safety of medicines during pregnancy/breastfeeding (table 12).

Approximately 80% imagined using the knowledge bank daily, weekly or monthly, and just as many stated that using such a knowledge bank would save them time. There were more HCPs that would like to access the knowledge bank via a website than a mobile app, although they were both popular options. In total, approximately 60% of the HCPs were native English speakers or thought English would be sufficient for them to be able to use the knowledge bank (table 12). Almost one third of the participating HCPs thought that more than 50% of their patients would be likely to use the knowledge bank, as it is Internet based.

Table 12. HCPs and information about medication use during pregnancy and lactation.

	Total (n=665)	GP (n=59)	Specialist (n=143)	Nurse (n=236)	Pharmacist (n=160)	Other HCPS (n=67)
Perceived usefulness of an open access knowledge bank on the safety of medications during pregnancy and lactation, 0-10^a (n=505)						
0-4	12 (2.4)	0 (0.0)	4 (3.4)	5 (2.8)	3 (2.4)	0 (0.0)
5-7	63 (12.5)	7 (14.9)	13 (11.0)	20 (11.2)	13 (10.4)	10 (27.0)
8-10	430 (85.1)	40 (85.1)	101 (85.6)	153 (86.0)	109 (87.2)	27 (73.0)
Median (25 th -75 th percentile)	10 (8-10)	10 (8-10)	10 (8-10)	10 (8-10)	10 (8-10)	10 (7-10)
How often imagine using knowledge bank (n=503)						
Daily	75 (9.3)	4 (8.5)	12 (10.3)	22 (12.4)	29 (23.2)	8 (21.6)
Weekly	222 (44.1)	26 (55.3)	58 (49.6)	76 (42.9)	55 (44.0)	7 (18.9)
Monthly	139 (27.6)	11 (23.4)	24 (20.5)	65 (36.7)	25 (20.0)	14 (37.8)
More seldom	65 (12.9)	6 (12.8)	22 (18.8)	13 (7.3)	16 (12.8)	8 (21.6)
Never	2 (0.4)	0 (0.0)	1 (0.9)	1 (0.6)	0 (0.0)	0 (0.0)
Would using such a knowledge bank save you time? (n=504)						
Yes	412 (81.7)	40 (85.1)	94 (79.7)	142 (80.2)	110 (88.0)	26 (70.3)
No	12 (2.4)	0 (0.0)	4 (3.4)	6 (3.4)	2 (1.6)	0 (0.0)
Don't know	80 (15.9)	7 (14.9)	20 (16.9)	29 (16.4)	13 (10.4)	11 (29.7)
When could you imagine using the knowledge bank?^b (n=505)						
Before a consultation	235 (46.5)	24 (51.1)	61 (51.7)	94 (52.8)	42 (33.6)	14 (37.8)
During a consultation	416 (82.4)	43 (91.5)	106 (89.8)	147 (82.6)	97 (77.6)	23 (62.2)
After a consultation	225 (44.6)	30 (63.8)	60 (50.8)	80 (44.9)	41 (32.8)	14 (37.8)
To learn more myself	346 (68.5)	29 (61.7)	71 (59.3)	140 (78.7)	79 (63.2)	27 (73.0)
To support teaching	205 (40.6)	18 (38.3)	58 (49.2)	66 (37.1)	48 (38.4)	15 (40.5)
Other situations	35 (6.9)	0 (0.0)	5 (4.2)	11 (6.2)	12 (9.6)	7 (18.9)
In what kind of situations could you imagine using the knowledge bank?^b (n=505)						
To counsel a woman who has used a medication before realising that she was pregnant	370 (73.3)	43 (91.5)	86 (72.9)	139 (78.1)	82 (65.6)	20 (54.1)
To inform the choice of treatment for a pregnant woman	420 (83.2)	45 (95.7)	98 (83.1)	148 (83.1)	111 (88.8)	18 (48.6)
To inform the choice of treatment for a lactation woman	440 (87.1)	45 (95.7)	112 (94.9)	147 (82.6)	111 (88.8)	25 (67.6)
To plan future treatment for a woman before she becomes pregnant	259 (51.3)	34 (72.3)	66 (55.9)	79 (44.4)	66 (52.8)	14 (37.8)
To plan future treatment for a woman before she begins lactation	273 (54.1)	28 (59.6)	65 (55.1)	101 (56.7)	61 (48.8)	18 (48.6)
To investigate potential reasons for birth defects and neonatal problems	182 (36.0)	11 (23.4)	63 (53.4)	56 (31.5)	38 (30.4)	14 (37.8)
Other situations	23 (4.6)	0 (0.0)	4 (3.4)	6 (3.4)	5 (4.0)	8 (21.6)

	Total (n=665)	GP (n=59)	Specialist (n=143)	Nurse (n=236)	Pharmacist (n=160)	Other HCPs (n=67)
I would like to access the knowledge bank via a website (n=489)						
Strongly Agree	276 (56.4)	27 (58.7)	71 (63.4)	96 (55.2)	65 (54.2)	17 (45.9)
Agree	161 (32.9)	13 (28.3)	32 (28.6)	59 (33.9)	44 (36.7)	13 (35.1)
Neutral	28 (5.7)	2 (4.3)	2 (1.8)	14 (2.3)	8 (6.7)	2 (5.4)
Disagree	4 (0.8)	0 (0.0)	2 (1.8)	1 (0.6)	0 (0.0)	1 (2.7)
Strongly Disagree	20 (4.1)	4 (8.7)	5 (4.5)	4 (2.3)	3 (2.5)	4 (10.8)
I would like to access the knowledge bank via a mobile app (n=488)						
Strongly Agree	194 (39.8)	16 (34.8)	55 (49.1)	64 (36.8)	46 (38.7)	13 (35.1)
Agree	137 (28.1)	15 (32.6)	36 (32.1)	41 (23.6)	36 (30.3)	9 (24.3)
Neutral	90 (18.4)	8 (17.4)	10 (8.9)	36 (20.7)	25 (21.0)	11 (29.7)
Disagree	29 (5.9)	2 (4.3)	7 (6.3)	13 (7.5)	6 (5.0)	1 (2.7)
Strongly Disagree	38 (7.8)	5 (10.9)	4 (3.6)	20 (11.5)	6 (5.0)	3 (8.1)
Would you be able to use a knowledge bank if it is only available in English? (n=489)						
Yes, English is my native language	100 (20.4)	14 (30.4)	26 (23.2)	28 (16.1)	27 (22.5)	5 (13.5)
Yes, English would be adequate	204 (41.7)	21 (45.7)	71 (63.4)	34 (19.5)	59 (49.2)	19 (51.4)
No, I would prefer at least a short summary in my own language with more extensive information in English	116 (23.7)	8 (17.4)	15 (13.4)	63 (36.2)	25 (20.8)	5 (13.5)
No, I would need all information in my own language to allow me to use it	69 (14.1)	3 (6.5)	0 (0.0)	49 (28.2)	9 (7.5)	8 (21.6)
Do you see any concerns in allowing the public to access the knowledge bank? (n=489)						
Yes	294 (60.1)	32 (69.6)	69 (61.6)	117 (67.2)	50 (41.7)	26 (70.3)
No	110 (22.5)	7 (15.2)	24 (21.4)	33 (19.0)	41 (34.2)	5 (13.5)
Don't know	85 (17.4)	7 (15.2)	19 (8.0)	24 (13.8)	29 (24.2)	6 (16.2)
What percentage of your patients do you think would be likely to use the knowledge bank, as is Internet based? (n=488)						
<1%	20 (4.1)	6 (13.3)	4 (3.6)	4 (2.3)	5 (4.2)	1 (2.7)
1-10%	66 (13.5)	8 (17.8)	22 (19.6)	15 (8.6)	16 (13.3)	5 (13.5)
11-20%	97 (19.9)	8 (17.8)	20 (17.9)	29 (16.7)	34 (28.3)	6 (16.2)
21-50%	98 (20.1)	6 (13.3)	18 (16.1)	47 (27.0)	21 (17.5)	6 (16.2)
>50%	154 (31.6)	15 (33.3)	33 (29.5)	64 (36.8)	30 (25.0)	12 (32.4)
Don't know	53 (10.9)	2 (4.4)	15 (13.4)	15 (8.6)	14 (11.7)	7 (18.9)

**Data presented as percentage of total (n=665), GP (n=59), specialist (n=143), nurse (n=236), pharmacist (n=160), other HCPs (n=67) in the first, second, third, fourth, fifth and sixth column, respectively. Numbers do not always add up due to missing numbers (percentages might therefore be less than 100): perceived usefulness of an open access knowledge bank on the safety of medicines during pregnancy and breastfeeding, 1-10 n=160, how often imagine using knowledge bank n=162, would using such a knowledge bank save you time? n=161, when could you imagine using the knowledge bank? n=160, in what kind of situations could you imagine using the knowledge bank? n=160, I would like to access the knowledge bank via a website n=176, I would like to access the knowledge bank via a mobile app n=177, would you be able to use a knowledge bank if it is only available in English? n=176, do you see any concerns in allowing the public to access the knowledge bank? n=176, what percentage of your patients do you think would be likely to use the knowledge bank, as is Internet based? n=177. Abbreviations: HCP, Healthcare Professional; GP, General Practitioner; a On a scale from 0 to 10, 0 being "Not valuable" and 10 being "Most valuable" b Respondents could choose more than 1 answer*

Results focus groups

General info

Six focus group interviews were performed. The focus group composition is presented in table 13.

Table 13. Focus group composition

	WOMEN	HEALTHCARE PROFESSIONALS
CROATIA	6 participants; 2 pregnant and 4 breastfeeding <ul style="list-style-type: none"> • 1 chronic patient (type 1 diabetes and hypertension), • 1 woman became pregnant through an IVF treatment • The other women did not use specific drugs during pregnancy, aside from dietary supplements • After pregnancy, some women had experience with the use of antibiotics 	9 participants <ul style="list-style-type: none"> • 7 gynecologists • a pharmacist • a general practitioner
FRANCE	3 participants, all breastfeeding. One woman has epilepsy	5 participants <ul style="list-style-type: none"> • 2 pharmacists • a neurologist • a general practitioner • a haptonomist and perinatal companion
THE NETHERLANDS	3 participants, all breastfeeding <ul style="list-style-type: none"> • 1 woman used macrogol (laxantia) during pregnancy. • The other women did not use medicines during pregnancy. • They have experience with drug use during breastfeeding 	6 participants <ul style="list-style-type: none"> • 2 midwives • 2 nurses • a gynaecologist • a professor in reproductive health

Information needs women

The women mentioned that it is important that there is information available on the safety of drug use during pregnancy and breastfeeding. They believe that women who have underlying conditions, should also have the opportunity to get pregnant.

A woman who used medicines during pregnancy: *“It is scary at first, especially regarding the*

risk of malformations, but if you are reassured by professionals, you have to go for it.” [FR Women 2]

When it comes to drug use during pregnancy and breastfeeding, women have questions about the safety of drug use in general, the effect of the drug on their child (malformations), the maximum dose that can be taken and for how long, the use of vitamins during pregnancy, and alternative drugs. One woman had specific questions about the effect of the pregnancy on her condition (diabetes mellitus).

“What worries me the most at the moment is the amount of insulin and why it is increasing rapidly every day.” [CR Woman 2]

Also, the effect of the drug on breastfeeding was mentioned. Women gave the example of the use of antibiotics and contraception. Questions were directly asked when the drug was prescribed. However, there was also a woman who mentioned that she had no questions:

“I didn’t ask anything special because I got an advice from a doctor. I trusted him for the recommendation of an antibiotic.” [CR Woman 1]

The women in the Netherlands specifically mentioned that there were also no questions that they were afraid to ask their HCPs.

Information needs HCPs

HCPs do feel that it’s their role to inform pregnant women about the use of drugs during pregnancy and breastfeeding.

“We give the booklet about self-medicines that can be use during pregnancy to every pregnant woman, so they can look it up themselves.” [NL HCP 3]

“Our role is to collect the information, to synthetize the data and to guide the patient on the problem, and to give her a final solution.” [FR HCP2]

Questions that HCPs had about drug use during pregnancy and breastfeeding were related to drug safety in general and during the specific stages of pregnancy, consequences for the child, if dose adjustments are necessary, if there are alternative drugs, interactions, if the drug passes into the mother’s milk, and if adaptations are needed for breastfeeding, for example temporary cessation. They would also like to know where the safety information is coming from and how much is known. Regarding the stages of pregnancy, HCPs would like to know in which stage a certain drug can or cannot be used.

“You might expect different influences during pre-conception and the period around conception and early organogenesis than later in pregnancy.” [NL HCP 6]

Another HCP also mentioned that information about drug use on fertility is important and that women at some age with chronic disease are undergoing various drug therapies that possibly might influence this.

HCPs are aware that in general there is little information available about the safety of drug use during pregnancy and breastfeeding.

“There are of course very few drugs about which you can say that they are safe, that you can use them. Usually there is nuance to it.” [NL HCP 4]

An HCP from France mentioned that some HCPs have little knowledge on this subject. For example, pharmacists, who are drug specialist but during their training there is little attention to the use and safety of drugs during pregnancy and breastfeeding. The Dutch HCP participants mentioned that from their experience, there is a different level of knowledge about the safety of drug use during pregnancy between primary and secondary HCPs. General practitioners, in particular are not aware of resources for information on this topic, they only use the national drug formulary, which has little concrete information.

Contact with the women: When HCPs are confronted with questions from women, they find it important to have clear and straightforward answers. In general, women are asking questions at all stages of pregnancy and breastfeeding. Specialist doctors’ experience is that women have questions already before pregnancy. While for example for midwives, who see pregnant women from the moment they are pregnant, questions are mostly discussed during the first consultation.

The HCPs mentioned that the women have similar questions as themselves. In addition to registered medicines, women also have questions about alternative medicines, vitamins, and cosmetic products.

There were differences between the participants concerning the attitudes of the women toward drug use. Some participants have the experience that women do have questions concerning drug use. There were also participants who experience that women do not ask any questions and are not aware of potential problems.

“During the first consultation you ask which medicines they use, and then sometimes you get a list of medicines that you are surprised they are not aware that it is not wise in pregnancy.” [NL HCP 4]

It was also experienced that women self-medicate.

“Pregnant and breastfeeding women often do not even ask us about medicines, but they take the medicine by themselves, without our knowledge or without the knowledge of the competent doctors.” [CR HCP 4]

These kinds of differences were thought to be population dependent. It was also thought that some women may be anxious in mentioning drug use while they are pregnant, especially with psycho-pharmaceuticals.

Participants mentioned that pregnant women use over-the-counter drug (self-medicines), for example nonsteroidal analgesics and multivitamins.

“In my opinion, this is a topic that we should talk about more often and more openly on this topic of safe drugs in pregnancy is precisely the topic of self-medicines. When it comes to drugs and medical products, the information is sufficient, but when it comes to dietary supplements, we have a bigger problem. They are not today's narrow topic, but they can be a problem.” [CR HCP 8]

HCPs decision making: For decision making around treatment of pregnant and breastfeeding women it was mentioned that each situation is different.

“You cannot say this is never allowed and this is always allowed, but you look carefully

balanced with different doctors and with the patient of course.” [NL HCP 4]

They take into consideration the knowledge there is on drug safety, information in the SmPC, the experience that they already have, alternative drugs, and the severity of the disease for which the woman uses the drug in relation to the teratogenic effect of the drug. They also discuss possible treatment options with the women.

“You notice that some people with the same information make different choices, because they themselves have a different view of life or feelings. And that is allowed, it takes time and then it is very nice if you have information of how much is known about that topic.” [NL HCP 4]

Used information sources by women

Sources: When women search for information about drug use during pregnancy and breastfeeding, they use the internet (Google, the pharmacy website, TIS website), consult their HCPs, and Facebook ‘mum groups’. The use of internet forums differs between the participating women. Some mentioned that they read it and that they identified other sources of information, like the TIS, through these forums, while other women dislike internet forums. It was also mentioned that comments on forums are sometimes difficult to interpret.

“I would never use instructions written on various forums, it's terrible for me and I don't really believe them, everything can be read there.” [CR Woman 1]

“I found a lot of help by just reading comments from different moms groups on Facebook. They share their experiences.” [FR Woman 1]

The patient information leaflet is less often used because the women find that this source provides conservative and incomplete information. There were also women who did not look for information. Their main reason was that they trusted what their HCP prescribed.

“I usually just started taking the drug. And I completely trust that they (the healthcare professional) know what they are doing.” [NL Woman 1]

Role HCP: HCPs have an important role when it comes to providing information about the safety of drugs during pregnancy and breastfeeding. Women contact their general practitioner, pharmacist, midwife, and the TIS (France and the Netherlands) when they are in need for information. The women believe that HCPs have good knowledge on this subject and they trust that the drug that the healthcare professional prescribed is safe during pregnancy.

“I had confidence in my doctor..” and “It's huge (the role of the healthcare professional) yes, I would use the internet, but I always trust the doctor for information.” [Cr Woman 3]

Women use the internet to look for information, but they also find it important to get feedback from their HCP about the information they found. A woman mentioned that:

“I first did online research for contraception and then asked the doctor about what are your experiences with these drugs?” [NL Woman 3]

Stage of pregnancy: The stage of the pregnancy that the women are in may depend on where women search for information. For example, in the Netherlands, women consult their midwife or gynaecologist on a regular basis. However, after delivery, the care is handled over to a health consultation office where the development of the child is followed on a regular basis. At this health

consultation office, the vaccines from the Dutch National Immunisation Programme are also administrated. Some women mentioned that during the pregnancy, they would ask questions to their midwife. However, for questions concerning breastfeeding, they would look it up on the internet, as they are not under the care of a specific HCP.

“I had to know if it (the drug) can also be combined with breastfeeding. The easiest way for me was to search for the product on the internet. I did not have the package leaflet, but well, I just looked up the product on the internet at the site of the marketed holder and thus found out that it can be used in combination with breastfeeding.” [NL Woman 3]

Conflicting info: Some women had experience with either differences in perception or conflicting information coming from different healthcare providers.

“This concerned antibiotics. Then it turned out that the taste of the milk could change and the baby could refuse breastmilk. Then I kindly asked for another type of antibiotic that wouldn't do that. Because I would really like to breastfeed and not immediately take the risk that the baby would refuse it.” [NL Woman 2]

“For me it concerned the choice of follow-on milk for my daughter who had a rash during the introduction of this milk. I had a different medical opinion compared to the pediatrician. I was very stressed and distraught. I started searching other sources, I researched and read information on the internet and then made an appointment with her doctor to change the artificial milk.” [FR Woman 1]

There were also women who didn't experience conflicting information. One did mention that she missed confirming information.

“More the lack of confirmation that it is good and that it is all possible.” [NL Woman 1]

“I didn't have contradictory information because the epileptologist and the neurologist exchange information with each other, so there was no problem.” [FR Woman 2]

Satisfaction and reliability: The women had different perceptions regarding satisfaction about the found or received information. One woman mentioned that she was satisfied with the information she found online.

“Yes, there was a better explanation as well, and not only as stated in the leaflet ‘consult your doctor’, but also a real explanation of what is safe and whether it can be used safely. And what dose you have to use for how long, so that was nice.” [NL Woman 3]

Another woman mentioned:

“Yeah, mostly I would find it all, it's just all scattered, it took me a long time.” [CR Woman 3]
Some women have also experienced that the information provided to them by HCPs was not correct.

“When I went to for TENS [pain therapy: transcutaneous electrical nerve stimulation] therapy at the clinic before, they wrote me, for example, ibuprofen of 600 mg, and I told her that I was breastfeeding, I can't do that.... and she then told me that she forgot.... So if you don't mention or ask, they just forget....” [CR Woman 5]

Used information sources by HCPs

Sources: There are several sources that are being used by HCPs to gain information about drug safety during pregnancy and breastfeeding: (electronic) text books (Briggs, Hale), information website (for example about breastfeeding), national drug formulary, Summary of Product Characteristics (SmPC), European guidelines, database from universities or other institutes, consultation of colleagues, and the internet. HCPs also consult the TIS by their website or by telephone.

For Dutch and France participants, the TIS is often used as a first step to find information. The Dutch participants furthermore mentioned that the TIS-website and the national drug formulary are used as a first step when they are looking for information. If they cannot find what they were looking for, they will either call the TIS or continue their search in European guidelines. Participants mentioned about the TIS-website that it is an advantage that information on a website is more up-to-date compared to books. Furthermore, it is easily accessible.

The SmPC is not a first-choice source as it is conservative and has little information.

“It (the SmPC) says ‘the drug has not been tested on pregnant women’, and it does not tell me anything, what will I say to the pregnant women?” [CR HCP 5]

One HCP from Croatia mentioned that SmPC is being used:

“..the description describes in detail whether the drug is appropriate.” [CR HCP 8]

HCPs do not use internet forums. This is however a source that they believe pregnant women like to use.

Conflicting information: When HCPs come across conflicting information they discuss this with other HCPs and the woman. Some participants also mentioned that they call the TIS or the pharmacovigilance centre to ask for more information. It was furthermore mentioned that discussion about conflicting information can be difficult.

“Through the association, some mothers say ‘the doctor says I can’t take this medicines but on the CRAT (French TIS) says I can. What is your opinion? Answer: We’re going to call the Regional Center of Pharmacovigilance. The question is asked the other way around: ‘I hear that I shouldn’t take it and yet is it really the case?’ [FR HCP 3]

Satisfaction and reliability: The level of satisfaction with the information found differed between the participants. Some mentioned they are satisfied, while others are moderately or not satisfied. The latter was mostly related to conflicting information and unclear conclusion.

“On the SmPC, when it gives its green light it’s great, but when it doesn’t give its green light, in the end, you don’t really get an answer ... We are therefore obliged to cross-check all the information and go and see the different sites, which requires additional research work.” [FR HCP 5]

Participants find information reliable when the source is a non-profit organisation, when there are experts who work there, and when the references are clearly described. The amount of data available and the number of patients who used the drug of interest in relation to teratology contribute to the reliability.

Needs and preferences of women for a knowledge bank

For the Croatian and French women and HCPs, it was asked what kind of knowledge bank they would prefer in relation to drug use during pregnancy and breastfeeding.

Information on knowledge bank: Women would like a freely accessible, validated website with information from HCPs. They would like to have information about specific therapies, differences for different stages of pregnancy, and dose and duration. It was also mentioned that it would be helpful to have a website where you can also contact a HCP by e-mail.

“Somehow the information should be segmented, before pregnancy, preparation for pregnancy, pregnancy and like that.” [Cr Woman 2]

“Information on dose and duration. If the information is complicated and if a medical opinion is needed, display a phone number or email to contact for a personalized opinion due to several possible situations.” [FR Woman 3]

Women find information reliable when the information on it comes from professionals and when there are references available.

“First of all, this page should have tips from doctors who are experts in their field and who are really objective...” [CR Woman 2]

Preferred search strategy: The women would like to search by symptoms and medicines.

“I would like to write down a term so that the possibilities of therapy open up to me, but also perhaps alternative therapies. [CR Woman 1]

Preferences and accessibility: They would prefer that the knowledge bank is available as website and as an app. It is also preferred that the knowledge bank is also available in the country’s language in order for the women to use it and it should be understandable for the public.

“I would not want to read professional medical information that is unclear to me. I don’t even read that [professional medical information] broad and concise information, because it’s not as appealing to me as I am not a doctor.” [CR Woman 3]

For accessibility it was suggested to put a link to the knowledge bank on a site that women often use. Or to make the knowledge bank visible on a search engine when women search for ‘a type of drug’ in combination with ‘pregnancy’. It can also be advised by healthcare professionals (generalists and specialists), social networks, and brochures.

The women would prefer that a neutral organization such as a university or institute should be responsible for the knowledge bank. It should be an organization independent from the pharmaceutical industry.

Needs and preferences of HCPs for a knowledge bank

Information on knowledge bank: HCPs would like to have a freely accessible, up-to-date database with information about the safety of drugs in the different stage of pregnancy and

breastfeeding. They would also like information about drug interactions and information on drugs that are used off label or in the doses not according to the approvals.

“.. something simple and easily accessible and useful would be a big plus since we have nothing now, it doesn't have to be an enormous project in the beginning.” [CR HCP 3]

One HCP mentioned that is preferred to not have too much text.

“You know what I'm going to tell you, I'm bothered by the excess information in these databases, why this information is repeated in many places, and it's not always necessary.” [CR HCP 7]

The information should also be understandable by the public. As the information may not always be easy to interpret by the women, it was advised to include a link to an HCP.

References and information about methodology that is being used to write the information pages are preferred. These do not necessarily have to be present in the first reading, but it would be good if they could find them. This would contribute to more confidence in the data provided.

“References also help to understand and to provide a better explanation to the patient.” [FR HCP 4]

They would not like to see advertising, pharmaceutical sponsors, comments, or a forum on the knowledge bank website.

Preferred search strategy: HCPs would like to search by medicines (molecule name and brand names) and by disease.

Preferences and accessibility: Ideas for accessibility were: flyers that can be distributed by HCPs, a display in pharmacies, a logo on the medicine boxes. The idea for the kind of organization that should be responsible differed between the HCPs. Some mentioned the TIS/pharmacovigilance centre of the country, while other thought the public should be responsible. One HCP mentioned that the sustainability can be a problem. It was suggested to organize a multidisciplinary team of people who are interested in the subject, or that the knowledge bank is maintained by a TIS after the project.

“I think we are a small country for something like that [develop knowledge bank]. You need to have a large population for a special knowledge database, Europe is a level to think about. So, we can't use databases from USA either, because some drugs are not registered in Europe.” [CR HCP 7]

Testing of the knowledge bank by women

In the Netherlands, the prototype of the knowledge bank has been shown to the participants. The information page for azithromycin was used as an example.

Impressions: All three women used a different device to open the knowledge bank; laptop, tablet, and mobile phone. They all found that that the knowledge bank is clear and straightforward. In their opinion, the knowledge bank should provide up-to-date information. This also contributes to the reliability.

“Well, what struck me is that there are also topics that are addressed with regard to COVID. So that makes me think, hey this is also a website that shares recent information.” [NL Woman 2]

The women mentioned that the website looks trustworthy and they liked the colours of the website. In the ‘About us’ section you can get more information, which is helpful. They would prefer that the knowledge bank is also available in the country’s language in order for the women to use it.

Information pages: All women missed a clear conclusion.

“I think starting with the conclusion and then the option of more information and research. when you are searching, you want to know right away that this is safe and not first plough through the whole research and then come to the conclusion and think, oh yes, it is safe.” [NL Woman 2]

“Yeah, a little how the Lareb [Netherlands Pharmacovigilance Centre – TIS] works. Then you immediately have a list of most safe, probably safe and unsafe. And best alternative. I think that’s just complete, I like that very much.” [NL Woman 2]

It was also mentioned that the advice given in the conclusion is not clear enough. The information page of azithromycin that was used as an example mentions ‘this drug can be used’. For the women it was still not clear if it is actually safe during pregnancy. They would like to see this specifically in the conclusion; ‘this drug is safe to use’. All women found it positive that there are references available for the information pages.

Use of the knowledge bank: The English language is an obstacle for the women to use the website. Because the information pages are not clear to them, they would probably not use the knowledge bank in its current form. They furthermore mentioned that this knowledge bank is ‘unknown’ to them. This makes it less reliable.

“Yes, for me also the unfamiliarity of how to get to the page. Then if you’re looking for something very specific, you’ll see references that make it reliable. But, I think that at the moment it is the unfamiliarity that says well, I don’t know that one. So, let me ignore it and fall back on sources that I do know.” [NL Woman 2]

When a midwife or general practitioner advises this knowledge bank, they would be more open to using it. Also, when the conclusion would be highlighted and clearer, they would consider using it.

Testing of the knowledge bank by HCP

Impressions: HCPs mentioned that the website looks nice and it is easy that you can directly start your search. They believe that the colours give a professional healthcare look. They were critical on the visuals that have been used, for example a female HCP with nail polish is not a good reflection of the reality as HCPs are not allowed to wear nail polish in the Netherlands.

In general, the HCPs found the aim of the knowledge bank unclear. They didn’t know if they could for example also find information on drug safety during breastfeeding.

“When you open it, it says ‘medicines in pregnancy’. Is that correct?” [NL HCP 1]

It was also unclear who is responsible for the knowledge bank. The organisations that work on this knowledge bank, including whether or not they are non-profit, and the fact that this is a European initiative, can be more transparent.

Information pages: For the information pages, they were positive about the references and that different languages can be chosen. The main issue was that most participants found it text heavy and that they missed a clear conclusion. They would like to see directly if a drug is safe to use.

[After clicking on the information page] *“Then I immediately come up with a text and then you have to read through the entire text and draw a conclusion from it. And that is quite difficult to do when you have someone in front of you who wants an answer as quickly as possible.”* [NL HCP 4]

For the conclusion, it was suggested to include a score, for example ‘red, orange, green’ or ‘1, 2, 3, 4, 5’, and information on how much and the quality of information that the conclusion was based on.

“But this is what I miss, what is so nice of the TIS-website, that you can see at a glance whether it is probably safe, probably not safe or absolutely not safe.” [NL HCP 4]

Participants mentioned that they missed information related to the different phases of pregnancy, including preconception.

“What I am actually missing is a preconception part about effects on sperm and the chance of pregnancy or orogeny. And maybe even before that ... Pregnancy really does consist of several phases...” [NL HCP 6]

Most participants furthermore mentioned that it would be good to split information meant for the general public and that for HCPs. One participant also looked at the information page about rheumatoid arthritis:

“.. the first story begins about what rheumatism is. I don't think that's something you look for in something like that. You don't want some kind of textbook.” [NL HCP 4]

Search functionality: Participants find that the search function should also work when the drug name is typed incorrectly.

“I already typed it incorrectly and then the system freezes.” [NL HCP 1]

“Because very often people don't know .. and you type it the way you interpret it.” [NL HCP 1]

Accessibility: In order to make people aware of this knowledge bank, it was suggested to add the link of the knowledge bank on a known, trustable website (like the TIS-website, national drug formulary website). This might also increase the trust people have in the content of the knowledge bank. In order to make the knowledge bank trustworthy, it was also suggested to clearly explain the role of each partner that collaborates in the knowledge bank. Maybe there is also a need for a campaign.

“As HCP we don't all know Lareb, general practitioners do not all know Lareb. If this European website just shows up like that between one of the many websites, than it is unclear to me if it is a good source.” [NL HCP 5]

Discussion

Main conclusions from survey

Women

- Almost all the women said they had needed information about medicines during pregnancy/breastfeeding
- As the first information source, medical doctors and the Internet were most used
- Almost half of the women reported their medical doctor as their preferred source of information
- More than half of the women have experienced finding contradictory information on medicines use during pregnancy/breastfeeding
- Forty percent reported having had difficulties understanding information given, most commonly because information was not precise enough.
- More than one third of the women reported having difficulties understanding information on medicines use during pregnancy/breastfeeding
- 80% of the women had English as their native language or thought English would be sufficient for them to be able to use the knowledge bank

HCPs

- More than half of the HCPs reported being asked about medicines use during pregnancy/breastfeeding daily or weekly
- Being asked about medicines use was more common among GPs, specialist physicians and pharmacists compared to other HCP groups
- More than half of the HCPs reported to often or sometimes having difficulties understand information on medicines use during pregnancy/breastfeeding
- Almost all the women and HCPs thought a European knowledge bank on the safety of medicines during pregnancy/breastfeeding would be very useful
- 60% of the HCPs had English as their native language or thought English would be sufficient for them to be able to use the knowledge bank

Main conclusions from the focus groups

- Pregnant and breastfeeding women and HCPs believe it is important that there is information available about the safety of drug use during pregnancy and breastfeeding.
- They were all positive about a European knowledge bank. Concerning this knowledge bank, it was thought to be important that the information is clear and understandable by HCPs and the public, like pregnant women. It should be clear on what studies the information on the knowledge bank was based on, and the pharmaceutical industry should not be involved in making any recommendations in order to make the information reliable. Information pages in local languages are preferred in order to reach a larger population.
- Questions that women and HCPs have related to the safety of drug use during pregnancy and breastfeeding are generally similar. In addition to HCPs, women had questions about the

use of vitamins and herbals. This was comparable with information from literature (3,4). HCPs were also interested in the safety of drugs used during different stages of pregnancy. There was a difference in attitude of the women related to drug use and questions they ask their HCPs. Some women discussed their questions with their HCP and search for information themselves, while others have no questions and trust in the knowledge of their HCP when it comes to drug use during pregnancy and breastfeeding.

- As it is described in literature, HCPs mentioned that women with more health problems are more likely to discuss the safety of drug use during pregnancy and breastfeeding with their HCP (5).

Comparison in relation to prior studies

In this survey and the focus groups, we found that most of the women had had the need for information about medicines during pregnancy or breastfeeding and that their HCP and Internet were the most used first information sources. In the survey, almost half of the women reported their medical doctor as their preferred source of information. In the focus groups, women mentioned that they have trust in their HCPs when it comes to the safety of drug use during pregnancy. In the case the women search for information themselves, HCPs are also used as a source to double check the information. These findings are in accordance with a former study where women expressed high information needs about medicines during pregnancy, and they relied on physicians (73%), pharmacy personnel (46%) and midwives or nurses (33%). The Internet was also a widely used information source (60%) (6). In another study, Internet, books and clinic pamphlets/brochures were the most frequent self-identified sources of information (7).

When searching for information online, the women were most commonly using search engines (45.0%). Several studies show that in general, up to 95% of women are using the Internet as a resource during pregnancy, and 60–75% of pregnant women reported use of a pregnancy-related smartphone app (3, 8, 9, 10). A study found that pregnant women were frequently searching the Internet for information concerning medicines (e.g. 74% of the women visiting a tertiary hospital in Belgium), most commonly via Google and other search engines, and sometimes without discussing the results with an HCP (11). Official national preconception websites are often not known by the women (12).

A recently published study found that women expressed the greatest interest in resources that facilitated connections to other women and their experiences (87.4%) (13). In our research, approximately 50% of the women in the present survey found it essential or important that the information was based on women's own experiences. In the focus groups there were differences in perception concerning the use of Internet forums. Some women prefer to get information from others, while there were also women who dislike the use of Internet forums as they don't trust the information described there.

These results together may indicate that some pregnant and breastfeeding women have a desire for fellowship when making decisions about medicines. However, concerns on the trustworthiness of information in internet women forums were also acknowledged.

HCPs use many sources for information, of which pregnancy and breastfeeding textbook, the national drug formulary, and the nation TIS were the one that are mostly used. Concerning the latter, this was not surprising since the TIS was one of the main setting of recruiting participants. There are few studies specifically investigating how physicians obtain information about teratogenic risks or convey this information to their patients. In one study, primary care clinicians expressed concerns about the variable quality of information that they encountered online regarding to teratogenic risks (14). The focus groups demonstrated that the TIS (in France and the Netherlands)

is an important source for HCPs to ask for information and discuss conflicting findings. It was noteworthy that both women and HCPs mentioned that the SmPC is not a first-choice source as it is conservative and has little information. This is in line with the finding from literature that in particular, physicians prefer resources that would provide more specific numerical information that they could use when explaining a medicine risk of teratogenic side effects to a patient (14).

Another important finding of the present survey was the majority of women that have experienced finding contradictory information on medicines use during pregnancy and breastfeeding. This is consistent with previous findings (6, 13). In addition, the survey found that more than one third of the women reported having difficulties understanding information on medicines use during pregnancy and breastfeeding. The focus groups furthermore indicated that some women also experienced receiving contradictory information from different HCPs. Hence, there should be an increased focus on giving women who are or want to become pregnant or are breastfeeding, clear and comprehensible information.

The women's desire for information from HCPs agrees well with other results from the present study, which show that more than 60% of the HCPs are being asked about medicines use during pregnancy daily or weekly. Fifty percent of the participating HCPs reported that they found it easy to find the needed information, however, some HCPs reported that they found it difficult to find the needed information, and many HCPs reported to sometimes or occasionally having difficulties interpreting information about medicines use during pregnancy/breastfeeding. The focus group results demonstrated that there is sometimes a difference in the competence of HCPs in finding the right information and being up-to-date about the several sources that are available. HCPs who receive questions about the safety of drug use during pregnancy or breastfeeding on a regular basis might be better informed compared to others, such as general practitioners or pharmacists.

Literature on HCPs' information needs on drug use during pregnancy and breastfeeding are scarce and quite old. Therefore, the findings of this study are of great importance. The results also indicate a great need for a common database on medicines use during pregnancy and breastfeeding. As the present survey and focus groups show that both women and HCPs are perceiving a future knowledge bank as very useful. Further focus should be to develop a knowledge bank that best suits their needs and preferences.

Strengths and limitations of the survey

Strengths of the study

There are several strengths of these conducted surveys. Firstly, by using a web-based approach, the questionnaires were accessible in a uniform way to a large number of women and HCPs across Europe and beyond. Internet penetration rates in Europe are high (89.4%) (15), making an online approach feasible and efficient. In addition, the questionnaires were anonymous, which may have made the women and HCPs more comfortable answering the questions. The questionnaire for women was shared on many websites commonly visited by pregnant and breastfeeding women, and several important external stakeholders were asked for their support in sharing the survey enabling perspectives from a broad population perspective. Lastly, the wide range of questions makes it possible to get an extensive view of the study participants, which will provide future directions for the ConcePTION ecosystem. An additional strength can be seen in the geographic scope of survey respondents, with many participants living outside the EU. For this reason, the knowledge bank could have a much wider impact than just in the EU, especially in countries where there is no TIS.

Limitations of the study

The surveys have also some important limitations that should be acknowledged. Firstly, the questionnaire was only available through internet websites; consequently, a conventional response rate cannot be calculated. Secondly, women and HCPs who decided to answer the surveys may differ from the general birthing population in Europe and European HCPs in several ways, and a selection bias of the target population cannot be ruled out. For example, over 70% of the women had a University degree whereas, 40 % of the 30-34-year-old women in the EU had completed tertiary education in 2019 (16). Epidemiological studies, however, indicate reasonable validity of web-based recruitment methods (17, 18). Furthermore, the survey was disseminated and publicised in the ENTIS network, possibly influencing the answers towards the teratology information services.

Some additional limitations are as follows:

The accuracy of replies depended on women and HCPs recall. Especially, as there were no exclusion criteria for the women's survey, for some of the participating women their last pregnancy could be many years ago. These women's answers may consequently not reflect today's situation regarding the needs of information about medicines use during pregnancy and breastfeeding.

In retrospect, more background variables could be advantageous in the women's survey, e.g. marital status, smoking status and income level. However, the women's survey was already quite comprehensive, and even more questions might have contributed to fewer completing the survey or possibly more missing answers among the respondents. Other studies have investigated special patient groups regarding information needs (4, 11, 13), however, due to the low number of participants in the various patient groups in this study, we mostly studied the participants as one group. This may have yielded different results than if we had studied each patient group separately. Another possible limitation is linked to the fact that there are no possibilities for asking questions when answering the questionnaires. Hence, there might have been women or HCPs misunderstanding some of the questions and thus giving incorrect answers. However, a pilot study was carried out in December 2019, which strengthens the assumption that the questions are interpreted correctly.

Strength and limitation of the focus group interviews

Doing qualitative research in focus groups rather than in individual interview settings allows observations of how and why individuals accept or reject opinions, ideas, comments and thoughts from the other participants in the group, and how these interactions stimulate the development of the topic at hand (19). A strength of our study was the inclusion of a variety of pregnant or breastfeeding women and HCPs from several European countries. It is expected that a wide range of factors that are important regarding information on the safety of drugs during pregnancy and breastfeeding are covered.

A limitation of this study was the way women and HCPs have been invited to participate. The national TIS was one of the main starting points for including women and HCPs in France and the Netherlands. The results are probable not representative for all pregnant or breastfeeding women and HCPs, but as with most qualitative studies these findings were not needed for confirmation, but to generate hypotheses. There were only two pregnant women involved in the focus groups. We do however believe that the women who are breastfeeding can still give a view on their thoughts during their pregnancy.

Due to the COVID pandemic, the focus groups needed to take place online instead of face to face. This might have negatively influenced the contribution of the participants as they might have hold

back in giving their thoughts. Also, online it is more difficult for the observer to read body language and to act on it. We were planning on having focus groups of 8 participants. This number was only reached for the focus groups with HCPs in Croatia. Especially for the focus groups with women in France and the Netherlands, it was difficult to include the women. Nevertheless, we believe that the discussions provided the information that we aimed for.

Conclusion

This study shows that pregnant and breastfeeding women and HCPs need information about the safe use of drugs. Currently, there is a lack of clear and comprehensible information sources for women in need of information about medicines use during pregnancy and breastfeeding. HCPs are widely consulted as source of information, but they are also experiencing difficulties in finding and interpreting information. Discrepancies and often conflicting information in different sources are a challenge reported by both women and HCPs. The Internet was a preferred source of information and has led to the preference for easily accessible but reliable online resources.

The pregnant, breastfeeding women and HCPs were positive regarding a European knowledge bank with information about the safe use of drugs during pregnancy and breastfeeding. The survey and focus group interviews provided insights on the needs and preferences for information. According to these, the information provided on the knowledge bank should be clear and understandable for both HCPs and the general public. The information pages should be easily found and have a clear conclusion. It is also important that the information is available in native languages. In order to increase the reliability and trust in the knowledge bank, it should be clear on what studies the presented information was based on, and the pharmaceutical industry should not be involved in making recommendations. In this way the knowledge bank will best meet the needs and preferences of the users.

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Appendix sub-task 5.1.1: Inventory

Appendix 1 – Name of TIS completing table

Data Source Name	Brief Description	Published Format	Exposures Included	Language	Target Audience	Data Source Website (if applicable)

Appendix 2 – Information source in European countries: questionnaire for industry

Different stakeholders disseminate different kinds of information about the safety of drug use during pregnancy and lactation and may use a number of different delivery methods to provide these details. The objective of the questionnaire is to make an inventory of the current information sources used in all European countries.

Please complete the questionnaire regarding the information sources about medication in pregnancy and or breastfeeding in your country.

Questions

1) In which country are you based/are you responsible for?

<input type="checkbox"/> Austria	<input type="checkbox"/> Slovenia	<input type="checkbox"/> Lithuania	<input type="checkbox"/> Greece
<input type="checkbox"/> Croatia	<input type="checkbox"/> United Kingdom	<input type="checkbox"/> Netherlands	<input type="checkbox"/> Italy
<input type="checkbox"/> Denmark	<input type="checkbox"/> Belgium	<input type="checkbox"/> Romania	<input type="checkbox"/> Luxembourg
<input type="checkbox"/> France	<input type="checkbox"/> Cyprus	<input type="checkbox"/> Spain	<input type="checkbox"/> Poland
<input type="checkbox"/> Hungary	<input type="checkbox"/> Estonia	<input type="checkbox"/> Bulgaria	<input type="checkbox"/> Slovakia
<input type="checkbox"/> Latvia	<input type="checkbox"/> Germany	<input type="checkbox"/> Czech Republic	<input type="checkbox"/> Sweden
<input type="checkbox"/> Portugal	<input type="checkbox"/> Ireland	<input type="checkbox"/> Finland	<input type="checkbox"/> Malta
<input type="checkbox"/> Norway	<input type="checkbox"/> Switzerland	<input type="checkbox"/> Other	

2) What is your role?

- Pharmacovigilance
- Medical information
- Regulatory
- Other (please specify):

3) Are you aware of sources of information about medication in pregnancy and or breastfeeding available in your country?

- Yes
- No

4) Based on your knowledge, where do general public (e.g. pregnant women) in your country get information about medicine use during pregnancy and breastfeeding (please specify those that apply with example and provider if it's mentioned)?

<input type="checkbox"/> Medical specialists (obstetricians/gynaecologists)	Example :
<input type="checkbox"/> Teratology information services or registries	Example :
<input type="checkbox"/> National or local hospital guidance	Example :

<input type="checkbox"/> Online databases	Example :
<input type="checkbox"/> Package inserts	Example :
<input type="checkbox"/> Desk references or textbooks	Example :
<input type="checkbox"/> Websites	Example :
<input type="checkbox"/> Treatment guidelines	Exemple :
<input type="checkbox"/> Social media	Exemple :
<input type="checkbox"/> Medical literature	Exemple :
<input type="checkbox"/> Other sources (specify: _____)	Example :

- 5) Based on your knowledge, where do HCPs in your country get information about medicine use during pregnancy and breastfeeding (please specify those that apply with example and provider if it's mentioned)?

<input type="checkbox"/> Medical specialists (obstetricians/gynaecologists)	Example :
<input type="checkbox"/> Teratology information services or registries	Example :
<input type="checkbox"/> National or local hospital guidance	Example :
<input type="checkbox"/> Online databases	Example :
<input type="checkbox"/> Package inserts	Example :
<input type="checkbox"/> Desk references or textbooks	Example :
<input type="checkbox"/> Websites	Example :
<input type="checkbox"/> Treatment guidelines	Exemple :
<input type="checkbox"/> Social media	Exemple :
<input type="checkbox"/> Medical literature	Exemple :
<input type="checkbox"/> Other sources (specify: _____)	Example :

- 6) Do you have a Teratology Information Service (TIS) centre (national centre that provides telephone advice on medication use during pregnancy and lactation) or similar available in your country or region?

- Yes
 No
 Don't know

- 7) Among the listed sources of information, please indicate the most or the least reliable?

Most reliable	Least reliable
<input type="checkbox"/> Medical specialists (obstetricians/gynaecologists)	<input type="checkbox"/> Medical specialists (obstetricians/gynaecologists)
<input type="checkbox"/> Teratology information services or registries	<input type="checkbox"/> Teratology information services or registries
<input type="checkbox"/> National or local hospital guidance	<input type="checkbox"/> National or local hospital guidance
<input type="checkbox"/> Online databases	<input type="checkbox"/> Online databases
<input type="checkbox"/> Package inserts	<input type="checkbox"/> Package inserts
<input type="checkbox"/> Desk references or textbooks	<input type="checkbox"/> Desk references or textbooks
<input type="checkbox"/> Websites	<input type="checkbox"/> Websites
<input type="checkbox"/> Other sources :	<input type="checkbox"/> Other sources :

8) Can you provide details in the table below about the online information sources used in your country?

Online information source name	Target audience (HCPs/general public (pregnant women)/ both)	Language(s) of the information (local or foreign)	Accessibility (free to use/requires subscription/pay-per-view)

Thank you for your participation to this survey

Appendix 3 – Inventory of information resources known to or used by ENTIS members and industry partners

Country	Stakeholder/Data Source Name/url	Brief description	Active on social media? (Y/N)	Format 1= open access website, 2= subscription access website, 3= combined open and subscription access website, 4= webchat, 5=phone service, 6= textbook, 7=database, 8= app, 9=email, 10=personal communication, 11=database, 12=periodic newsletter/journal, 13=forum	Audience 1=HCPs 2=patients/general public 3=both 4=other	Scope 1=pregnancy 2=breasfeeding 3=both 4=broad	Language * 1=local, 2=Local and english, 3=Local, english and other, 4=International
International	Marketing authorisation holder SmPC	Official pharmaceutical information	N	1	1	4	4
Estonia	Republic of Estonia Agency of medicines www.ravimiamet.ee	HA	N	1	3	4	2
Finland	Teratologinentietopalvelu www.hus.fi	TIS	Y	1, 4, 5	3	3	3
Romania	Agentia Nationala a Medicamentului si a Dispozitivelor Medicale din Romania www.anm.ro	HA	Y	1	4	4	2
Norway	Trygg Mammamedsin www.tryggmammamedsin.no	HA funded service, individual advice.	N	1	2	3	1
Norway	Relis www.relis.no	HA	Y	1	1	4	1
Slovakia	SUKL www.sukl.sk	HA	Y	1	3	4	2
Hungary	OGYEI http://ogyei.gov.hu/gyogyszeradatbazis	National Institute of Pharmacy and Nutrition. Hungarian HA drug database	N	1, 11	3	4	2
Ireland	Health Service Executive http://www.hse.ie/eng/services/list/3/maternity/combinedcare.html	HA. Maternity section of broader website	Y	1	3	1	2
Ireland	NMIC (national medicines information centre) http://www.stjames.ie/NMIC/Index.html	Cinical enquiry answering service for prescribers. Therapeutics bulletin and monthly therapeutics newsletter.	Y	1, 5, 9	1	1	2

Lithuania	The State Agency of Medicines, Drug Registry http://vapris.vvkt.lt/vvkt-web/public/medications	Register of medicinal products. Submission of ADRs by patients and HCPs.	N	1,7	3	4	2
Latvia	The State Agency of Medicines, Drug Registry http://www.zva.gov.lv/zvais/zalu-registrs/	Register of medicinal products. Submission of ADRs by patients and HCPs.	Y	1	3	4	2
Germany	Berlin TIS www.embryotox.de Embryotox app	TIS	N	1,8	3	3	1
Germany	AWMF Leitlinien (Association of the Scientific Medical Societies in Germany) https://www.awmf.org/awmf-online-das-portal-der-wissenschaftlichen-medizin/awmf-aktuell.html	Society producing clinical guidelines.	N	1	1	4	2
Germany	BfArM Rote Hand Briefe https://www.bfarm.de/SiteGlobals/Forms/Suche/EN/Servicefunctionsearch_Formular.html?resourceId=3496626&input_=3496626&pageLocale=3497216&templateQueryString=rote+hand+briefe&submit.x=0&submit.y=0	Information of the Federal Institute for Drugs and Medical Devices	N	1	1	4	2
Germany	Rohde/Schaefer; Psychopharmakotherapie in Schwangerschaft und Stillzeit: Möglichkeiten und Grenzen	Recommendations regarding the use of psychiatric medications	N	6	1	4	2
UK	National Institute for Health and Care Excellence (NICE) https://www.nice.org.uk/	Evidence-based recommendations developed by independent committees, including professionals and lay members, and consulted on by stakeholders.	Y	1	1	4	2
UK	Tommy's www.tommys.org/pregnancy	Patient organisation	Y	1	3	1	2
North America	American Herbal Products Association Botanical Safety Handbook	Information on herbal products	N	6	1	4	2
Germany	Friese, Mylonas, Schulze, Infektionserkrankungen der Schwangeren und des Neugeborenen	Textbook about infectious diseases during pregnancy and neonatal period including treatment	N	6	1	1	1
Germany	Enders, Infektionen und Impfungen in der Schwangerschaft	Textbook about infectious diseases during pregnancy and neonatal period including treatment	N	6	1	1	1
Germany	Berlin TIS VigilanceONE	Berlin TIS Database for search and evaluation of Follow Ups including exposures and outcomes including adverse pregnancy outcomes	N	7	4	1	1

North America	North American AED press release http://www.aedpregnancyregistry.org/wp-content/uploads/The-NA-AED-Pregnancy-Registry-AES-2019.pdf	Preliminary results of the north American AED- registry	N	1	3	1	2
International	ENTIS/Otis	e-tox discussions	N	9	4	1	2
International	ENTIS https://www.entis-org.eu/	ENTIS webpage	N	1	3	1	2
N/A	Textbook of Human Lactation (by Hale and Hartmann)	Summary of published research and recommendations regarding the use of medicines during lactation.	N	6	1	2	2
North America	National Library of Medicine- Pubmed https://www.ncbi.nlm.nih.gov/pubmed/	Free search engine primarily accessing the MEDLINE database	Y	3	1	4	2
Finland	Medbase Ltd Gravbase, Lactbase https://www.terveysportti.fi/apps/raim/	Summary of published research and recommendations regarding the use of medicines during pregnancy and lactation.	Y	2	1	3	2
Finland	Duodecim health portal (Finnish) https://www.terveysportti.fi/terveysportti/koti	Scientific association national evidence-based information on treatment of illnesses	N	2	1	4	2
Finland	Drugs and pregnancy project www.thl.fi	Database based on the Finnish Medical Birth Register and Prescription register	Y	10	1	1	3
Sweden	Janusinfo www.janusinfo.se	TIS. Data on the Swedish Medical Birth Register	Y	1	1	3	2
Sweden	Lakemedelsindustriforeningens Service AB www.Fass.se	Industry organisation providing product information	N	1	3	4	2
Sweden	Karolinska Drug Information Center www.Drugline.se	Short summaries	N	1	3	3	2
Netherlands	de (digitale) kennisbank van de Teratologie Informatie Service Lareb www.zwangerenmedicijn.nl or http://www.lareb.nl/tis-knowledge	TIS knowledgebank	Y	1	3	3	1
UK	Royal College of Obstetricians and Gynaecologists (RCOG) www.rcog.org.uk	Professional organisation	Y	1,	3	1	2
UK	NHS http://www.nhs.uk/conditions/pregnancy-and-baby/medicines-in-pregnancy	HA	Y	1	2	4	2
UK	UK Drugs in lactation advisory service (UKDILAS) http://www.sps.nhs.uk/articles/ukdilas	HA funded service	Y	1,5	1	2	2
France	CRAT http://www.lecrat.fr/	TIS Summary recommendations during pregnancy and breastfeeding. No references	N	1	1	3	1

France	Delaloye « Médicaments, grossesse et lactation » https://www.revmed.ch/Medicaments/Medicaments-grossesse-et-lactation	Summary recommendations during pregnancy and breastfeeding presented as tables, referenced.	N	6	1	3	1
France	Annie-Pierre Jonville-Béra, Thierry Vial « MÉDICAMENTS ET GROSSESSE : PRESCRIRE ET ÉVALUER LE RISQUE »	Summary recommendations during pregnancy, referenced	N	6	1	1	1
France	Prescrire- la revue prescrire https://english.prescrire.org/en/Summary.aspx	Non-profit educational organisation producing Monthly medical journal	N	1, 12	1	4	2
Italy	Italia medicines agency (AIFA) www.aifa.gov.it http://www.farmaciegravianza.it/	Bi-monthly Drug info bulletin (Pharmacovigilance magazine Reazoni (focused on adverse reactions).	Y	1	3	4	1
International	World Health Organisation (WHO) VigiBase https://www.who-umc.org/vigibase/vigibase/	World Health Organisation (WHO) global Individual Case Safety Report (ICSR) database.	Y	7	1,4	4	3
France	Agence national sécurité du médicament et des produits de santé French National Pharmacovigilance database (FPVD)	Database	N	7	1	4	1
North America	OTIS Mother-to-baby Fact Sheets https://mothertobaby.org	Knowledgebank	Y	1	3	3	3
North America	IBM Watson Health REPRORISK System in Micromedex 2.0. It comprises four databases: REPROTOX®, REPROTEXT®, TERIS, and Shepard's Catalog. www.micromedexsolutions.com	Literature review style summaries of peer-reviewed published studies	N	2	1	3	2
North America	IBM Watson Health DRUGDEX® in Micromedex 2.0 www.micromedexsolutions.com	Drug Information documents	N	2	1	4	2
N/A	Herbal Medicines in Pregnancy and Lactation: An evidence-based approach (by Edward Mills)	Literature review style summaries of peer-reviewed published studies	N	6	1	3	2
UK	UKTIS Summary monographs: www.uktis.org BUMPS leaflets: www.medicinesinpregnancy.org	TIS	Y	1,2	3	1	2
UK	British National Formulary (BNF) http://www.bnf.org/products/bnf-online	National Formulary	Y	3	1	4	2
UK	The Breastfeeding Network www.breastfeedingnetwork.org.uk	Patient organisation	Y	1	3	2	2
UK	MIMIS pregnancy treatment options; MIMS treatment in pregnancy www.mims.co.uk	Knowledge Bank	N	2	1	1	2
N/A	Drugs in Pregnancy and Lactation (by Briggs, Freeman and Yaffe).	Literature review style summaries of peer-reviewed published studies	N	6	1	3	2

Spain	CIMA https://cima.aemps.es/cima/publico/home.htm	Summary of the characteristics of the drugs	N	1	1	4	1
North America	Dailymed https://dailymed.nlm.nih.gov/	Official provider of FDA label information	N	1	1	4	2
Spain	e-lactancia http://www.e-lactancia.org/	Knowledgebank	Y	1	1	2	2
Germany	Paulus WE, Lauritzen C. Medikamente und Schadstoffe in Schwangerschaft und Stillzeit	Literature review style summaries of peer-reviewed published studies	N	6	1		1
Italy	AIFA Italian medicines agency http://www.farmaciegravidanza.it/	HA	Y	1	3	1	2
Italy	Telefono rosso http://www.policlinicogemelli.it/telefono-rosso/	TIS	Y	1, 5	3	1	1
Italy	Istituto mario negri/Ospedale Papa Giovanni XXIII 800 883 300	Phone contact istituto mario negri/Ospedale Papa Giovanni XXIII 800 883 300	N	5	3		1
Italy	Associazione Italiana Studio Maformazioni Onlus (ASM) Filo Rosso www.asmonlus.it	Knowledge bank	Y	1	3	1	1
Denmark	www.promedicin.dk	Knowledge bank	Y	1	3	4	1
Denmark	http://www.bispebjerghospital.dk/afdelinger-og-klinikker/klinisk-farmakologisk-afdeling/om-afdelingen/trvg_mor/Sider/default.aspx	Hospital	N	1??	3	4	1
Netherlands	www.apotheek.nl	Pharmacist information bank	N	1, 8	3	4	2
Netherlands	www.voedingscentrum.nl	Nutrition center	Y	1	2	4	2
Netherlands	www.borstvoeding.com	Breastfeeding knowledge center	Y	1, 5	2	2	2
Netherlands	www.nci.nl	Center		3	2		1
Netherlands	Netherlands Huisartsen Genootschap www.nhg.org	Association	N	1,3	1	4	2
Netherlands	V&VN http://www.venvn.nl/	Professional Association	Y	2	1	4	2
Netherlands	Royal Dutch Medical Association http://www.knmg.nl/	HA	n	2	1	4	2
Netherlands	NVL http://www.nvlborstvoeding.nl/	Association	Y	3	3	2	2
Netherlands	Federatie Medisch Specialisten www.richtlijnendatabase.nl	Knowledgebank	Y	1	1	4	2
Netherlands	College of Perinatal Care (Erfocentrum) http://www.strakswangerworden.nl	Website developed on behalf of Ministry of Health, Welfare and Sport.	N	1	2	1	3
France	Vidal Eureka sante www.vidal.fr	Scientific information	N	1	3	4	1

France	Agence nationale de securite du medicament et des produits de sante (ANSM) www.ansm.sante.fr	HA	Y	1	3	4	2
France	Doctissimo www.doctissimo.fr	Scientific Information	Y	1	2	3	1
Germany	www.rote-liste.de	Pharmaceutical drugs register	N	1	3	4	1
North America	Pregistry www.pregistry.com	Knowledgebank	Y	1,4,5,8,9,13	2	1	2

* Where local language is english, this was coded as 2. HA= Health authority, TIS= Teratology information service

Appendix 4 – Description of stakeholders

Stakeholder	Country	Description
Farmacotherapeutisch Koms (FK)	NL	<p>The FK lists all medicines available in the Netherlands that are registered as 'medicines for humans' at the Medicines Evaluation Board (CBG) or the European Medicines Agency (EMA) and are listed in the tax file of Z-Index, which is updated every month. The most important source for the pharmaceutical texts in the FK are the SPC texts of the MEB and EMA. In addition, sources are consulted as official guidelines (NHG, Federation of Medical Specialists). Other sources include the Dutch TIS and widely recognized textbooks and medical literature. It provides among other things information about pregnancy and breastfeeding.</p> <p>The goal of the FK is to promote the appropriate use of medicines. To this end, it provides (aspiring) doctors with practice-oriented and decision-supporting information about medicines and their applications.</p> <p>It is financed by the Zorginstituut Nederland. Zorginstituut Nederland is an advisory and executive organization in the field of healthcare. The Zorginstituut is governed and financed by the Ministry of Health, Welfare and Sport (VWS).</p>
TIS	NL	<p>The TIS website is part of the LAREB website. The website is for the public and for HCP's. TIS is financed by the Ministry of Health, Welfare and Sport.</p>
Richtlijnen NVOG	NL	<p>The NVOG is the Dutch scientific association for Obstetrics and Gynaecology.</p> <p>The NVOG's mission is to provide the best quality of care for women at all stages of life. In this capacity she wants to monitor the quality of women's health care in general and the gynecological, obstetric, oncological and reproductive medicine (sub) specialties in particular. As part of their work they developed guidelines (richtlijn) to support healthcare professionals and healthcare users. These guidelines can be found on the website. Part of the guidelines is information about treatment options.</p> <p>Finances: A fixed amount per hour worked has been reserved in the medical specialist hourly rate to manage the structural financing of the quality policy among which the guidelines.</p>
Stichting ZEHG	NL	<p>The ZEHG Foundation (Pregnancy Sickness and Hyperemesis Gravidarum) ensures that more information is available about this disease and supports women who suffer or have suffered from (severe) morning sickness and HG. On the website they provide information about the treatment of HG and morning sickness.</p> <p>Finances: It is a non-profit organisation. The ZEHG Foundation is completely dependent on donations and sponsorship</p>
borstvoeding.com	NL	<p>It calls itself the knowledge center about breastfeeding. Its goal is to support and advise breastfeeding mothers. It is founded and lead by lactation consultants. It has several articles about drug use during breastfeeding. Finances: Borstvoeding.com is a non-profitorganisation.It gets finances through advertisements and donations. Breastfeeding.com is sponsored by the milkflask manufacturer Medela.</p>

Fass	SW	Fass has for more than 50 years been a trusted source of information on medicinal products in Sweden. The Fass services are widely used by healthcare professionals and the general public with approximately 4,2 million visits/month. In 2001 the Fass webpage, Fass.se, was launched. Today Fass is a digital platform with web pages, apps and web integrations designed to provide information on medicinal products directly to healthcare professionals, the general public as well as to healthcare information systems and pharmacy systems. Fass is provided by Läkemedelsindustriföreningen who is the trade association for the research-based pharmaceutical industry in Sweden. The answers in this form regards only the parts of Fass that provides information on medicines in connection with pregnancy and breastfeeding.
Janusmed	SW	A website providing information on different aspects of drug treatment, e.g. interactions, impaired renal function, pregnancy and breastfeeding. It is hosted by Region Stockholm but financed by all health regions in Sweden. The pregnancy and breastfeeding part are mainly directed for HCPs but also for pregnant and breastfeeding women. The answers in the form regard only the two subsections-of the homepage that covers medications during pregnancy and breastfeeding.
Svensk reumatologisk förening	SW	The Swedish Society of Rheumatology is a specialist organization that organizes congresses, have an information bulletin, scholarships and that also produce guidelines. They have a special guideline regarding pregnancy and breastfeeding in women with rheumatic disorders. The answers in this form regards only this clinical guideline.
Svensk gastroenterologisk förening	SW	The Swedish Society of Gastroenterology (SGF) is a specialist organization dealing with gastrointestinal diseases. They organize congresses, have a newsletter and publish guidelines. One guideline regards pregnancy and breastfeeding in women with inflammatory bowel disease. The answers in this form regards only this clinical guideline.
1177.se: Subsection: Graviditet och läkemedel	SW	This is a very broad webportal for all health regions in Sweden directed to the public. It covers many diseases with advice on selfcare and contact information to different health care facilities. They also have one subsection regarding drug treatment during pregnancy and lactation. The answers in the form regard only this subsection of the homepage.
Läkemedelsupplysningen	SW	<u>Läkemedelsupplysningen</u> (Drug information services) hosted by the Swedish Medical Products Agency (MPA) mainly provide advice regarding drug treatment to the public via telephone, but they also have some information published on their homepage. They receive quite a lot of questions regarding pregnancy and lactation, and they also publish some common pregnancy and lactation questions on their homepage. The answers in this form regards all their services concerning medicines in connection with pregnancy and breastfeeding.
Le Crat	FR	“Centre de Référence sur les Agents Tératogènes” is a public structured part of the Public Hospital Armand-Trousseau in Paris, and is one of the French TIS centers. Its main mission is to inform HCPs and patients about teratogen effects of medicines.
CNGOF	FR	(Collège National des obstétriciens et gynécologues français) French association, its main objective is the development and progress in all their forms of gynecology and obstetrics, with the

		essential principle of the unity of the discipline of gynecology and obstetrics. To accomplish its mission, the CNGOF relies on a scientific committee and a board of directors representative of the discipline. He regularly writes practice guidelines .
La Leche League	FR	Of note, articles on specific drugs use during breastfeeding have restricted access, but some general articles related to drug intake and breastfeeding are available on the French website la LLL.
Doctissimo	FR	
BNF	UK	The BNF is a joint publication of the British Medical Association and the Royal Pharmaceutical Society. It is published under the authority of a Joint Formulary Committee. It provides key information on the selection, prescribing, dispensing and administration of medicines. Little or no information is given on medicines which can be purchased by the public. The BNF uses around 60 expert clinical advisers to help with clinical content. The editorial team have all worked as pharmacists or possess a pharmacy degree and a further relevant post graduate qualification. The BNF is entirely funded from sales made by the joint publishers, the BMJ Group and Pharmaceutical Press.
UKTIS	UK	The UK Teratology information service is commissioned by Public Health England and hosted within the NHS. UKTIS aims to support the appropriate use of medicines in pregnancy. UKTIS provides telephone advice to HCPs considering treatment options for their patients or require advice on management of a pregnancy after exposures to medicinal products. UKTIS produces detailed systematic reviews of the available evidence (available to HCPs as monographs as part of a subscription) and also patient-focused information sheets which complement the full reviews. These shorter summaries are available on a public facing website 'BUMPS- Best use of medicines in pregnancy'. UKTIS is funded by PHE.
UKDILAS	UK	The UK drugs in lactation advisory service is provided via the UK Medicines Information Network by the Trent and West Midlands Regional Medicines Information Centers. The service provides evidence-based information for every medicine in the UK and has risk assessed this in terms of safety during breastfeeding. This information is available on the SPS website and via an enquiry answering service for HCPs.
RCOG	UK	Guidelines committee works in parallel with the RCOG Women's network and relevant professional societies to identify a relevant guideline. The scope is approved by the RCOG guidelines committee. Information for the public is developed in parallel with professional guidelines.
Tommy's	UK	Tommy's is an organisation which supports research into causes of baby loss. Tommy's website has a PregnancyHub which provides expert-led pregnancy information. This hub receives around 2 million visits every month. Within that pregnancy hub there is information on medicines use in pregnancy. Tommy's has also produced a clinical guideline for delivering preconception advice for women with severe mental health conditions. They also have various resources for pregnant women – a blog, an app, newsletters etc.
NHS website	UK	The NHS website is the UK's biggest health website with more than 50 million visits every month. It is funded by the Department of Health and Social care. The Empower the Person Board defines and

		<p>manages the strategic direction and priorities of the NHS website. The clinical Information Advisory Group is responsible for setting editorial and data quality standards for the NHS website and for providing overall clinical governance for the service.</p>
The breastfeeding network	UK	<p>The BfN aims to be an independent source of support and information for breastfeeding women and others. They do not accept funding from sources which have a commercial interest in infant feeding. The BfN has a website which has drug factsheets, a shop with publications and training materials which can be bought, a blog, social media presence, e learning for GPs, training and peer support network. They also have a helpline and live chat function on the website. Drug factsheets are fully referenced.</p>

Appendix 5 - IMI ConcePTION Stakeholder communication survey

Different stakeholder groups undertake communications about the safety of medicines and drug use during pregnancy and breastfeeding.

This survey aims to identify the scope and purpose of the information provided by stakeholders, the methods of information dissemination and the processes involved in collating data from different sources.

Thank you for your participation!

*Mandatory



I am happy to answer this survey. I understand that my data will be used in the analysis conducted by Subtask 5.1.1 for IMI ConcePTION and for no other purpose. The results of this analysis may be published. *

- Yes
 No

Name of organisation/individual *

How is this information being collected? If you have been asked to complete this survey as an organisation please select 'the organisation has completed the form directly'. *

- the organisation has completed the form directly
 from the website of the organisation
 email interview
 phone interview
 Other: -----

Date of information collection *

dd/mm/yyyy: -----

What category does the organisation fit into? *

- National formulary
 Teratology information service
 Organisation that creates SmPC/PIL (e.g. the manufacturer)

- Organisation providing recommendations to healthcare professionals
- Organisations providing recommendations/advice to patients
- Other:-----

What country is the organisation based in? *

- Netherlands
- Sweden
- France
- United Kingdom
- Other:-----

Does the organisation have a website? If yes, please provide link to website.

Who is the target audience of the organisation's communications? Please give details if 'other'*

- Pregnant women
- Breastfeeding women
- Healthcare professionals
- Other:-----

If healthcare professionals are an audience, please specify which.

- Obstetricians
- General practitioners (GPs)
- Midwives
- Nurse practitioners
- Pharmacist (hospital, community or GP practise)
- Specialist doctors
- Other:-----

What is the scope of the communications? *

- Pregnancy
- Breastfeeding
- Other:-----

What does the organisation communicate about (in relation to the pregnancy and/or breastfeeding)? Please give details if 'other', *

- Medicines
- Vaccines
- Chemicals
- Cosmetics
- Radiopharmaceuticals
- Medical procedures (e.g. x-ray)
- Maternal medical conditions (chronic conditions that the mother has)
- Breastfeeding issues/medical problems (e.g. mastitis, tongue-tie)
- Gestational medical conditions (e.g. UTIs, gestational diabetes)
- Other:-----

Are your communications in the context of a specific disease/condition? *

- Yes
- No

Sometimes

If yes, which disease/condition?-----

What routes of communication does the organisation use? *

- Open access website
 Free subscription access website
 Paid for website
 Combination of open access and subscription access website
 TV or Radio
 Informal communication via phone or email
 Formal documented communication via phone or email
 Conference
 Education training and exam programme
 Social media
 Scientific journals
 Mailing list
 Public forum (where general public can discuss situation with others and potentially moderators)
 Print (i.e. Product label/package insert)
 Autre :

What modes of communication does the organisation use? Please indicate the audience for each mode of communication you use. Please also indicate which is your primary and second most important modes of communication.

	For HCPs	For breastfeeding women	For pregnant women	For 'other' audience	This is the primary mode of communication	This is the second most important mode of communication
Clinical guidelines	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Patient information sheets (PIL)/SPC	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Statements and reports (e.g. press releases)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Systematic reviews/short research summaries	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Verbal advice	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Written advice (e.g. email)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Newsletters	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Short social media messages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Conference poster/abstract/presentation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lectures/educational materials	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Scientific manuscripts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Please detail other modes of communication used and the audience they are aimed at.

Which data sources are used to synthesise the information for your primary communication mode? If 'other' please specify. *

Clinical trials

- Preclinical animal studies data
- Preclinical cell studies data
- Specialist website (e.g. REPROTOX, lactmed, Janusmed)
- Personal communications (e.g. with doctor, pharmacists and experts in the field)
- Teratology information services
- Text book
- Forum
- Published Observational studies
- Unpublished observational studies (including own studies and registries)
- Exposure databases
- Regulatory guidance
- Summary of product characteristics (SPC)
- Pharmacovigilance (PV) system (e.g. PBRER, PV database, etc).
- Other:-----

Is there one information resource which is used by the organisation most of the time? If so, please give its name here.

Which processes does the organisation use to collate information for the primary mode of communication? *

	Always/mandatory	Most of the time	Sometimes/adhoc	Never	N/A	Unknown
There is Public/target audience consultation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
An oversight/steering committee is in place	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Experts are consulted on content	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There is Internal peer review	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There is systemic review of evidence	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There is grading of the quality of the evidence using a scale	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
There is	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

publication of methods and transparency of process (e.g. standard operating procedure on a website)						
There is transparency on data sources used (e.g. are communications fully referenced)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
A standard operating procedure is followed in the collation of information and production of materials	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Communications have formal accreditation (by an organisation, for example (e.g. NICE, in the UK))	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Communication materials are produced in partnership with another organisation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Health Authorities review and approval	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
None of the above, no collation of information is made- we only disseminate information from other sources (via links on websites and social media, for example)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Is the primary communication method reviewed and updated? If yes, how often and in what context (e.g. when new evidence arises that changes the message of the communication)? *

No

- Yes, more frequently than annually
- Yes, annually
- Yes, every two years
- Yes, every 5 years
- Yes, less frequently than every 5 years
- Yes, when new evidence could change the message of the communications or change in the B/R assessment
- Other:-----

What is the language level of your primary communications? *

- Plain Language
- Specialist language
- Other:-----

What language are your communications available in? *

- English
- Swedish
- Dutch
- French
- Other:-----

If there is anything more you would like to tell us regarding communication routes, modes and processes used by the organisation? Please tell us here. State N/A if not applicable. *

Additional comments

Appendix sub-task 5.1.2: Information discrepancies

Methods

Table 1. Information sources analyzed – patients

Regulatory sources	<ul style="list-style-type: none"> • Package Information Leaflet (PIL) for NL, SW, FR and UK
Scientific sources	<ul style="list-style-type: none"> • Teratology Information Services (TIS) or national knowledge bases <ul style="list-style-type: none"> ○ Lareb.nl (NL) ○ Janusmed.sll.se (SE) ○ Lecrat.fr (FR) ○ BUMPS, medicinesinpregnancy.org, (UK) ○ Mother to Baby, mothertobaby.org (US) • National drug formularies <ul style="list-style-type: none"> ○ Farmacotherapeutischkompas.nl (NL) • Non-commercial official web sites understandable for patients, e.g. <ul style="list-style-type: none"> ○ 1177.se (SW)
Blogs/forums/social media	<ul style="list-style-type: none"> • Different sites depending on the drug and discussion
News articles	<ul style="list-style-type: none"> • Various articles in e.g. tabloids, public service media and easily understandable scientific journals
Commercial web sites	<ul style="list-style-type: none"> • Most commonly used <ul style="list-style-type: none"> ○ Doctissimo.fr (FR) ○ Drugs.com (EN) ○ WebMD.com (EN)

Table 2. Information sources analyzed – HCPs

Regulatory sources	<ul style="list-style-type: none"> • Summary of Products Characteristics (SmPC) for NL, SW, FR and UK
Drug formularies	<ul style="list-style-type: none"> • Available for NL and UK <ul style="list-style-type: none"> ○ Farmacotherapeutisch Kompas: for physicians (NL) ○ KNMP Informatorium: for pharmacists (NL) ○ BNF, British National Formulary (UK)
Scientific sources	<ul style="list-style-type: none"> • Teratology Information Services (TIS) or national knowledge bases <ul style="list-style-type: none"> ○ Lareb.nl (NL) ○ Janusmed.sll.se (SE) ○ Lecrat.fr (FR) ○ UK Teratology Information Services via Toxbase (UK) for pregnancy ○ Specialist Pharmacy Services, SPS, for lactation (UK)
Treatment guidelines	<ul style="list-style-type: none"> • National or regional guidelines from medical associations, health care providers or authorities, e.g. <ul style="list-style-type: none"> ○ NICE or Royal College of Obstetricians and Gynecologists, RCOG, (UK) ○ Haute Autorité de Santé, HAS, (FR)
Main medical journal	<ul style="list-style-type: none"> • Following journals in each language <ul style="list-style-type: none"> ○ Nederlands Tijdschrift voor Geneeskunde, NTvG, (NL) ○ Läkartidningen (SE) ○ Prescrire (FR) ○ BMJ with associated journals (EN)

Results – distribution of pregnancy and lactation recommendations

Patient information resources

Table 3. Pregnancy and lactation recommendation categories by type of recommendation and by medicine. Patient data resources

Type of recommendation	Adalimumab		Fingolimod		Ibuprofen		Methylphenidate		Olanzapine		Ondansetron		TOTAL BY TYPE OF STATEMENT	
	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)
Can be used	1 (4)	12 (60)	0	0	0	13 (62)	0	4 (18)	1 (6)	5 (33)	3 (12)	1 (6)	5 (4)	35 (31)
Individual benefit-risk assessment	18 (78)	6 (30)	2 (9)	3 (17)	4 (17)	5 (24)	13 (54)	7 (32)	13 (72)	4 (27)	15 (60)	7 (44)	65 (47)	32 (29)
Should not be used	1 (4)	2 (10)	20 (87)	15 (83)	4 (17)	3 (14)	5 (21)	7 (32)	1 (6)	6 (40)	3 (12)	8 (50)	34 (25)	41 (37)
Not classifiable	2 (9)	0	1 (4)	0	2 (8)	0	6 (25)	4 (18)	3 (17)	0	1 (4)	0	15 (11)	4 (3)
Trimester specific	1 (4)	0	0	0	14 (58)	0	0	0	0	0	3 (12)	0	18(13)	0
TOTAL	23	20	23	18	24	21	24	22	18	15	25	16	137	112
No available information	3	5	4	7	2	3	4	4	6	10	4	9	23	38

Table 4. Analysis of pregnancy recommendations per data source for medicines with no predominant recommendation (all languages). Patient data sources

	Methylphenidate	Ibuprofen
Regulatory data sources	100% BRA (n=5)	100% Different recommendations by trimester (n=4)
Scientific data sources	56% BRA (n=5) 33% SNBU (n=3) 11% Not classifiable (n=1)	78% Different recommendations by trimester: (n=7) 22% BRA (n=2)
Social media	40% BRA (n=2) 60% Not classifiable (n=3)	33% Different recommendations by trimester: (n=1) 67% Not classifiable (n=2)
News article	100% Not classifiable (n=1)	25% BRA (n=1) 75% SNBU (n=3)
Website for patients	25% BRA (n=1) 50% SNBU (n=2) 25% Not classifiable (n=2)	50% Different recommendations by trimester: (n=2) 25% BRA (n=1) 25% SNBU (n=1)

Abbreviations: BRA = Benefit Risk Assessment; SNBU = Should Not Be Used

Table 5. Analysis of lactation recommendations per data source for medicines with no predominant recommendation (all languages). Patient data sources

	Methylphenidate	Olanzapine	Ondansetron
Regulatory data sources	20% Can be used (n=1) 60% BRA 60% (n=3) 20% SNBU (n=1)	100% SNBU (n=4)	25% BRA (n=1) 75% SNBU (n=3)
Scientific data sources	13% Can be used (n=1) 38% BRA (n=3) 38% SNBU (n=3) 13% Not classifiable	50% Can be used (n=4) 38% BRA (n=3) 13% SNBU (n=1)	14% Can be used (n=1) 43% BRA (n=3) 43% SNBU (n=3)
Social media	25% Can be used (n=1) 75% Not classifiable (n=3)	Not available	Not available
News article	100% SNBU (n=1)	Not available	Not available
Website for patients	25% Can be used (n=1) 25% BRA (n=3) 50% SNBU (n=2)	33% Can be used (n=1) 33% BRA (n=1) 33% SNBU (n=1)	60% BRA (n=3) 40% SNBU (n=2)

Abbreviations: BRA = Benefit Risk Assessment; SNBU = Should Not Be Use

Table 6. Pregnancy and lactation recommendation categories by type of recommendation and by data source. Patient data sources

Type of recommendation	Regulatory data sources		Scientific data sources		Social media		News article		Website for patients		TOTAL BY TYPE OF STATEMENT	
	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)
Can be used	0	5 (20)	1 (2)	16 (39)	3 (18)	4 (40)	1 (6)	4 (57)	0	6 (21)	5 (4)	35 (31)
Individual benefit-risk assessment	14 (52)	7 (28)	28 (58)	14 (34)	3 (18)	1 (1)	7 (41)	0	13 (46)	10 (34)	65 (47)	32 (29)
Should not be used	8 (30)	13 (52)	8 (17)	10 (24)	0	2 (20)	6 (35)	3 (43)	12 (43)	13 (45)	34 (25)	41 (37)
Not classifiable	0	0	1 (2)	1 (2)	10 (59)	3 (30)	3 (18)	0	1 (4)	0	15 (11)	4 (3)
Trimester specific	5 (18)	0	10 (21)	0	1 (6)	0	0	0	2 (7)	0	18 (13)	0
Total	27	25	48	41	17	10	17	7	28	29	137	112
No available information	0	0	1	2	8	15	8	17	6	4	23	38

HCP information resources

Table 7. Pregnancy and lactation recommendation categories by type of recommendation and medicine. HCP resources

Type of recommendation	Adalimumab		Fingolimod		Ibuprofen		Methylphenidate		Olanzapine		Ondansetron		TOTAL BY TYPE OF RECOMMENDATION	
	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)
Can be used	1 (6)	9 (64)	0	0	0	10 (66)	0	1 (8)	1 (5)	4 (29)	0	0	2 (2)	25 (31)
Individual benefit-risk assessment	15 (88)	4 (29)	0	1 (8)	1 (6)	3 (20)	13 (72)	4 (31)	18 (95)	4 (29)	9 (47)	4 (33)	57 (54)	19 (24)
Should not be used	0	1 (7)	15 (100)	10 (84)	2 (12)	1 (7)	3 (17)	8 (612)	0	6 (42)	2 (11)	8 (67)	21 (20)	34 (43)
Not classifiable	1 (6)	0	0	1 (8)	0	1 (7)	2 (11)	0	0	0	1 (5)	0	4 (4)	2 (2)
Trimester specific	0	0	0	0	14 (82)	0	0	0	0	0	7 (37)	0	21 (20)	0
TOTAL	17	14	15	12	17	15	18	13	19	14	19	12	105	80
No available information	5	8	7	10	3	5	3	8	2	7	1	8	21	46

Table 8. Analysis of recommendations per data source for medicines with no predominant recommendation (all languages). HCP data sources

	Ondansetron (pregnancy)	Olanzapine (lactation)
Regulatory data sources (SmPC)	75% Different recommendations by trimester (n=3) 25% SNBU (n=1)	100% SNBU (n=4)
Drug formulary	33% Different recommendations by trimester (n=1) 67% BRA (n=2)	33% Can be used (n=1) 67% SNBU (n=3)
Scientific sources (TIS)	25% (n=1) Different recommendations by trimester 75% BRA (n=3)	75% Can be used (n=3) 25% BRA (n=1)
Treatment guidelines	25% (n=1) Different recommendations by trimester 25% BRA (n=1) 25% SNBU (n=1) 25% Not classifiable (n=1)	50% Can be used (n=1) 50% BRA (n=1)
Medical journal	25% (n=1) Different recommendations by trimester 75% BRA (n=3)	100% BRA (n=1)

Abbreviations: BRA = Individual Benefit Risk Assessment; SNBU = Should Not Be Used

Table 9. Pregnancy and lactation recommendation categories by type of recommendation and by data source (all languages and medicines). HCP data sources

Type of recommendation	SmPC		Drug formularies		Scientific data sources		Treatment guidelines		Main national medical journal		TOTAL BY TYPE OF RECOMMENDATION	
	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)	Pregnancy n (%)	Lactation n (%)
Can be used	0	5 (21)	0	6 (33)	0	9 (39)	2 (8)	4 (33)	0	1 (33)	2 (2)	25 (31)
Individual benefit-risk assessment	12 (50)	2 (8)	1 (56)	4 (22)	17 (77)	9 (39)	9 (38)	3 (25)	9 (53)	1 (33)	57 (54)	19 (24)
Should not be used	5 (21)	17 (71)	4 (22)	8 (45)	2 (9)	4 (17)	6 (25)	4 (33)	4 (23)	1 (33)	21 (20)	34 (43)
Not classifiable	0	0	0	0	0	1 (5)	2 (8)	1 (9)	2 (12)	0	4 (4)	2 (2)
Trimester specific	7 (29)		4 (22)	0	3 (14)	0	5 (21)	0	2 (12)	0	21 (20)	0
TOTAL	24	24	18	18	22	23	24	12	17	3	105	80
No available information	0	0	6	6	2	1	3	15	10	24	21	46

Results– detailed discrepancies analysis

Table 10. Medicines with totally divergent pregnancy or lactation recommendations between patient’s data sources

	Should not be used	Can be used
Pregnancy recommendations		
Adalimumab	1 website for patients (FR)	1 social media (FR)
Ondansetron	PIL (NL)	Social media (NL)
	PIL (FR)	Social media and news article (FR)
Lactation recommendations		
Olanzapine	PIL (NL)	1 scientific source and 1 social media (NL)
	PIL and 1 website for patients (FR)	All other sources (FR)
	PIL (EN)	1 scientific source (EN)
Ibuprofen	PIL, 1 social media and 1 website for patients (EN)	1 scientific source and 1 news article (EN)
Methylphenidate	1 scientific source and 1 website for patients (NL)	1 website for patients (NL)
Adalimumab	1 website for patients (NL)	PIL and 2 scientific sources (NL)
	1 website for patients (FR)	PIL, 1 scientific source and 1 news article (FR)
Ondansetron	PIL, 1 scientific and 1 website for patients (EN)	1 scientific source (EN)

EN=English, FR=French, NL=Dutch, SW=Swedish

Table 11. Medicines with totally divergent lactation recommendations between HCP's data sources

	Should not be used	Can be used
Olanzapine	SmPC and Drug formulary for physicians (NL)	TIS and Drug formulary for pharmacists (NL)
	SmPC (FR)	TIS (FR)
	SmPC and Drug formulary (EN)	Treatment guidelines (EN)
Ibuprofen	SmPC (FR)	TIS and Medical journal (FR)
Methylphenidate	SmPC (SW)	TIS (Janusmed) (SW)
Adalimumab	Treatment guidelines (FR)	SmPC and TIS (FR)

Table 12. Pregnancy and lactation recommendations per medicine from the TIS centers (information for health care professionals and patients combined)

		NL: Lareb	SW: Janused	FR: Le Crat	EN (UK): UKTIS/BUMPS for pregnancy and SPS for lactation	EN (US): Mother to baby
Fingolimod	Pregnancy	SNBU	SNBU	NA	NA	NA
	Lactation	SNBU	BRA	NA	SNBU	NA
Olanzapine	Pregnancy	BRA	BRA	BRA	BRA	Can be used
	Lactation	Can be used	BRA	Can be used	BRA	Can be used
Ondansetron	Pregnancy	First trimester: BRA, second and third trimester: Can be used	BRA (whole pregnancy)	BRA (whole pregnancy but especially before 10 weeks)	BRA	BRA (whole pregnancy)
	Lactation	BRA	BRA	SNBU	BRA	BRA
Ibuprofen	Pregnancy	First and second trimester: BRA Third trimester: should not be used"	BRA (during the whole pregnancy but more strictly during the last trimester)	First and second trimester: BRA Third trimester: Should not be used.	<i>Information for HCPs:</i> BRA (whole pregnancy, but very strict in third trimester) <i>Information for patients (BUMPS):</i> First and second trimester: BRA Third trimester: SNBU	First and second trimester: BRA Third trimester: SNBU
	Lactation	Can be used	Can be used	Can be used	Can be used	BRA
Methylphenidate	Pregnancy	BRA	BRA	BRA	BRA	BRA
	Lactation	BRA	Can be used	SNBU	BRA	Can be used
Adalimumab	Pregnancy	BRA	BRA	BRA	BRA	BRA
	Lactation	Can be used	BRA	Can be used	BRA	Can be used

Abbreviations: UKTIS=United Kingdom Teratology Information Services, BUMPS=Best Use of Medicine in Pregnancy, SPS=Specialist Pharmacy Services; BRA = Individual benefit Risk Assessment, SNBU = Should Not Be Used

Comparing PIL with TIS recommendations

Table 13. Pregnancy recommendations per medicine – PIL vs TIS centers/national knowledge bases

PIL consistent with TIS	Fingolimod ^a , olanzapine, methylphenidate, adalimumab (all languages), ibuprofen (NL, FR, UK), ondansetron (UK)
PIL more conservative than TIS	Ondansetron (NL, SW, FR), ibuprofen (SW)
PIL less conservative than TIS	No cases

^a No information was available for fingolimod from TIS in French and English (UK)

Table 14. Lactation recommendations per drug – PIL vs TIS centers/national knowledge bases^a

PIL consistent with TIS	Fingolimod ^b (NL), ondansetron (SW, FR), methylphenidate (NL, FR)
PIL more conservative than TIS	Ibuprofen (all languages), olanzapine (all languages), fingolimod ^b (SW), ondansetron (NL), methylphenidate (SW)
PIL less conservative than TIS	Adalimumab (SW)

^a Data in 3 languages were analyzed for lactation: NL, SW and FR

^b No information was available for fingolimod from TIS in French

Appendix sub-task 5.1.3: End-Users' experiences

Appendix 1 - Literature review results

Authors:

Rebecca Moore (EIWH)

Vanessa Moore (Eurohealth)

Bonaventure Ikediashi (26, The Synergist),

Ludivine Douarin (39-Sanofi)

Stéphanie Tcherny-Lessenot (39-Sanofi)

Sashka Hristoskova (38 – Novartis),

Review Protocol

For the ConcePTION WP5 subtask 5.1.3, the objective is to collect information on end users experience with the current information about the safety of drugs during pregnancy and breastfeeding, and to assess what their preferences would be in receiving such information in the future, both regarding content of the information and how it is delivered/made accessible to them.

The literature review was done to assess the available data from previous studies. We wanted to collect available high-quality studies where the end-user's experience with information about the safety in medicines had been assessed. We defined end-users as pregnant or breastfeeding women and/or healthcare professionals (HCPs).

In order to conduct the most comprehensive search to detect relevant existing studies we undertook a broad multi-method research protocol including literature searches of relevant databases, grey-literature searches, scanning conference publications and hand scanning key journals.

Database Review

The relevant databases that were searched were MEDLINE, Embase, CINAHL, PsychINFO, PubMed and DARE.

Search terms

The following search terms were used: 'teratology' + 'teratogenicity' + 'teratogenesis' + 'pregnancy' + 'information' + 'risk' + 'safety' + 'experience' + 'medicine' + 'prescription' + 'end-user' + 'leaflet' in different combinations. Our mixture of searches detected wide varying numbers of publications. The search term 'leaflet' and 'end-user' had to be removed as they made the search too narrow.

To identify articles only concerned with breastfeeding, we used the search terms: lacta* +breastfe* + 'information' + 'risk' + 'safety' + 'experience' + 'medicine' + 'prescription' in different combinations.

Inclusion criteria

The criteria used for inclusion were: Publications between 01 Jan 2000 and 10 Aug 2019; English Language; no geographical limit; address our specific question (must address the end-users experience regarding information of safety of medicines during pregnancy or breastfeeding); be a published peer-reviewed article. To broaden our search as much as possible we decided to include empirical works, theoretical works and conceptual frameworks and models.

Exclusion Criteria

We excluded publications that were not looking specifically at end-user experience; however, no measurement type was excluded. This part of the search also excluded organizational projects and conference

papers.

Findings

Within the different search combinations and evaluating the results, we were able to identify 16 articles that matched the inclusion criteria. To broaden the result, multiple searches were conducted and hundreds of articles were sifted through by hand. Articles where the abstract suggested that there could be important information within the article were also extracted and grouped in two broad categories: health literacy and pregnancy (n.5) and risk perception and pregnancy (n.11) This was done to ensure that some important articles that could be helpful to build a picture of what information is important to end users were not omitted.

In a second step, these articles were further scrutinized. In the process, 5 additional articles were identified from the reference lists of the articles: (n.3) related to users' information needs and preferences, and (n.2) under the risk perception category, while 3 articles were eliminated because it was discovered they did not match the inclusion criteria or contain any information relevant to user's information needs.

Finally, the articles were regrouped into three categories: Users' information Needs, Users' Preferences and Risk Perception. The summaries are presented below.

Terminology and definitions (for example for risk perception) as in the original articles were used when developing this literature summary. Each article was reviewed by 2 independent reviewers.

User Preferences

Healthcare professionals' preferences

Literature on healthcare providers' use of information sources in the context of pregnant women advice is very scarce and quite old and show that HCPs were using different sources of information that they considered reliable enough. One study on Dutch GPs and pharmacists displayed the different sources of information used and the differences between these two types of HCPs. Information sources most frequently used by GPs are the National Health Insurance System Formulary, consultation of pharmacists, and at a lesser extent the Briggs textbook on drugs in pregnancy and breastfeeding, national guidelines and consultation of the manufacturer. For pharmacists, the most frequently used sources are the National Health Insurance System Formulary and consultation of the manufacturer and to a lesser extent the Briggs textbook and national guidelines. Internet was used quite frequently by both groups to look for scientific evidence and reports for consensus groups (20).

Another study on physicians who used a teratology information service in Canada showed that the top four sources of information were the Compendium of Pharmaceuticals and Specialties, textbooks, journals, and colleagues (21). In these years, the use of the internet to search for scientific information was limited and may not reflect current practices. A study in the US of primary care physicians confirmed the perception of the reliability of the Briggs textbook and a growing use of internet as the preferred source of information to get access to up to date information including ongoing studies (14).

Pregnant women's preferences

Sources of information

Studies in pregnant women listed healthcare providers - including midwives, obstetricians, general practitioners, pharmacists and specialists for women with chronic disease - as the primary source for information, followed by the internet (6, 11- 13, 22).

Other sources of information indicated by pregnant women are hospital websites, internet, booklets and at less extent scientific sources, pregnancy forums, family, friends and leaflet or information printed on the

packaging (6, 12, 22). Pregnant women expressed interest in resources that facilitated connections to other women and their experiences (13).

Use of internet

A literature review conducted on internet use by pregnant women looking for pregnancy information and found that the internet has become one of the most frequently used sources of information by pregnant women in recent years (23). Women with high education levels, who are nulliparous and employed are more likely to search for information on the internet. English speaking women are also more likely to use the internet (22). Questions about the safety of medicines during pregnancy are common among pregnant internet users. They considered the information as reliable and useful especially when the retrieved information was consistent across sources including information brought by midwives.

Perception and value of scientific sources

A study evaluated how pregnant women perceived and valued the scientific resource Drugs and Birth Defects in Sweden (24). Pregnant women considered the information as easy to understand and valuable in complementing information shared by the health care staff and to make decisions. Reading this information led to a decrease in anxiety for almost half of pregnant women, but it led to an increase in anxiety for one quarter - lower education level being associated with increased anxiety. Midwives considered this information as valuable for pregnant women and used them for regular visits more often than among physicians.

Issue of conflicting information

In conducted surveys, from a quarter to over half of pregnant women reported encountering conflicting information, doing additional research for information in publicly available resources, or communicating online with others with similar experiences, or getting increased anxiety that may be associated to a decision not to use the medicines (6, 13).

Information needs

Health Care Professionals' information needs

Limited number of publications referred to how physicians obtain information about teratogenic risks or convey this information to their patients. One study evaluated rheumatologists' information needs on the treatment of rheumatoid arthritis (RA) in pregnant women, by means of a semi-structured interview. Dutch rheumatologists regard the available information as being sufficient to guide treatment of RA in women who are pregnant or wish to become pregnant, despite inadequate evidence on safe use of medicines during pregnancy. The conclusion was that there are several options to reduce this problem. First, pregnancy risk categorizations, such as the US FDA risk categorization, need to be regularly updated. Secondly, there is a need for a good monitoring system, to follow all young patients with rheumatic disease, to enable the collection of information on safe medicines use during pregnancy (25).

In an older article dating from 2002-2003, physician's information seeking behaviour was examined, in particular regarding teratogen information. Nearly half of the physicians researched their question prior to calling Motherisk, and 106 (91%) ie. not necessarily calling Motherisk for new information, but rather for reassurance, and passed on the information received to their patient verbatim. The top four resources for information were: 1) The CPS (PDR), 2) textbooks, 3) journals and 4) colleagues. Only 8% used the Medline for gathering information. Of note, considering that this study was conducted in 2002-2003, these resources consulted by physicians do not anymore reflect current practices (21).

One study gathered primary care clinicians (PCP)'s perspective on teratogenic counselling, and provided interesting information on how to support their efforts to provide information about teratogenic risks to their patients (14). Clinicians expressed concerns about the variable quality of information that they encountered online, challenges identifying resources that had the level of detail they felt was necessary for communicating

with their patients, and in particular desire for resources that would provide more specific numerical information that they could use when explaining a medicine risk of teratogenic side effects to a patient and challenges they faced in communicating risk of teratogenicity in a way that would be meaningful to their patients. Ideally, they would like references that provided information the same way they intended to convey that information to their patient.

Clinicians provided several suggestions for ways to facilitate counselling about medicines' teratogenic risks in their primary care settings. These included assistance in identifying medicines that pose teratogenic risks. Clinicians made frequent mention of the internet as a preferred source of information. A number of PCPs felt that decision support built into electronic medical records could be helpful if it was timed to coincide with computerized order entry of prescription medicines. Finally, PCPs expressed interest in access to patient education materials that would allow them to efficiently convey information about teratogenic risks to their patients (14).

For breastfeeding, a survey of Australian community pharmacists on their perspectives of medicine use and safety while breastfeeding, found that generally the issue was discussed, and the pharmacists had confidence in their ability to advise patients, however their knowledge was sometimes varying (26).

Similarly, a survey of Australian GPs to determine their knowledge, attitudes and practices on medicines and breastfeeding, found that in general, GPs felt it was a complex issue. There was certainty in prescribing for issues such as mastitis, however less straight-forward situations required a lot of inputs and consideration. The study found that without evidence-based information, GPs sometimes recommend cessation of breastfeeding unnecessarily, as they manage risk of prescribing by gathering information and assessing the possible effects on the breastfed infant – if the evidence is not there, they cannot make the decision (27).

One study analysed calls to Australian medicines call centres, and looked at the enquiries being made by consumers and by health care professionals. Most of the consumer calls concerned easily accessible or over-the-counter medicines, while the health care professionals (mostly GPs, followed by community pharmacists and nurses) generally enquired about prescription medicines such as antidepressants. The question themes were similar for both cohorts, mainly concerned with medicines safety, risk minimisations, and milk supply, but both point to the need to understand themes driving medicines help-seeking related to breastfeeding and to address the information gap (28).

Pregnant women's information needs

Information sources

Women expressed high information needs about medicines during pregnancy, and they rely on physicians (73%), pharmacy personnel (46%) and midwives or nurses (33%). The internet is also a widely used information source (60%) about medicines during pregnancy (24). In another study, the internet, books and clinic pamphlets/brochures were the most frequent self-identified sources of information (29). Pregnant women are frequently searching the internet for information concerning medicines (e.g. 74% of the women visiting a tertiary hospital in Belgium), most commonly via Google and other search engines, sometimes without discussing the results with an HCP (12). Official national preconception websites are often not known by the women (12).

In general, up to 95% of women are using the internet as a resource during pregnancy, and 60–75% of pregnant women reporting use of a pregnancy-related smartphone app. One study's participants expressed preferences for personal communications to meet such information needs, so developers should consider employing technologies that support rich interactions, such as video chat tools or social media groups (3).

Distinct features of women with chronic diseases

Women with chronic disease have some distinct features which could influence risk perception, and possibly also medicines information needs, compared to pregnant women in the general population. Different surveys

have evaluated information needs of women with chronic diseases such as epilepsy, or chronic autoimmune inflammatory conditions across the pregnancy continuum (11, 13) and multiple sclerosis (MS) patients' awareness of disease modifying therapies (DMT) teratogenic risks (4). Topics of interest encompassed topics related to pregnancy and their chronic conditions, ranging from their ability to become pregnant, how symptoms might change during pregnancy, how the disease and the use of drugs may affect their unborn children, and their ability to breastfeed and care for their baby. Many respondents reported difficulty finding the information they need. Epileptic women regarded the neurologist as their primary source of information regarding antiepileptic drugs (AEDs), while most women browsed the Internet for health and pregnancy related information in general. Conversely, for MS patients, HCPs (the neurologist and the MS nurse) represented the most frequently used and important sources of information about MS in general, but for the knowledge about information related to potential teratogenic effects of DMT, the respondents turned to the internet, social media, and other sources just as often as to their healthcare professionals. This is pointing to an unmet need for very specific information related to family planning. Also, there was a low awareness of teratogenic risk during DMTs it was pointed out, and no knowledge of potential exposure to healthy partners of male patients. There is a high need for increasing awareness among prescribers and patients on the risk of teratogenicity and the need for specific measures in monitoring to mitigate the risk (4). PILs were especially consulted by epileptic women at initiation of a medicine or experience of new symptoms suspected to be adverse effects. A challenge with PILs was that texts were perceived as difficult to interpret (11). Over half (56.9%) of women with chronic autoimmune inflammatory conditions reported receiving conflicting information from different doctors, and a majority of those respondents reported doing their own research. Respondents expressed the greatest interest in resources that facilitated connections to other women and their experiences (87.4%) (13).

Health literacy needs

The need for medicines information among pregnant women increases with the number of health problems and use of both prescription and OTC medicines as well as herbal preparations. Also, when complications arise, pregnant women and their caregivers may be faced with uncertain outcomes, difficult decisions, and evolving information needs (3). Women with higher education were 3.0 times (95% CI 1.2-7.5) more likely to seek advice than women with less than a high school education (28). Also, single (OR = 0.3; 95% CI 0.1-0.7) and multiparous (OR = 0.4; 95% CI 0.1-0.9) women were less likely to seek advice than married and nulliparous patients, respectively (29). Therefore, women with lower health literacy express a higher need for medicines information. Indeed, low health literacy in childbearing women affects the women's pregnancy knowledge and potentially the health of the baby. They are more likely to be non-adherent to pharmacotherapy than their high-level counterparts. Pregnant women with low health literacy were less likely to use the Internet as frequently as pregnant women with high health literacy. They had more personal barriers to information seeking such as not knowing how to take care of themselves during pregnancy and not knowing how to use the Internet (12).

Women with lower health literacy are primary targets for intensified counselling, and more broadly, non-highly educated women (12,30,31). Interventions to promote information-seeking skills and to improve access to information, particularly the Internet, may be helpful for pregnant women with low health literacy (32). Patient counselling should be initiated early in (or before) pregnancy (16). Clinicians and healthcare workers should be conscious of this in all of their consultations with pregnant women, and should guide them towards reliable websites, and discuss online-retrieved information during counselling. Provision of volumes of information alone does not satisfy issues of patient empowerment (33). Those who wish to improve the health of mother and baby should be cognizant of this statistic when designing and developing new solutions across technological, social, financial, policy and business domains (12,34).

Risk Perception

Health care professionals' risk perception

Three of the studies found that physicians had an inaccurate risk perception associated with drug use (21,35,36), thus informing their decision to prescribe lower doses of drugs (21). One study reported a high-

risk perception by physicians (35), which is influenced by information received from drug information centres, thus indicating the importance of drug information centres. This was contrary to another study which reported that most Physicians correctly estimate teratogenic risk for common medicines (37). In another study (38), healthcare professionals (physicians, nurses, pharmacists and hospital workers) had high teratogenic risk perception which varied with the kind of drugs and the source of information. One study found that incorrect information regarding medicines safety from social media could influence risk perception during pregnancy (39).

Pregnant women's risk perception

Six of the studies reviewed suggest an inaccurate perception of risk associated with drug use in pregnancy. One of the studies conducted among pregnant and recent mothers reported that most of them underestimated the risk associated with migraine medicines (5). In another study conducted by the Italian Teratology service, it was found that the perception of teratogenic risk was high among pregnant women (40). Similarly, one study conducted in Canada (41), found that pregnant women who had exposures to medicines had a higher risk perception compared to other women in the group who had no exposures. Also, a study conducted in Denmark reported a high risk perception of medicines use during pregnancy for fear of inflicting the child with a disease and malformations (42). A different study which evaluated risk perception with the use of penicillin showed a tendency to overestimate teratogenic risk (43). These findings are consistent with a literature review which found an overestimation of teratogenic risk of medicines by pregnant women (44). However, one large-scale multinational study which surveyed participants from 18 countries reported a low risk perception (45).

Several factors affect the perception of teratogenic risks. Age is one of them. In the Canadian study, older women reported a higher risk perception compared to younger women in the study. Similarly, lower risk perception scores were recorded by younger women in the multinational survey (45). Other factors which influence risk perception in pregnant women include; 1) limited health literacy, which has been reported to negatively affect the perception of medicines in pregnancy (34), and counselling provided by HCPs, which has been found to reduce risk perception of pregnant women (41).

Breastfeeding women's risk perception

A review of articles on breastfeeding women's risk perception was conducted, however there are not many studies on this issue in general. Limited information was found on breastfeeding and alternative medicines. One study in Western Australia found that the use of herbal medicines is common among breastfeeding women, but that there was a lack of information regarding their safety and efficacy. A majority of the women surveyed believed there was a lack of information, while 43% believed herbal medicines to be safer than conventional medicines. Only 29% told their doctor about their use of herbal medicines, and 72% had refused or avoided conventional medicines due to concerns about the safety of their infant (46).

Conclusion

Most of the studies reviewed show that most pregnant women rely on their health care practitioners (Doctors, Pharmacists and Midwives) for information about medicine use during pregnancy. Inaccurate risk perception by pregnant women and HCPs may be an indication of unmet information needs during pregnancy. It is thus important that these health care practitioners are equipped with the relevant information to enable them to provide accurate information and counselling to women about teratogenic effects of drugs, thus helping to create a more accurate perception of the risks during pregnancy. Teratology information centers can play an important role in ensuring HCPs have the required information by providing education materials that can be used by these HCPs. More information is needed to understand current information sources and needs of HCPs about the use of medicines during pregnancy.

The increase in internet use have been accelerated by the global expansion of smart phones and other devices in the last decades. Pregnant women often turn to the internet to seek information which contain often conflicting information. It is therefore important that good quality information is accessible through the

internet and should be easily visible and searchable for these users. More research is needed to understand internet use, such as the specific sites visited and also their perception of how reliable they find information from the internet.

Appendix 2 - Preparatory Survey Results

https://share.novartis.net/:b:r/sites/WP5/Task%2051/Subtask%205.1.3/Survey/WP5.1.3%20Survey%201%20Analysis%2003.02.2020_FINAL.pdf?csf=1&web=1&e=eljUeD

Appendix 3 - Survey Questionnaire HCP

Introduction

The safety of medicine use during pregnancy and breastfeeding - Healthcare professional's information needs and preferences

Women who are pregnant and breastfeeding, or who are planning a pregnancy, need information about the medicines they take, or intend to take. We want to know about healthcare professionals' needs and preferences for such information so that we can develop better information and tools for you in the future.

This survey is part of ConcePTION, an Innovative Medicines Initiative (IMI) funded project. One of the goals is to develop a European-wide "knowledge bank" or database containing information on medicine use during pregnancy and breastfeeding. The aim is to provide both healthcare professionals and the public with an open access information resource, compiled by experts in pregnancy and breastfeeding pharmacovigilance. The knowledge bank will provide reliable and accurate up-to-date and evidence-based safety information for women who use medicines during pregnancy or breastfeeding. To make the knowledge bank as useful as possible, we kindly ask you to answer the following questions.

This survey is led by The Synergist on behalf of the other IMI ConcePTION project's members (which act as joint data controllers and are listed here). By filling out this survey, you consent to the ConcePTION project using data generated from this survey in ConcePTION's publications on this topic. If you want to know more about how we process data, please have a look at our Data Protection Notice.

Your participation is important to help us develop better information and tools for women and healthcare professionals in the future. In order to continue our research, we ask for your email address to possibly invite you to further studies or surveys, however this is completely optional.

Questions marked with * require answers. Choose your language: IT - FR - NL - DE - ES - SWE - RO

About yourself

1. In which country do you practice?*

Drop down of all countries

2. My native language is*

3. What is your profession?*

- Obstetrician / Gynaecologist
- General Practitioner

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- Paediatrician
- Anaesthesiologist
- Other specialist physician
- Midwife
- Nurse
- Pharmacist
- Other (please specify)

4. How old are you?*

- <30
- 31-40
- 41-50
- 51-60
- >61

Information needs

5. How often do you get asked about medicine use during pregnancy or breastfeeding? *

- Daily
- Weekly
- Monthly
- Less than once a month
- Never

6. Where do you get information about medicine use during pregnancy and breastfeeding? (Please specify those that apply)*

- Medical specialists (e.g. obstetricians / gynaecologists)
- Teratology information services or registries
- National or local hospital guidance
- Online databases
- Medicine packaging (medicine label or patient information leaflet)
- Desk references or text books
- Websites
- Other sources

Please provide more details about the information source(s) you used

Text box

7. How easy is it for you to find the information you need?*

- Very easy
- Easy
- Neither easy nor difficult
- Difficult
- Very difficult
- Varies from case to case

8. When do your patients usually look for information about medicine use in pregnancy or breastfeeding?

Please select all that apply:*

- Before their pregnancy
- During their pregnancy
- After their pregnancy
- When breastfeeding
- Varies from case to case

9. What type of information about medicine use are you usually looking for? Please select all that apply:*

- Optimal dosage for treatment
- Foetal safety / potential effects on the child
- Dose excreted to breastmilk / safety during breastfeeding (including possible side effects)
- Information about the medical condition the medicine is used for
- Other (please specify)

10. If you use different sources to compare information, what do you compare?*

- Dosage or use of the medicine
- Safety for the child during pregnancy
- Dose excreted to breastmilk / safety during breastfeeding (including possible side effects)
- Side effects for the mother
- Information about the medical condition the medicine is used for
- Not applicable
- Other (please specify)

Please explain if yes

Textbox

11. Have you found contradictory information about medicine use during pregnancy and breastfeeding?*

- Yes, often
- Yes, sometimes
- No

12. How often do you have difficulty interpreting information about medicine use during pregnancy or breastfeeding?*

- Always
- Often
- Sometimes
- Occasionally
- Never

13. If you experienced difficulties, please explain why. (Select all that apply):*

- The information was too detailed
- The information was not precise enough
- The information did not fulfil my information needs
- The information was not sufficiently evidenced-based
- The information did not present the risks well
- I did not understand the way the information was presented
- Other (please specify)

14. Do you have a Teratology Information Service (TIS) centre (national centre that registers birth defects) or similar available in your country or region)?*

- Yes
- No
- Don't know

15. Is the information from the Teratology Information Service sufficient to meet your needs?*

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- Yes, always
- Yes, occasionally
- Often not
- Don't know

16. Please explain your answer above.

17. How often do you use an information service or database for questions about medicine use before or during pregnancy and breastfeeding?*

- Daily
- Weekly
- Monthly
- More seldom
- Never

Knowledge Bank

One of the goals is to develop a European-wide “knowledge bank” or database containing information on medicine use during pregnancy and breastfeeding. The information in the knowledge bank would be compiled by experts in the field of pregnancy/breastfeeding pharmacovigilance. It would also provide reliable, accurate and up-to-date evidence-based safety information for women who use medicines during pregnancy or breastfeeding.

18. How useful would an open access “knowledge bank” or database be to you? Please select a number from 1 to 10, 1 being “Not valuable” and 10 being “Most valuable”*

19. How often could you imagine using this * knowledge bank?

- Daily
- Weekly
- Monthly
- More seldom
- Never

20. Would using such a knowledge bank save you time?*

- Yes
- No
- Don't know

21. When could you imagine using the knowledge bank? Please select all that apply:*

- Before a consultation
- During a consultation
- After a consultation
- To learn more myself
- To support teaching
- Other (please specify)

22. In what kinds of situations could you imagine using the knowledge bank? Please select all that apply:*

- To counsel a woman who has used a medicine before realising that she was pregnant
- To inform the choice of treatment for a pregnant woman
- To inform the choice of treatment for a breastfeeding woman
- To plan future treatment for a woman before she becomes pregnant
- To plan future treatment for a woman before she begins breastfeeding

- To investigate potential reasons for birth defects and neonatal problems
- Other (please specify)
-

The following questions concern how you would like to access the knowledge bank

23. I would like to access the knowledge bank via a website*

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

24. I would like to access the knowledge bank via a mobile app*

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

25. Would you be able to use a knowledge bank if it is only available in English?*

- Yes, English is my native language
- Yes, English would be adequate
- No, I would prefer at least a short summary in my own language with more extensive information in English
- No, I would need all information in my own language to allow me to use it

26. Describe how you would like the knowledge bank to present risk information. For example, would you need short text summaries, risk classifications (such as by colour: red for known risk, yellow for potential risk, green for low or no risk) or background references?*

Textbox

27. The knowledge bank will be available to the public. Do you see any concerns in allowing the public to access it?*

- No
- Don't know
- Yes, please specify

28. The knowledge bank will be internet based. What percentage of your patients do you think would be likely to use it?*

- <1%
- 1-10%
- 11-20%
- 21-50%
- >50%
- Don't know

29. Your participation is critical in helping us solve the information gap in medicine use during pregnancy and breastfeeding. Would you be willing to take part in future studies on this topic as part of the ConcePTION project? If yes, please enter your email address:

Appendix 4 - Survey Questionnaire Women

Introduction

Women's needs and preferences for information about the safety of medicines during pregnancy and breastfeeding

Women who are pregnant and breastfeeding, or who are planning to get pregnant, need information about their medicines. To be able to develop better information and tools for women in the future, we ask for your input. The aim of this survey is to understand what kind of information women need, and how you and other women prefer to receive that information.

This survey is part of ConcePTION, a research project funded by the Innovative Medicines Initiative (IMI). This survey is led by The Synergist on behalf of the other IMI ConcePTION project's members (which act as joint data controllers and are listed here). We collect your personal data only if you explicitly consent to the ConcePTION project processing your data, and using data generated from this survey in ConcePTION's publications on this topic. If you want to know more about how we process data, please have a look at our Data Protection Notice.

Your participation is important to help us develop better information and tools for women like you in the future. In order to continue our research, we ask for your email address to possibly invite you to further studies or surveys, however this is completely optional.

Questions marked with * require answers. Choose your language: IT - FR - NL - DE - ES - SWE - CZ - RO

1. I explicitly agree to ConcePTION's members processing the health data I will provide for this project.*

- Yes
- No

Introductory questions

2. In which country do you live?*

Drop down of countries

3. My native language is*

4. Are you currently*

- Thinking about getting pregnant
- Trying to get pregnant
- Pregnant
- Breastfeeding
- Other (please specify)

5. How many times have you been pregnant? (including unsuccessful pregnancies) *

Text box

6. Was your last pregnancy more than 10 years ago? *

- Yes
- No

7. How old are you?*

Text box

8. What is your highest level of education?*

- Secondary School

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- High school degree or equivalent
- Professional degree
- Bachelor's degree
- Master's degree
- Doctorate
- Other (please specify)

9. Are you a healthcare professional (nurse, pharmacist, physician, midwife, other)?*

- Yes
- No

10. Select your healthcare profession in the drop-down list

- Obstetrician / Gynaecologist
- General Practitioner
- Paediatrician
- Anaesthesiologist
- Other specialist physician
- Midwife
- Nurse
- Pharmacist
- Other (please specify)

11. Do you have any pre-existing or chronic medical conditions?*

- Yes
- No

12. Please select your medical condition in the drop-down list*

13. Do you have any genetic disorders in the family?

- Yes
- No
- Do not know

14. Do you take any medicines regularly?*

- Yes
- No

Please specify
Text box

15. What do you take the medicines for?

- to treat a chronic medical condition
- to treat a pregnancy related condition e.g. nausea and vomiting, heartburn, constipation
- for other types of conditions

Your need for information

16. Have you needed information on the safety of certain medicines before or during pregnancy or breastfeeding?*

- Yes
- No

Your need for information

17. When did you need information?*

- When thinking about getting pregnant
- When trying to get pregnant
- When pregnant
- When breastfeeding

18. Where did you look for this information first?*

- Family/friends
- Medical doctor
- Midwife/Nurse
- Pharmacy personnel
- Alternative medicine shop personnel
- Internet (searching online, in social media or specific websites)
- Calling birth defect information service (not available in all countries)
- Print media (e.g. magazines, newspapers)
- Information leaflet about medicine use during pregnancy or breastfeeding from your doctor's office
- Medicine packaging (medicine label or patient information leaflet)
- Other (please specify)

19. Where did you find information online?*

- Discussion forums
- Search engines
- Social media
- Online magazines
- Patient organisation websites
- Scientific articles
- Patient information leaflet
- Birth defect information service (not available in all countries)
- National medical services
- Other (please specify)

20. Please give examples for the online sources you selected above

21. Did you discuss the information you found online with your doctor, midwife, pharmacist or other healthcare professionals? *

- Yes
- No

22. Did you go online to check for information you received from your doctor, midwife, pharmacist or another health care professional?*

- Yes
- No

23. When you started looking for information, what information did you try to find? (Select all that apply)*

- Can the medicine make it difficult to become pregnant?
- Is it safe for my baby if I take this medicine when I am pregnant?
- Is it safe for my baby if I take this medicine when I am breastfeeding?
- How much of this medicine can I take when I am pregnant?
- How much of this medicine can I take when I am breastfeeding?
- How to treat a disease or condition I had when I was pregnant or breastfeeding
- Experiences or advice from women who have used the same medicine during pregnancy or breastfeeding
- Other (please specify)

24. If you used information from more than one source, do you think the information was similar? (in terms of content, not appearance) *

- Yes, the same or similar (only wording or detail level was different)
- No, part of the information was different
- No, the information was completely different
- Not applicable

25. Is there anything you looked for, that you couldn't find a useful answer for?*

- I found everything I needed
- Don't know
- I could not find a useful answer to the following (please specify below)

26. If you were NOT able to find a useful answer, what did you do? (Select all that apply)*

- I decided not to get pregnant
- I decided to terminate a pregnancy
- I decided not to take the medicine
- I decided to take the medicine anyway
- I became anxious
- I discussed with my doctor, midwife or pharmacist
- I looked for a new information source (please specify:)
- Other (please specify)

Your information preferences

27. Did you find it difficult to understand information about how safe it is to use medicines before or during pregnancy or breastfeeding?*

- Yes
- No
- Don't know
-

28. Was it because (Select all that apply):*

- Information was too detailed
- Information was not precise enough
- Information did not include scientific results
- The presentation was not clear
- I did not understand the words they used
- Other (please specify)

29. Which of the following information sources is the easiest to access, understand, most trustworthy, and best tailored to your needs?*

	Medical doctor	Midwife/ Nurse	Pharmacy personnel	Birth defects information services (not available in all countries)	Medicine packaging (medicine label or patient information leaflet)	Scientific article written by researchers	Patient organisations	Pregnant women with the same experience as you	Internet	Don't know
Easiest to access	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Easiest to understand	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most trustworthy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Best tailored to my needs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

If Internet was selected, please specify which website(s)

30. For you to trust a source of information, how important is the following?*

	Essential	Important	Neither important nor unimportant	Not important
The information is written or verified by a medical doctor (e.g. general practitioner, obstetrician or gynaecologist)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The information is written or verified by a healthcare professional (e.g. nurse, midwife, or pharmacist)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The information comes from an official source (an established government source, a medical professional or hospital)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The information is based on women's own experiences	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The information is based on medical doctors' experiences with patients	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The information is based on results from clinical trials or clinical studies	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The information is recent (last 5 years)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Other (please specify)	<input type="text"/>			

31. In an ideal world, which source would you turn to for questions about using medicines during pregnancy and breastfeeding?*

- My midwife or nurse
- My medical doctor
- My pharmacist
- Birth defect information service (not available in all countries)
- Patient organisations
- Print media (e.g. magazines, newspapers)
- The companies that develop medicines
- Other (please specify)

32. Please explain your answer above

33. Do you know of any organisations that specialise in providing information about how safe it is to use medicines during pregnancy and breastfeeding?

- No
- Yes, please specify

Help us build your ideal tool

It can be difficult to find reliable and consistent information about how safe medicines are to use when you are pregnant or breastfeeding. We are developing a European-wide knowledge bank that will provide searchable and reliable advice. To make sure this knowledge bank as useful as possible, we want to know what you think is important.

34. How useful would a European knowledge bank with up-to-date information on the safety of medicines during pregnancy and breastfeeding be to you?*

- Very useful
- Somewhat useful
- Neither useful nor not useful
- Not that useful

- Not useful at all
- Don't know

35. In what situations could you imagine using such a knowledge bank? (Select all that apply)*

- To prepare for a visit to see my doctor, midwife, pharmacist, or other healthcare professionals
- To double check information I found somewhere else
- To get a second opinion on recommendations made by my doctor, midwife, pharmacist, or other healthcare professional
- To decide if I should use a medicine while pregnant or breastfeeding
- Other (please specify)

36. How would you like to access this knowledge bank?*

- Website
- Mobile app
- Through my healthcare provider (e.g. doctor, midwife, pharmacist)

37. Would you be able to use information from the knowledge bank if it is only available in English?

- Yes, English is my native language
- Yes, English would be adequate
- No, I would prefer at least a short summary in my own language
- No, I would need all information in my own language

38. Your participation is critical in helping us solve the information gap in medicine use during pregnancy and breastfeeding. Would you be willing to take part in future studies on this topic as part of the ConcePTION project? If yes, please enter your email address:

Appendix 5 - Focus group instructions

The focus groups contained the following steps:

Step 1. Introductory questions

- An outline of the program of the focus group was given to the participants.
- Check that all participants were asked to sign a country specific consent form.
- Participants were asked to tell a little about themselves. For HCPs this can be something about their profession, year of experience etc. For pregnant and breastfeeding women this can be something about their pregnancy or personal life such as names of children, work experience and place of living.

Step 2a Key questions pregnant and breastfeeding women

What you want to know	Broad engagement question	• If not covered in the broader discussion, ask questions to explore themes
What kind of information do women need around medicine use during pregnancy and breast feeding and why	What are your thoughts on pregnancy and medicines?	<ul style="list-style-type: none"> • Did you take any medicines during your pregnancy or during breastfeeding? • What made you decide to use or not to use any drugs during pregnancy or breastfeeding? • What questions did you have around your medicine use? • When did you have questions about the safety of drug use during pregnancy and breastfeeding? • How did you address these questions?
What information sources do women trust and why	Where did you go for information?	<ul style="list-style-type: none"> • Did you look for information online? • How did you find the information source? What search terms did you use? • Why did you use that source? • Is there a source you wouldn't use? Why? • Were you satisfied with the information you found? Why or why not? • What did you do when encountering conflicting information? • What did you do with the information you found? • What was the role of the healthcare professional in providing you with information regarding drug use during pregnancy and breastfeeding? • How did the information given/found influence your medicine use?

<p>Needs and preferences for a knowledge bank</p>	<p>How would you prefer to get information about drug use during pregnancy and breastfeeding?</p>	<ul style="list-style-type: none"> • If you could create a website with information about drug use during pregnancy and breastfeeding, what kind of information should this ideal website contain? • How would you prefer to search for information? What would you search for? What terms would you prefer to search by? • How should this information be presented to you? (Examples of websites or apps they like, for what reasons?) • Is there any information you would not want to or need to see on this website? • How can you make this website accessible and searchable for women like you? • What kind of organisation should be responsible for providing this information in your opinion?
<p>User testing of the knowledgebank</p>	<p>OR</p> <ul style="list-style-type: none"> • I would like to ask you to go to a test website that we have built. The observer will share the link to the website with you in the chat • Please browse around the website and let us know your thoughts • I will now ask you to search information for the drug azithromycin. The observer will provide you with the spelling in the chat. Please read the text and let us know your thoughts. 	<ul style="list-style-type: none"> • What are your impressions of the website? • What do you think about the lay-out? • What do you think about the navigation? • What do you think about the different types of information on the website? • What do you think about the text? • Does the text fulfil your information needs? Please elaborate • What do you think about the structure of the text (summary, detailed information) • What do you think about the language and readability of the text?

Step 2b. Key question healthcare professionals

<p>What you want to know</p>	<p>Broad engagement question</p>	<p>If not covered in the broader discussion, ask questions to explore themes</p>
<p>What kind of information do HCPs need around medicine use during pregnancy and breast feeding and why</p>	<p>What kind of information do you need to inform and advise pregnant and breastfeeding women about safe drug use?</p>	<ul style="list-style-type: none"> • What questions do pregnant and breastfeeding women have when visiting you? • What additional questions do you have around medicine use during pregnancy and breastfeeding? • When in the pregnancy/breastfeeding period do most of the questions arise? • How do you address these questions? • What considerations do you make in advising pregnant and breastfeeding women to use or not to use drugs?

What information sources do HCPs trust and why	Where do you go for information?	<ul style="list-style-type: none"> • Did you contact another healthcare professional? If yes, who did you contact and why? • Did you look for information online? If yes, why did you use that source? • Is there a source you wouldn't use? Why? • Are you satisfied about the information you find on safe drug use during pregnancy and breastfeeding? • What do you do when encountering conflicting information? • What makes information reliable to you? • What do you do with the information you find? • How did the information given/found influence your recommendation to the patient?
Needs and preferences for a knowledge bank	How would you prefer to get information about drug use during pregnancy and breastfeeding?	<ul style="list-style-type: none"> • If you could create a website with information about drug use during pregnancy and breastfeedings, what kind of information should this ideal website contain? • How would you prefer to search for information? What would you search for? What terms would you prefer to search by? • Is there any information you would not want to see or would not need to see on this website? • How can you make this website accessible and searchable for all HCPs? • What kind of organisation should be responsible for providing this information in your opinion?

Step 3. Ending questions

Summary question is asked after you have summarized the main conclusions of the key questions.

Is this an adequate summary?

Finally, after the summarizing question, you finish the discussion with a **final question**.

Have we missed something?