Review

Women's Beliefs about Medicines and Adherence to Pharmacotherapy in Pregnancy: Opportunities for Community Pharmacists?

Medication-taking during pregnancy: opportunities for community pharmacists?

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Abstract

Background

During pregnancy women might weigh benefits of treatment against potential risks to the unborn child. However, non-adherence to necessary treatment can adversely affect both mother and child. To optimize pregnant women's beliefs and medication adherence, community pharmacists are ideally positioned to play an important role in primary care.

Objective

This narrative review aimed to summarize the evidence on 1) pregnant women's beliefs, 2) medication adherence in pregnancy, and 3) community pharmacists' counselling during pregnancy.

Method

Three search strategies were used in Medline and Embase to find original studies evaluating women's beliefs, medication adherence and community pharmacists' counselling during pregnancy. All original descriptive and analytic epidemiological studies performed in Europe, North America and Australia, written in English and published from 2000 onwards were included.

Results

We included 14 studies reporting on women's beliefs, 11 studies on medication adherence and 9 on community pharmacists' counselling during pregnancy. Women are more reluctant to use medicines during pregnancy and tend to overestimate the teratogenic risk of medicines. Risk perception varies with type of medicine, level of health literacy, education level and occupation. Furthermore, low medication adherence during pregnancy is common. Finally, limited evidence showed current community pharmacists' counselling is insufficient. Barriers hindering pharmacists are insufficient knowledge and limited access to reliable information.

Conclusion

Concerns about medication use and non-adherence are widespread among pregnant women. Community pharmacists' counselling during pregnancy is insufficient. Further education, training and research are required to support community pharmacists in fulfilling all the opportunities they have when counselling pregnant women.

1. Introduction

During pregnancy, a substantial number of women have pregnancy-related disorders or preexisting morbidities which may require pharmacological treatment. Although prevalence estimates of medication use during pregnancy vary between studies, it is well established that maternal use of medicines is common during this period [1-3]. Recent studies have shown that eight out of ten women take at least one prescription or over-the-counter (OTC) medicine during pregnancy [4], with paracetamol being the most common OTC exposure (65%) [5, 6]. Medication use during pregnancy poses important challenges to the women and their physicians, since the benefits of pharmacological treatment have to be weighed against potential risks to the unborn child. Although teratogenicity has been shown for some medicines such as thalidomide, isotretinoin and valproic acid [7-9], safety data for more subtle pregnancy outcomes and for longer-term effects on child development remain scarce. Still, medicines are frequently needed during pregnancy, for example to treat pre-existing conditions like asthma or epilepsy, acute conditions like infections or fever, or to treat pregnancy-related disorders like nausea and vomiting, hypertension or gestational diabetes.

Prior research has shown that at least half of the pregnant women need information about medicines during pregnancy [10]. Unfortunately, inaccurate information and inconsistencies between sources has been observed, potentially leading to increased and unjustified anxiety among pregnant women, unrealistic risk perception of drug exposure, or even abrupt discontinuation of needed pharmacotherapy [6, 11-13]. Because non-adherence to necessary pharmacotherapy can adversely affect both mother and child, understanding its extent across various diseases in pregnancy is essential for fetal-maternal health.

From a societal point of view, there are many reasons for utilizing pharmaceutical expertise in community pharmacy care of pregnant women. Firstly, antenatal care in most countries does not provide prenatal care until gestational weeks 8-12 [14]. Despite this, women can experience pregnancy-related ailments prior to their first consultation (typically nausea and vomiting) [15], making pharmacists the first healthcare professionals pregnant women encounter. Furthermore, previous studies have reported that pregnant women rely on pharmacists as one of the most used sources of information about medicines during pregnancy [6, 10]. Due to their easy accessibility and wide distribution in the community, pharmacists are ideally positioned to play an important role in primary pregnancy care. In addition, studies in non-pregnant patients have shown the effectiveness of pharmacists' counselling on medication adherence, persistence, clinical management and therapeutic outcomes [16-22]. This is important since two recent studies have shown medication-related problems (MRP) frequently occur among pregnant women [23, 24]. These MRP were largely resolved by pharmacists correcting misperceptions, providing information, and empowering the women to make safe decisions about medication use [23]. The potential contribution of pharmacists to improve fetal-maternal health has been recognized by the International Pharmaceutical Federation (FIP), stating that pharmacists can detect the use of potential teratogenic medicines and counsel pregnant women on alternative medicines [25]. In order to take up this role, pharmacists need to maintain and improve professional performance. Therefore, pharmacy education and continuous professional development are essential to optimize pharmacists' knowledge, communication skills and problem-solving competencies.

From a global public health perspective, safe and rationale medication use during pregnancy is essential to improve fetal-maternal health, and this can be accomplished via a better understanding of pregnant women's beliefs and barriers to optimal medication adherence. Likewise, knowledge about current pharmacists' counselling practice and about the barriers they experience in counselling is useful to further develop the profession. Therefore, this narrative review aimed to summarize quantitative evidence on the following three aspects: 1) pregnant women's beliefs about medicines and risk perception; 2) pregnant women's medication adherence and persistence in real-world setting; 3) and community pharmacists' counselling practice during pregnancy and the barriers they encounter. In the discussion, future perspectives with regard to pharmaceutical care research, continuous education and undergraduate training are provided.

2. Methods

Three search strategies were used in MEDLINE and EMBASE in May 2018 to find original studies evaluating beliefs about medicines and medication adherence among pregnant women as well as community pharmacists' counselling during pregnancy. MeSH and Emtree terms and text words were used to retrieve relevant articles. Reference lists of identified studies were examined in order to identify other potential articles. An overview of the concepts (combined via AND) and corresponding search terms (combined via OR) for each of the three search strategies can be found in the Supplementary Material.

All original descriptive and analytic epidemiological studies from Europe, North America and Australia, written in English and published from 2000 onwards were included. Reviews, Delphi studies, qualitative research, case reports and case series, editorials and commentaries, and conference abstracts were excluded. For the topic 'medication adherence', only studies describing one of the following aspects were included: adherence and persistence; acute and chronic medicines; adherence prevalence estimates and factors associated with low adherence. Studies exploring medication discontinuation in pregnancy were not included. Clinical trials on adherence to HIV treatment during pregnancy, and pharmacists' counselling related to contraception and emergency contraception, vitamin use and lifestyle changes (smoking or alcohol cessation) were beyond the scope of the manuscript as well.

Two reviewers (MC & AL) independently selected the retrieved articles based on inclusion and exclusion criteria. Discrepancies in judgement were evaluated by a third independent reviewer (VF) to reach consensus on the final list of included articles. Of these, full texts were collected and read in full.
For each review section, we extracted data on authors, publication year, study country, study period, data source, study population, study type and design, number of study participants, main outcome measure and main findings.

3. Results

3.1 Beliefs about medicines among pregnant women

A total of 504 studies were initially retrieved in the literature search. After application of the exclusion criteria and removing duplicates, we identified 14 papers on beliefs about using medicines during pregnancy (see Table 1). These studies were conducted in a variety of countries with Norway producing four papers and on a variety of therapeutic areas. The number of participants in the studies ranged from 95 – 8131 pregnant or recently pregnant (within 5 years) women. The most prevalent data collection method was a self-completed questionnaire distributed either in person or via a website aimed at pregnant women. Different measures were used ranging from scales as the Beliefs about Medicines (BMQ; measuring beliefs about medicines in general and during pregnancy), to Visual Analogue Scales (VAS; measuring risk perception), as well as self-generated questions.

Most studies found that women were more reluctant to use medicines during pregnancy and tended to overestimate the teratogenic risk of medicines. Willingness to initiate or continue medication use, however, depended on their severity of illness and whether they were pregnant or had recently delivered at the time they reported on beliefs about medicines in pregnancy [26-32]. The most common fear in using medicines during pregnancy appeared to be the risk of harming the unborn child [6, 27, 29, 30]. The framing of this information appeared important for the overall assessment of risk [33], while the first person to give participants this information was more likely to influence their final decision [34].

Overall, there appears to be high consistency within the studies that women with a lower literacy and education levels overestimate the teratogenic risk of medicines to a greater extent than their counterparts [28, 35-37]. Only one study did not support this finding [6]. Two studies indicated that women who were healthcare professionals rated the risk of taking medicines during pregnancy lower than those with no healthcare background or occupation [28, 37].

The majority of studies highlighted that the perceived risk of taking medicines during pregnancy does not apply to all categories of medicines equally. In these studies, women frequently reported antidepressants and anxiolytics as those with the highest risk, and antibiotics and paracetamol with the lowest risk or greatest benefit [27, 35, 37, 38].

Table **1**: Characteristics and main findings of included studies related to 'beliefs about medicines'.

Authors & publication year	**Country & period**	**Study population**	**Study type & design, N**	**Main measure**	**Main findings**
EUROPE					
Duggan *et al.* 2014 [36]	Ireland, 2012	Pregnant women attending the antenatal clinic at Cork University Hospital antenatal unit between 4th – 24th January 2012	Cross-sectional questionnaire study N = 404	REALM and BMQ	Lower level of education and lower literacy level associated with stronger beliefs about the harm of medicines.
Heitmann *et al.* 2016 [26]	Norway, 2014/15	Pregnant women and women with a child ≤ 1 year old. Experienced nausea or vomiting in most recent pregnancy	Cross-sectional web-based questionnaire study N = 712	Self-generated questions on attitudes towards medicines	Women who were more likely to use medicines thought that it was better for the fetus to use medicines and get better than leave the illness untreated. Majority of women reported a higher threshold for using medicines while being pregnant. Severity of symptoms was an important consideration for taking medicines. The majority of women taking conventional medicines were anxious about the effect on the fetus and used less than required as a result.

Authors & publication year	Country & period	Study population	Study type & design, N	Main measure	Main findings
Mulder *et al.* 2018 [27]	Netherlands, 2013	Pregnant women attending a Dutch obstetric care facility	Cross-sectional self-reported questionnaire study N = 136	Self-generated questions on risk perception	Pregnant women were most concerned about birth defects, miscarriage or giving birth to a child with an allergic disease as a result of their drug use. Highest perceived risk for antidepressants, sedatives and NSAIDs. Highest benefit for antibiotics, antifungals and antacids. Risk perception was highest in the first two trimesters. No other demographics influenced perceived risk. Lower benefit scores correlated with being single, smoking, nulliparous and no family history of birth defects.
Nordeng *et al.* 2010 [28]	Norway, 2008	Currently pregnant women	Self-completed structured web-based questionnaire N = 866	Part BMQ plus self-generated study specific questions	Most women were more cautious taking medicines during pregnancy. A large proportion believed that even if ill they should abstain from taking medication they would have otherwise taken if not pregnant. Physicians consent needed prior to taking natural remedies (majority of respondents). Education and occupation (health related versus non-health related) appeared to have some impact on beliefs.

Authors & publication year	Country & period	Study population	Study type & design, N	Main measure	Main findings
Nordeng *et al.* 2010 [6]	Norway, 2008	Pregnant women and women with a child ≤ 5 years old	Self-completed structured web-based questionnaire N = 1793	Self-generated questions on risk perception	The majority of women (87.5%) estimated correctly that the general risk of malformation is ≤5%. Most women, however, overestimated the risks of drugs and other exposures during pregnancy. Risk was perceived as highest for smoking, alcohol, sedatives/anxiolytics and antidepressants. Higher perceived risk from women who were older, had a higher level of education, choosing not to use a drug during pregnancy and primiparity. Most common reason for not using a drug was fear of harming the unborn child. 76.6% reported they needed information on drug use and 60% found this information conflicting between different sources.
Twigg *et al.* 2016 [29]*	UK, 2011/12	Pregnant women and women with a child ≤ 1 year old	Self-completed structured web-based questionnaire N = 1120	BMQ plus self-generated questions on risk perception	72.8% of women reported avoiding the use of medicines during pregnancy. Most common reasons for avoiding were: fear of harming the unborn child, medication not recommended and stating that they would endure as much as possible before taking medicines. Women who did not take medication perceived greater risk than those who did take medicines. 46.3% required more information about medicines use in pregnancy.

Authors & publication year	Country & period	Study population	Study type & design, N	Main measure	Main findings
Widnes *et al.,* 2013 [38]	Norway, 2010/11	Women attending a regular ultrasound scan in week 17-19 of pregnancy and their associated general practitioner (GP)	Self-completed questionnaire study Women: N = 171 GPs: N= 74	Self-generated questions on medicine labels	Out of 6 medicines (5 conventional and 1 herbal) participants thought paracetamol and dexchlorpheniramine were the safest. GPs gave a lower risk score than pregnant women. Little confidence in the herbal preparation. Scores for the clarity of the explanatory text indicated the text was appropriately phrased.
Patel *et al.,* 2012 [30]	UK, 2012	Nulliparous and multiparous women requiring antenatal therapy with enoxaparin in a hematological clinic	Self-administered questionnaire N = 95	BMQ	Perceived necessity of enoxaparin antenatally outweighed concerns. 88.4% stated enoxaparin not an issue as long as their baby's health was protected.
CANADA					
Jasper *et al.,* 2001 [33]	Canada, 2001	Successive callers to the Motherisk Program telephone pregnancy information line	Telephone structured interview N = 105	Self-generated questions on risk perception	Negatively framing information about fetal risk increases the perception of teratogenicity and the likelihood of not wanting to take the drug. Women who received positively framed information had a lower risk perception.

Authors & publication year	Country & period	Study population	Study type & design, N	Main measure	Main findings
Bonari *et al.,* 2005 [34]	Canada, 2004	Three groups of Motherisk Program telephone callers taking 1) antidepressants, 2) gastric medicines and 3) taking short term antibiotics	Before and after questionnaire and interview study N = 100 in each group	Risk perception analogue scale & CES-D	Pre-counselling: 87% (antidepressants), 56% (gastric) and 22% (antibiotics) of women rated the risk of medicines as greater than 1-3%. Significant decrease in risk perception from before to after the counselling service. 15% chose to discontinue antidepressant regardless of advice from Motherisk The first opinion received by the participants regarding safety appeared to be an important influence towards the eventual decision to continue or discontinue therapy. Demographics did not correlate with the decision to continue therapy.
USA					
Goodman, 2009 [31]	USA, 2006/7	Convenience sample of women in their third trimester attending an obstetric clinic	Self-administered questionnaire N = 509	Self-generated questions on risk perception	For the treatment of depression only 35.6% put medication as a top three option. Only 7.3% would consider this as first choice. 66% thought that taking medication for depression whilst pregnant was probably not or definitely not acceptable. Those who had used psychotropic medication before and had lower depression scores were more likely to say that medication use was acceptable.

Authors & publication year	Country & period	Study population	Study type & design, N	Main measure	Main findings
AUSTRALIA					
Selinger *et al.,* 2013 [32]	Australia, 2012	Female patients with IBD aged 18-45 from two tertiary outpatient IBD clinics	Self-administered questionnaire N = 145	Self-generated questions on risk perception	The majority of women stated that all medicines for IBD should be avoided during pregnancy. However, a majority also stated that if medicines are controlling symptoms they should be continued during pregnancy. Negative attitudes towards medicines and symptoms were associated with lower pregnancy-related knowledge scores.
MULTINATIONAL					
Petersen *et al.,* 2015 [37]*	Multi-national, 2011/12	Pregnant women and women with a child ≤ 1 year old	Self-completed structured web-based questionnaire N = 8131	Self-generated questions on risk perception	Rated antidepressants, alcohol, smoking and thalidomide as most harmful. Lower education level had higher perceptions of risk. Female healthcare professionals had a lower perception of risk. Some geographic differences in risk perception.
Lupattelli *et al.,* 2014 [35]*	Multi-national, 2011/12	Pregnant women at any gestational age	Self-completed structured web-based questionnaire N = 4999	Self-generated questions on risk perception	Women with low health literacy reported higher risk perceptions for medicines and more negative beliefs about medicines. Antidepressants were given the highest risk rating.

Abbreviations: REALM=Rapid Estimate of Adult Literacy in Medicine; BMQ=Beliefs about Medicines questionnaire; CES-D=Center for Epidemiologic Studies Depression Scale; IBD=Inflammatory Bowel Disease; *all part of the same data collection – studies presented here represent different sub-analyses of the data.

3.2 Medication adherence during pregnancy

A total of 275 studies were initially retrieved in the literature search. After application of the exclusion criteria and removing duplicates, 11 studies on medication adherence in pregnancy were identified (see Table 2). All studies were observational either based on primary (7 studies) or secondary data sources (2 studies) or both (2 studies). A single study explored the consequence of low medication adherence on pregnancy outcomes [39]. The remaining ten studies were descriptive, reporting prevalence of medication adherence and risk factors for low adherence. Most studies had a small sample size (42-804 women). Medication adherence was mainly measured via self-reported instruments such as the Morisky Medication Adherence Scale (MMAS) or as percentage of filled prescriptions (%), with a threshold of 80% for low/high adherence.

Two studies explored medication adherence in the context of maternal depression [40, 41]. Rates of low adherence to prescribed antidepressants were 45.0 and 48.8%. In both studies, low adherence was positively associated with greater severity of maternal psychiatric symptoms. Two studies explored adherence to progesterone or acetylsalicylic acid for prevention of adverse pregnancy outcomes [39, 42]. Low adherence was 33.7 to 46.3% for progesterone or acetylsalicylic acid, respectively, and no maternal risk factors were identified. Five studies explored medication adherence in the context of treatment of somatic disorders such as asthma, cardiovascular and inflammatory disorders [30, 43-46]. In one of those studies reporting adherence to heparin injections in women with thrombotic disorders, adherence rate was as high as 97.9% [30]. Another study showed that, under a special treatment management program, medication adherence to asthma medication was 73.0% [45]. Low medication adherence was commonly reported by pregnant women treated for rheumatic or inflammatory diseases (range 32.8-55.6%), as well as in women treated for epilepsy (40.0%) [43, 44, 46]. A single study explored medication adherence in the context of hypothyroidism in pregnancy [47]. Here, 16.9% of pregnant women demonstrated low medication adherence. The one study from Australia reported low medication adherence as a pooled estimate for a range of different disorders, which was found as high as 59.1% [48]. In the sole claims-based US study exploring the consequence of low medication adherence in pregnancy, there was no statistically significant association between adherence to progesterone and rates of prematurity, but study power was low [39].

Maternal characteristics (i.e., age, parity, smoking, lack of the use of folate, personality traits), women's beliefs and perceptions on medication exposure, and not least specialist counselling about continuation of medical treatment in pregnancy, seemed to be important determinants of medication adherence in pregnancy [40, 43, 44, 46, 47]. These factors were differentially associated with medication adherence depending on the type of maternal disease.

Table **2:** Characteristics and main findings of included studies related to 'medication adherence'.

Authors & publication year	**Country & period**	**Data source**	**Study population**	**Study type & design, N**	**Main measure**	**Therapeutic area**	**Main findings**
EUROPE							
Baarnes *et al.,* 2016 [45]	Denmark 2012	Outpatient clinical records within the 'asthma management program' and self-completed questionnaire	Pregnant women referred to the outpatient respiratory clinic, with diagnosed asthma and prescribed bronchodilators	Descriptive, prospective cohort N = 114	Self-reported adherence, and MPR	Asthma	Self-reported adherence: 73% MPR: 46% Significant positive association between self-reported adherence and MPR.
Abheiden *et al.,* 2016 [42]	Netherlands 2015-2016	Tertiary university hospital records and self-reported paper-based questionnaire	Pregnant women with an indication for use of low-dose acetylsalicylic acid	Descriptive, cross-sectional N = 42	SMAQ BBQ	Prevention of recurrent hypertension and fetal growth restriction	Self-reported adherence: SMAQ non-adherence: 46.3% BBQ non-adherence: 21.4% No association between adherence and age, race, BMI, education, maternal disease or indication.

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Therapeutic area	Main findings
Patel *et al*., 2012 [30]	Unspecified country and period, probably UK	Self-reported diary and paper-based questionnaire	Pregnant women referred to the hematology clinic in need of enoxaparin	Descriptive, prospective cohort N = 95	Adherence rate ≥ 80% according to self-completed diaries with times of injection, verified through laboratory tests	VTE, anti-phospholipid syndrome, switch from long-term warfarin	High adherence=97.9% No association of adherence with race, history of recurrent miscarriage, and frequency of the injections.
Julsgaard *et al.,* 2011 [44]	Denmark 2000-2006[a]	National Registries (Patient, Medical Birth, Prescription) and self-reported paper-based questionnaire	Pregnant women with ulcerative colitis having given birth in 2000–2005	Descriptive, retrospective cohort N = 62	Adherence rate ≥ 80% consumption of prescribed medicines	Ulcerative colitis	High adherence: 59.7% Significant negative association of low adherence with receiving counselling regarding medical treatment. No association of low adherence with multiparity, unplanned pregnancy, and smoking.
Nielsen *et al.,* 2010 [43]	Denmark 2000-2006[a]	National Registries (Patient, Medical Birth, Prescription) and self-reported paper-based questionnaire	Pregnant women with Crohn disease having given birth in 2000–2005	Descriptive, retrospective cohort N = 55	Adherence rate ≥ 80% consumption of prescribed medicines	Crohn disease	High adherence: 67.3% Significant negative association of low adherence with multiparity and having planned the pregnancy. No association of low adherence with receiving counselling regarding medical treatment.

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Therapeutic area	Main findings
USA							
Hydery *et al.,* 2017 [39]	USA 2011-15	Administra-tive claim records, Massachusetts Medicaid	Pregnant women filling progesterone prescriptions in Massachusetts	Analytical, retrospective cohort N = 169	Adherence as PCD of ≥ 0.8	Prevention of premature birth	High adherence=66.3% Term vs. preterm delivery: PCD ≥ 0.8: 58.0% vs 42.0% PCD< 0.8: 70.2% vs 29.8% p=0.124 No association between adherence and race, type and number of comorbidities.
Wu *et al.,* 2014 [41]	USA 2004-2009	Administra-tive claim records, South Carolina Medicaid	Pregnant women with a depression diagnosis within 280 days prior to delivery	Descriptive, retrospective cohort N = 804	Non-persistence, as a 2 week gap between consecutive prescriptions	Depression	Non-persistence to treatment: 45.0% Non-persistence was significantly, positively associated with nonwhite race, antidepressant use in the year prior to pregnancy, and number of office visits. Non-persistence was negatively associated with hospitalization.
AUSTRALIA							
Sawicki *et al.,* 2011 [48]	Australia 2009	Self-reported paper-based questionnaire	Pregnant women attending the outpatient clinics of RWH	Descriptive, cross-sectional N = 181	MMAS-4	Asthma, blood-related disorders, diabetes, vitamin/mineral deficiencies, hypertension	Self-reported low adherence: 59.1% High adherence: 40.9% Significant, positive association of low adherence with having asthma, and using non-prescribed dietary minerals.

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Therapeutic area	Main findings
MULTINATIONAL							
Juch *et al.,* 2016 [47]*	Multi-national with 18 countries 2011-2012	Web-based, self-completed questionnaire	Pregnant women with self-reported hypothyroidism	Descriptive, cross-sectional N = 213	MMAS-8	Hypothyroidism	Self-reported adherence: Low=16.9%, Medium=44.1%, High=39.0% Significant, positive association of low adherence with younger maternal age, and no use of folic acid. Higher adherence significant positively correlated with conscientious personality and perception that the benefit of pharmacotherapy outweighed the risks.
Lupattelli *et al.,* 2015 [40]*	Multi-national with 18 countries 2011-2012	Web-based, self-completed questionnaire	Pregnant women with self-reported psychiatric disorders	Descriptive, cross-sectional N = 160	MMAS-8	Depression, anxiety, other psychiatric disorders	Self-reported adherence: Low=48.8%, Medium=35.6%, High=15.6% Significant positive association of low adherence with smoking during pregnancy, elevated antidepressant risk perception, and depressive symptoms; negative association with psychotropic polytherapy. Higher adherence positively correlated with the perception that the benefit of pharmacotherapy outweighed the risks.
Lupattelli *et al.,* 2014 [46]*	Multi-national with 18 countries 2011-2012	Web-based, self-completed questionnaire	Pregnant women with self-reported somatic chronic disorders	Descriptive, cross-sectional N = 210	MMAS-8	Somatic chronic disorders: cardiovascular, rheumatic, bowel disorders, diabetes, epilepsy	Overall self-reported low adherence: 36.2% Adherence, cardiovascular disorders: Low=32.9%, Medium=35.4%, High=31.7%

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Therapeutic area	Main findings
							Adherence, rheumatic disorders: Low=55.6%, Medium=28.9%, High=15.5% Adherence, bowel disorders: Low=36.1%, Medium=27.8%, High=36.1% Adherence, diabetes: Low=17.1%, Medium=45.7%, High=37.2% Adherence, epilepsy: Low=40.0%, Medium=44.0%, High=16.0% Significant, positive association of low adherence with multiparity, no folic acid use, and beliefs that it is better to abstain from medicines or use herbals during pregnancy. No association of adherence with region of residency and FDA-assigned pregnancy categories D/X

Abbreviations: MPR=medical possession rate; SMAQ=simplified medication adherence questionnaire; BBQ= Beliefs and Behaviour Questionnaire; VTE=Venous thromboembolism; PCD=proportion of days covered; RCT=Randomized Clinical Trial; NPV=Nausea and vomiting of pregnancy; PUQE= delta of pregnancy unique-quantification of emesis score; RWH= The Royal Women's Hospital; MMAS-4=4 items Morisky Medication Adherence Scale; MMAS-8=8 items Morisky Medication Adherence Scale; FDA=Food and Drug Administration; [a]in these two studies, women giving birth between 2000 and 2005, having the disease of interest, were first selected. In 2006, they received a paper-based postage questionnaire; *all part of the same data collection – studies presented here represent different sub-analyses of the data.

3.3 Community pharmacists' counselling of pregnant women

A total of 310 studies were initially retrieved in the literature search. After application of the exclusion criteria and removing duplicates, we obtained only four studies evaluating pharmacists' counselling practice during pregnancy. Three of these studies were published more than 10 years ago. As shown in Table 3, all studies were descriptive and cross-sectional with samples of 110-276 pharmacists, mainly practicing in community pharmacies. Three out of four studies presented various scenarios to pharmacists and questioned them about their counselling on pharmacological as well as non-pharmacological treatment, and referral to a physician [49-51]. Differences were observed between pharmacists in Serbia, Norway and France in response to common ailments [49, 50]. OTC medicines were recommended by the majority of pharmacists (>60%) in treatment of pain and common cold symptoms including sore-throat, runny nose and fever [49-51]. Recommendation of homeopathy was the most prevalent response among French pharmacists to treat allergic rhinitis (>70% of participants) and cough (>50% of participants) [50]. In several scenarios, referring to a physician was the most prevalent suggestion: heavy legs and back pain (>63% of pharmacists in Norway), and morning sickness (>57% of pharmacists in France) [49, 50].

One multinational study in the Netherlands, Canada and Iceland investigated pharmacist's behavior upon a visit of a mystery patient asking for information about specific drug use related to pregnancy. Referral to a physician has been suggested by most pharmacists (90-100%) upon questions with regard to fluoxetine use in week 6 of pregnancy and with regard to metronidazole and carbamazepine use by women planning to get pregnant [52].

Five studies were identified specifically targeting barriers and concerns pharmacists experience when counselling pregnant women (see Table 4). All studies were descriptive with regard to concerns and barriers; some also included information on facilitators. Four studies used self-completed questionnaires to collect information. The number of pharmacists involved in these studies ranged from 43-472. Different barriers and areas of concerns, including symptoms and products of concern, related to the counselling of pregnant women have been identified. Gaps in knowledge about treatment of specific conditions in pregnancy and inadequate undergraduate knowledge-base were the most frequently reported barriers [53-55]. Additionally, two papers reported inaccessibility and absence of information related to medicines' use during pregnancy as a common problem [55, 56].

The study by Hutchinson has shown that *"experiential education"* (experience gained in practice) contributed to knowledge about OTC medicines counselling in pregnancy [55]. Continuing professional development courses have also been recognized as very important to increase the knowledge base related to this specific issue [53, 55]. A more recent assessment of the use and perceived added-value of a helpline for pharmacists (teratology information service Motherisk, developed in Canada) showed it is a good example of quickly providing needed information to pharmacists related to safety issues in pregnancy [57].

Table **3**: Characteristics and main findings of included studies related to the level of pharmacists' counselling of pregnant women.

Authors & publication year	**Country & period**	**Data source**	**Study population**	**Study type & design, N**	**Main measure**	**Main findings**
EUROPE						
Odalovic *et al.,* 2016 [49]	Serbia 2012; Norway 2014	Web-based, self-completed questionnaire	Community and hospital pharmacists	Descriptive, cross-sectional N = 276 - Serbia: 119 - Norway: 157	Level of counselling of medicine (M), supplement (S), non-pharmacological treatment (NPhT), referral to physician (RP)	*Serbia* back pain: 5.3% (S) – 71.2% (M) heavy legs: 10.1% (RP) – 49.9% (NPhT) nausea: 11.8% (S) – 50.5% (M) common cold: 8.4% (RP) – 63.8% (M) constipation: 1.4% (RP) – 54.5% (NPhT) *Norway* back pain: 0% (S) – 63.7% (RP) heavy legs: 1.3% (S) – 71.3% (RP) nausea: 13.4% (M) – 70.7% (NPhT) common cold: 12.1% (RP) – 80.9% (M) constipation: 11.5% (S) – 92.4% (M)
Damase-Michel *et al.,* 2004 [50]	France 1999	Face-to-face interview with paper-based open questionnaire	Community pharmacists and pharmacy technicians	Descriptive, cross-sectional N = 130	Level of counselling of homeopathy (H), phytotherapy (Ph), allopathy (A), non-pharmacological treatment (NPhT), referral to physician (RP)	back pain: 0.8% (Ph) – 83.8% (A) headache: 0% (Ph) – 93.8% (A) sore-throat: 2.4% (NPhT) - 60.3% (A) runny nose: 0% (Ph) – 66.4% (A) dry cough: 0.8% (Ph, NPhT) – 80.3% (H) productive cough: 1.6% (Ph, NPhT) – 50.8% (H) fever and aches: 0.8% (NPhT) – 75.4% (A) constipation: 0% (RP) – 93.8% (A) morning sickness: 0.8% (Ph) – 57.7% (RP) heartburn: 0% (Ph) – 88.5% (A) heavy legs: 3.1% (H) – 85% (NPhT): allergic rhinitis, 1st trim: 0% (Ph) – 73.0% (H) allergic rhinitis, 3rd trim: 0% (Ph) – 74.6% (H)

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Main findings
Lyszkiewicz *et al.,* 2001 [52]	Netherlands, Canada, Iceland Period unknown	Mystery shopper with standardize data collection form completed immediately upon leaving the pharmacy	Community pharmacists and pharmacy technicians	Descriptive, cross-sectional N = 120 (40/country)	Level of counselling of stop the drug (SD), continue the drug (CD), referral to physician (RP)	Fluoxetine (pregnancy week 6): SD: 10-25% CD: 10-35% RP: 90-100% Metronidazole (planning of pregnancy): SD: 10-70% CD: 0-40% RP: 90-100% Carbamazepine (planning of pregnancy): SD: 0-5% CD: 5-30% RP: 65-100%
USA						
Schrempp *et al.,* 2001 [51]	Nebraska 1998- 1999	Self-completed questionnaire	Community pharmacists	Descriptive, cross-sectional N = 110	Level of counselling of OTC product; pharmacists comfort level with counselling of pregnant women; factors that influence pharmacists' counselling	cough: 45% cold: 43% analgesic: 62% laxative: 46% diarrhea: 36% insomnia: 17% heartburn: 56% There were no statistical differences in counselling frequencies by geographic region, gender, academic degree (doctorate in pharmacy; bachelor in science), and age

Abbreviations: OTC=over the counter

Table **4:** Characteristics and main findings of included studies related to pharmacists' barriers and areas of concerns when counselling pregnant women.

Authors & publication year	**Country & period**	**Data source**	**Study population**	**Study type & design, N**	**Main measure**	**Therapeutic area**	**Main findings**
EUROPE							
Hutchinson *et al.,* 2001 [55]	Scotland Period unknown	Structured telephone interview	Community pharmacists	Descriptive, cross-sectional N = 43	Pharmacists areas of concern, knowledge base for counter-prescribing* in pregnancy, additional information readily accessible	All	*Symptoms of concern:* congestion, flu-like symptoms, ingestion in last trimester, pain from broken lag, recurring headache, sickness, thrush. *Products of concern:* Analgesia stronger than paracetamol, or requests for codeine/paracetamol or ibuprofen, antihistamines, ranitidine, herbals. *Barriers:* Gaps in undergraduate knowledge: 67% did not feel that undergraduate education contributed to their knowledge base for counter-prescribing* in pregnancy. The most used reference source was BNF (91%), but deficit in information has been reported about drugs use during pregnancy.
Zehnder *et al.,* 2004 [56]	Switzerland 2001	Web-based, self-completed questionnaire	Community pharmacists	Descriptive, cross-sectional N = 108	Types of drug information used by pharmacists in daily practice	All	*Barriers:* The most used reference source was Swiss drug reference book, but deficit in information has been reported about drugs use during pregnancy.

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Therapeutic area	Main findings
CANADA							
Tan *et al.,* 2011 [57]	Canada 2009-2010	Standardized form for data collection from calls received by Teratogenic information service (TIC)	Pharmacists, pharmacists' assistants, technicians, pharmacy students who calls TIC	Descriptive N = 472 calls	Types of calls received	All	*Products of concern:* antibiotics (14.3%), gastrointestinal drugs (13.5%) and psychiatric drugs (9.3%) *Products of safety concerns:* steroids (40 calls); SSRI/SNRI (33 calls); nitrofurantoin (18 calls), opioids (15 calls)
USA							
McAuley *et al.,* 2009 [54]	Ohio Period unknown	Self-completed e-questionnaire	Community and hospital pharmacists	Descriptive, cross-sectional N = 152	Pharmacists knowledge	Epilepsy	*Barriers:* Gaps in knowledge: More than 70% of pharmacists correctly answered four of the six pregnancy-related statements (folic acid= 77%, healthy babies=83%, continued AED adherence during pregnancy=87%, choice of AED during pregnancy=71%. Pharmacists who interacted with the most patients per month had the highest scores.

Authors & publication year	Country & period	Data source	Study population	Study type & design, N	Main measure	Therapeutic area	Main findings
MULTINATIONAL							
Bains *et al.,* 2014 [53]	Canada, Uganda and Qatar 2012-2013	Web-based, self-completed questionnaire	Community, hospital, and academia pharmacists and resident pharmacists	Descriptive, cross-sectional N = 273	Pharmacists knowledge, training opportunities and resources available related to fetal-maternal medicines	All	*Barriers:* Mean knowledge assessment score of pharmacists in Canada, Qatar and Uganda were 63%, 53% and 58%, respectively. Gaps in undergraduate knowledge: 71% (Canada), 48% (Qatar) and 56% (Uganda) of pharmacists indicated that they had obtained instruction or training in fetal-maternal medicine throughout their undergraduate program. Gaps in undergraduate knowledge: 27% (Canada), 52% (Qatar) and 33% (Uganda) of pharmacists (strongly) agreed that their entry-to-practice degree provided sufficient training to respond to drug information requests and to care for patients with issues related to fetal-maternal medicine.

Abbreviations: BNF=British National Formulary; TIC=Teratogenic Information Service; SSRI/SNRI=Selective Serotonin/Norepinephrine Reuptake Inhibitor; AED=anti-epileptic drugs; *Counter-prescribing: pharmacists prescribing products over-the-counter without reference to a physician prescription.

4. Discussion

4.1 Main findings

This review provides important insights into pregnant women's beliefs and medication adherence, as well as in community pharmacists' counselling of pregnant patients. The available evidence suggests that pregnant women have a high threshold for using medicines during pregnancy [26, 28, 29]. Similar to studies among non-pregnant women [58-60], individual negative beliefs and high risk perception of drug exposure are important predictors of medication avoidance during pregnancy [26, 29]. Heitmann *et al.* in 2016 found more positive beliefs towards medicines among pregnant women who took them; this is in line with the observation of Twigg *et al.* in 2016 who found lower risk perception scores among women using medicines in pregnancy than women not using medicines. Furthermore, risk perception seemed to vary with the type of medicine, level of health literacy, education level and occupation [27, 28, 35-38]. Overall, the most common fear in using medicines during pregnancy appeared to be the risk of harming the unborn child [6, 27, 29]. This finding underlines the fact that pregnancy is a unique situation where the individual takes both maternal and fetal health into consideration.

With regard to medication adherence during pregnancy, low adherence was common, although rates varied substantially between studies and indications. Only one study reported high adherence rates among more than 80% of pregnant study participants [30]. Of note, studies addressing the consequences of poor medication adherence in pregnancy on fetal-maternal health are almost non-existing, suggesting an urgent need of more research in this area. Moreover, the available literature suggests that low medication adherence during pregnancy is of special concern among women with psychiatric, rheumatic, or bowel disorders, and not least among women with epilepsy. While low adherence for rheumatic or bowel disorders may be explained by a quiescent phase of these disorders in pregnancy, the suboptimal treatment of psychiatric disorders or even epilepsy during pregnancy, deserves clinical attention. In one qualitative study, women taking antiepileptic drugs had restrictive attitudes towards taking medicines for indications other than epilepsy [61]. This shows that in pregnancy women may rank the importance of their chronic/acute conditions, and adequately medicate only one of those.

Multiple studies reported a positive association between unfavorable maternal characteristics (i.e., smoking, lack of the use of folate) and low medication adherence [40, 46, 47], despite variations were evident depending on the pharmacological treatment considered. Nevertheless, as also shown in the non-pregnant population [62], women's beliefs about their prescribed medicines were consistently found to be the most important determinants of medication adherence [40, 46, 47]. Specialist counselling about continuation of drug treatment during pregnancy played an important role in the context of adherence for treatment of bowel disorders [44], but was not so in relation to Crohn disease [43].

Counselling is essential to reduce concerns and correct misperceptions about medicines in pregnancy. According to Bonari in 2005, telephone advice of Canadian pregnant women by trained teratology information specialists significantly reduced women's risk perception [34]. Interestingly, the way the information is transferred to the women is also important [63], as positively framed information has been associated with lower perception of risk [33]. Pharmacists are often the first health care professionals (HCPs) pregnant women meet. Since the first person a pregnant woman speaks with regarding the use of medicines might have the greatest impact on her decision

[34], community pharmacists play an important role to optimize medication use during pregnancy. However, the limited evidence presented in the current review shows that community pharmacists' practice with regard to counselling pregnant women on safe and effective medicines' use, as observed in the studies, is still insufficient [49-52]. Pharmacists hesitate to advise medicines for common ailments during pregnancy, recommend less appropriate products and refer frequently to a physician, without taking any responsibility. Barriers hindering pharmacists to bring pharmaceutical care into daily practice were insufficient knowledge on the topic and limited access to reliable information [53-56]. The differences in pharmacists' counselling observed between countries might be due to differences in availability of products and in regulation and duration of pharmacy undergraduate programs.

When searching for reliable information or support on safe medicines during pregnancy, several high-quality websites are freely available to pharmacists. These include evidence-based resources and national teratology information services such as www.mothertobaby (Organisation of Teratology Information Specialists), www.uktis.org (UK), www.motherisk.org (Canada), www.lareb.nl (The Netherlands), www.janusinfo.se (Sweden), www.tryggmammamedisin.no and www.relis.no (SafeMommyMedicine, Norway), www.lecrat.fr (France) and www.cybele.be (Belgium). A recent report has shown that such information services can quickly provide needed information to pharmacists [57]. However, such services do not exist in every country yet. Establishing a recognized reference center in each country was urged for by the European Board and College of Obstetricians and Gynecologists (EBCOG) in 2016 [64]. Additionally, EBCOG also recommended the elaboration of research on the safe use of medicines in pregnancy.

4.2 Methodological considerations

To our knowledge, the current review is the first attempt to discuss pregnant women's beliefs, risk perception and medication adherence in relation to community pharmacists' counselling during pregnancy. In order to collect suitable references, English written articles published from 2000 onwards were derived from databases Medline and Embase. Only studies conducted in Europe, North America and Australia were eligible for inclusion. Qualitative studies, reviews, Delphi studies, case reports and case series, editorials, commentaries, and conference abstracts were excluded. The quality of the individual studies and risk of bias across studies was not assessed specifically. Most studies on medication adherence and beliefs relied on women's self-enrollment in the study, and thus the risk of selection bias cannot be ruled out. It is therefore possible that our summarized results may in fact represent an underestimation of the true prevalence of low medication adherence and negative medication beliefs in pregnancy. Indeed, the sample of the included studies more often included women with higher education than the general birthing population in the country. This should be kept in mind when interpreting the results. Generally, the paucity of published studies on beliefs about medicines and medication adherence during pregnancy makes is difficult to draw sound conclusions, especially given the small sample sizes and the heterogeneity of study methods utilized. This has barely improved since previous reviews on medication adherence during pregnancy were published in 2012 [65, 66]. The application of different study methods also prevents efficient comparison of study findings [67]. Another limitation is that this was a review of quantitative studies, and therefore provides no insight into women's motives of negative beliefs and/or drivers for low medication adherence. Lastly, only four studies on community pharmacists' counselling practice were found;

three of those were published more than 10 years ago. The included studies on barriers were performed in different settings with low numbers of participants, hence limiting the generalizability of the findings.

Importantly, none of the included scales or instruments were specifically tailored to pregnancy nor validated in that population. These findings emphasize the urgent need to develop psychometric instruments that can validly measure medication adherence among pregnant women. The development, validation and implementation of pregnancy-specific questionnaires for studies evaluating women's beliefs is also encouraged, e.g. continuing on the pregnancy-specific statements of the Beliefs about Medicines Questionnaire that was developed by Nordeng in 2010 [28]. The use of these instruments could allow international comparison of data, including the impact of cultural beliefs, socio-demographic backgrounds and organization of health care on beliefs and risk perception. Future initiatives should also study the consequences of (unjustified) negative beliefs about medicines on medication adherence during pregnancy, and as previously mentioned, of low adherence on maternal and child pregnancy outcomes. The development, implementation and evaluation of strategies to reduce concerns, correct misperceptions and improve medication adherence during pregnancy is warranted.

4.3 Implications

The results from this review not only have clinical implications for community pharmacists, but for all HCPs. All HCPs should be aware of pregnant women's beliefs and perceptions about medicines during pregnancy. Negative beliefs on medicines and low health literacy can impair medication adherence and, consequently, fetal and maternal well-being. Given the unique situation of a pregnancy, women will balance their decisions about medication use between personal benefits of treatment and the potential harmful effect of medicines on the unborn child. Hence, pregnant women should be encouraged to discuss their beliefs and concerns with HCPs. Equally important, HCPs need to provide evidence-based information regarding medicines in pregnancy and to provide counselling to prevent misperception about medicines and overestimation of teratogenicity. In case a woman who is planning to get pregnant uses chronic medicines, counselling needs to be initiated prior to conception ('preconception care').

The findings presented in the current review clearly emphasize the major opportunities for pharmaceutical care research, continuous evidence-based education and undergraduate training with regard to medication counselling during pregnancy. So far, no randomized controlled studies on the impact of interventions to improve community pharmacists' knowledge, competencies and/or counselling practice related to pregnancy have been performed. However, training of pharmacists' counselling competencies has been shown to positively affect the quality of patient care [68]. Hence, pregnancy-related interventions, using blended learning programs, need to be developed and tested. Assessment of community pharmacists' performance in a real-life context using mystery shoppers should be considered [52, 69]. These interventions should be performed in controlled studies, either with a before-after or RCT design.

The results further call upon universities and on professional organizations involved in continuous professional development of community pharmacists. In order to overcome the barriers and areas of uncertainty, universities and organizations should focus more on fetal-maternal medicine and corresponding pharmacotherapy in their

courses. Academic assessment of counselling competencies can be performed using Objective Structured Clinical Examinations (OSCE) [70]. OSCEs have been highly recommended for competency assessments and evaluate higher stages of performance [71-73] .

5. Conclusion

This review has found that concerns about medication use in pregnancy and non-adherence are widespread among pregnant women. The limited evidence also shows that community pharmacists' counselling practice during pregnancy is insufficient, with insufficient knowledge and limited access to reliable information as main barriers. Furthermore, there is an urgent need for research and development of methods tailored to measure adherence and beliefs about medicines in pregnancy. As easily accessible health care professionals, community pharmacists play an important role in primary care by correcting misperceptions, providing evidence-based information, optimizing medication adherence and empowering pregnant women to make safe decisions about medication use, especially related to minor ailments and OTC medicines. However, the current review suggests that further education, training and research are required in order to support community pharmacists in fulfilling all the opportunities they have when counselling pregnant women.

6. Conflict of interest

The authors declare no conflict of interest.

7. Acknowledgements

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8. References

[1] Daw JR, Hanley GE, Greyson DL, Morgan SG. Prescription drug use during pregnancy in developed countries: a systematic review. Pharmacoepidemiol Drug Saf, 2011; 20: 895-902.

[2] Mitchell AA, Gilboa SM, Werler MM, Kelley KE, Louik C, Hernandez-Diaz S. Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. Am J Obstet Gynecol, 2011; 205: 51.e1-8.

[3] Palmsten K, Hernandez-Diaz S, Chambers CD, Mogun H, Lai S, Gilmer TP, Huybrechts KF. The Most Commonly Dispensed Prescription Medications Among Pregnant Women Enrolled in the U.S. Medicaid Program. Obstet Gynecol, 2015; 126: 465-73.

[4] Lupattelli A, Spigset O, Twigg MJ, Zagorodnikova K, Mardby AC, Moretti ME, Drozd M, Panchaud A, Hameen-Anttila K, Rieutord A, Gjergja Juraski R, Odalovic M, Kennedy D, Rudolf G, Juch H, Passier A, Bjornsdottir I, Nordeng H. Medication use in pregnancy: a cross-sectional, multinational web-based study. BMJ Open, 2014; 4: e004365.

[5] Werler MM, Mitchell AA, Hernandez-Diaz S, Honein MA. Use of over-the-counter medications during pregnancy. Am J Obstet Gynecol, 2005; 193: 771-7.

[6] Nordeng H, Ystrøm E, Einarson A. Perception of risk regarding the use of medications and other exposures during pregnancy. European Journal of Clinical Pharmacology, 2010; 66: 207-214.

[7] Lenz W, Knapp K. Thalidomide embryopathy. Arch Environ Health, 1962; 5: 100-5.

[8] Lammer EJ, Chen DT, Hoar RM, Agnish ND, Benke PJ, Braun JT, Curry CJ, Fernhoff PM, Grix AW, Jr., Lott IT, et al. Retinoic acid embryopathy. N Engl J Med, 1985; 313: 837-41.

[9] Weston J, Bromley R, Jackson CF, Adab N, Clayton-Smith J, Greenhalgh J, Hounsome J, McKay AJ, Tudur Smith C, Marson AG. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. Cochrane Database Syst Rev, 2016; 11: Cd010224.

[10] Hameen-Anttila K, Jyrkka J, Enlund H, Nordeng H, Lupattelli A, Kokki E. Medicines information needs during pregnancy: a multinational comparison. BMJ Open, 2013; 3: e002594.

[11] Peters SL, Lind JN, Humphrey JR, Friedman JM, Honein MA, Tassinari MS, Moore CA, Mathis LL, Broussard CS. Safe lists for medications in pregnancy: inadequate evidence base and inconsistent guidance from Web-based information, 2011. Pharmacoepidemiol Drug Saf, 2013; 22: 324-8.

[12] De Santis M, De Luca C, Quattrocchi T, Visconti D, Cesari E, Mappa I, Nobili E, Spagnuolo T, Caruso A. Use of the Internet by women seeking information about potentially teratogenic agents. Eur J Obstet Gynecol Reprod Biol, 2010; 151: 154-7.

[13] Hameen-Anttila K, Nordeng H, Kokki E, Jyrkka J, Lupattelli A, Vainio K, Enlund H. Multiple information sources and consequences of conflicting information about medicine use during pregnancy: a multinational Internet-based survey. J Med Internet Res, 2014; 16: e60.

[14] WHO. WHO recommendations on antenatal care for a positive pregnancy experience. 2016.

[15] Adam MM. Maternal morbidity. In: Adam MM, Eds. Perinatal epidemiology for public health practice. Springer, 2009; pp. 49-101.

[16] Taitel M, Jiang J, Rudkin K, Ewing S, Duncan I. The impact of pharmacist face-to-face counseling to improve medication adherence among patients initiating statin therapy. Patient Prefer Adherence, 2012; 6: 323-9.

[17] Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. Jama, 2006; 296: 2563-71.

[18] Mehuys E, Van Bortel L, De Bolle L, Van Tongelen I, Annemans L, Remon JP, Brusselle G. Effectiveness of pharmacist intervention for asthma control improvement. Eur Respir J, 2008; 31: 790-9.

[19] Mehuys E, Van Bortel L, De Bolle L, Van Tongelen I, Annemans L, Remon JP, Giri M. Effectiveness of a community pharmacist intervention in diabetes care: a randomized controlled trial. J Clin Pharm Ther, 2011; 36: 602-13.

[20] Tommelein E, Mehuys E, Van Hees T, Adriaens E, Van Bortel L, Christiaens T, Van Tongelen I, Remon JP, Boussery K, Brusselle G. Effectiveness of pharmaceutical care for patients with chronic obstructive

pulmonary disease (PHARMACOP): a randomized controlled trial. Br J Clin Pharmacol, 2014; 77: 756-66.
[21] Viktil KK, Blix HS. The impact of clinical pharmacists on drug-related problems and clinical outcomes. Basic Clin Pharmacol Toxicol, 2008; 102: 275-80.
[22] Bergkvist Christensen A, Holmbjer L, Midlov P, Hoglund P, Larsson L, Bondesson A, Eriksson T. The process of identifying, solving and preventing drug related problems in the LIMM-study. Int J Clin Pharm, 2011; 33: 1010-8.
[23] Smedberg J, Brathen M, Waka MS, Jacobsen AF, Gjerdalen G, Nordeng H. Medication use and drug-related problems among women at maternity wards-a cross-sectional study from two Norwegian hospitals. Eur J Clin Pharmacol, 2016; 72: 849-57.
[24] Thompson R, Whennan L, Liang J, Alderman C, Grzeskowiak LE. Investigating the Frequency and Nature of Medication-Related Problems in the Women's Health Unit of an Australian Tertiary Teaching Hospital. Ann Pharmacother, 2015; 49: 770-6.
[25] FIP. Statement of Policy on the effective utilisation of pharmacists in improving maternal, newborn and child health (MNCH). 2013.
[26] Heitmann K, Solheimsnes A, Havnen GC, Nordeng H, Holst L. Treatment of nausea and vomiting during pregnancy —a cross-sectional study among 712 Norwegian women. European Journal of Clinical Pharmacology, 2016; 72: 593-604.
[27] Mulder B, Bijlsma MJ, Schuiling-Veninga CCM, Morssink LP, van Puijenbroek E, Aarnoudse JG, Hak E, de Vries TW. Risks versus benefits of medication use during pregnancy: what do women perceive? Patient preference and adherence, 2018; 12: 1-8.
[28] Nordeng H, Koren G, Einarson A. Pregnant Women's Beliefs About Medications—A Study Among 866 Norwegian Women. Annals of Pharmacotherapy, 2010; 44: 1478-1484.
[29] Twigg MJ, Lupattelli A, Nordeng H. Women's beliefs about medication use during their pregnancy: a UK perspective. International Journal of Clinical Pharmacy, 2016; 38: 968-976.
[30] Patel JP, Auyeung V, Patel RK, Marsh MS, Green B, Arya R, Davies JG. Women's views on and adherence to low-molecular-weight heparin therapy during pregnancy and the puerperium. J Thromb Haemost, 2012; 10: 2526-34.
[31] Goodman JH. Women's attitudes, preferences, and perceived barriers to treatment for perinatal depression. Birth, 2009; 36: 60-9.
[32] Selinger CP, Eaden J, Selby W, Jones DB, Katelaris P, Chapman G, McDondald C, McLaughlin J, Leong RW, Lal S. Inflammatory bowel disease and pregnancy: lack of knowledge is associated with negative views. J Crohns Colitis, 2013; 7: e206-13.
[33] Jasper J, Goel R, Einarson A, Gallo M, Koren G. Effects of framing on teratogenic risk perception in pregnant women. Lancet, 2001; 358: 1237-8.
[34] Bonari L, Koren G, Einarson TR, Jasper JD, Taddio A, Einarson A. Use of antidepressants by pregnant women: evaluation of perception of risk, efficacy of evidence based counseling and determinants of decision making. Arch Womens Ment Health, 2005; 8: 214-20.
[35] Lupattelli A, Picinardi M, Einarson A, Nordeng H. Health literacy and its association with perception of teratogenic risks and health behavior during pregnancy. Patient Educ Couns, 2014; 96: 171-8.
[36] Duggan L, McCarthy S, Curtis LM, Wolf MS, Noone C, Higgins JR, O'Shea S, Sahm LJ. Associations between health literacy and beliefs about medicines in an Irish obstetric population. J Health Commun, 2014; 19 Suppl 2: 106-14.
[37] Petersen I, McCrea RL, Lupattelli A, Nordeng H. Women's perception of risks of adverse fetal pregnancy outcomes: a large-scale multinational survey. BMJ Open, 2015; 5: e007390.
[38] Widnes SF, Schjott J, Eide GE, Granas AG. Teratogenic risk perception and confidence in use of medicines in pairs of pregnant women and general practitioners based on patient information leaflets. Drug Saf, 2013; 36: 481-9.
[39] Hydery T, Price MK, Greenwood BC, Takeshita M, Kunte PS, Mauro RP, Lenz K, Jeffrey PL. Evaluation of Progesterone Utilization and Birth Outcomes in a State Medicaid Plan. Pharmacotherapy, 2017; 37: 1328-1334.

[40] Lupattelli A, Spigset O, Bjornsdottir I, Hameen-Anttila K, Mardby AC, Panchaud A, Juraski RG, Rudolf G, Odalovic M, Drozd M, Twigg MJ, Juch H, Moretti ME, Kennedy D, Rieutord A, Zagorodnikova K, Passier A, Nordeng H. Patterns and factors associated with low adherence to psychotropic medications during pregnancy--a cross-sectional, multinational web-based study. Depress Anxiety, 2015; 32: 426-36.

[41] Wu J, Davis-Ajami ML. Antidepressant treatment persistence in low-income, insured pregnant women. J Manag Care Spec Pharm, 2014; 20: 631-7.

[42] Abheiden CN, van Reuler AV, Fuijkschot WW, de Vries JI, Thijs A, de Boer MA. Aspirin adherence during high-risk pregnancies, a questionnaire study. Pregnancy Hypertens, 2016; 6: 350-355.

[43] Nielsen MJ, Norgaard M, Holland-Fisher P, Christensen LA. Self-reported antenatal adherence to medical treatment among pregnant women with Crohn's disease. Aliment Pharmacol Ther, 2010; 32: 49-58.

[44] Julsgaard M, Norgaard M, Hvas CL, Buck D, Christensen LA. Self-reported adherence to medical treatment prior to and during pregnancy among women with ulcerative colitis. Inflamm Bowel Dis, 2011; 17: 1573-80.

[45] Baarnes CB, Hansen AV, Ulrik CS. Enrolment in an Asthma Management Program during Pregnancy and Adherence with Inhaled Corticosteroids: The 'Management of Asthma during Pregnancy' Program. Respiration, 2016; 92: 9-15.

[46] Lupattelli A, Spigset O, Nordeng H. Adherence to medication for chronic disorders during pregnancy: results from a multinational study. Int J Clin Pharm, 2014; 36: 145-53.

[47] Juch H, Lupattelli A, Ystrom E, Verheyen S, Nordeng H. Medication adherence among pregnant women with hypothyroidism-missed opportunities to improve reproductive health? A cross-sectional, web-based study. Patient Educ Couns, 2016; 99: 1699-707.

[48] Sawicki E, Stewart K, Wong S, Leung L, Paul E, George J. Medication use for chronic health conditions by pregnant women attending an Australian maternity hospital. Aust N Z J Obstet Gynaecol, 2011; 51: 333-8.

[49] Odalovic M, Milankovic S, Holst L, Nordeng H, Heitmann K, Tasic L. Pharmacists counselling of pregnant women: Web-based, comparative study between Serbia and Norway. Midwifery, 2016; 40: 79-86.

[50] Damase-Michel C, Vie C, Lacroix I, Lapeyre-Mestre M, Montastruc JL. Drug counselling in pregnancy: an opinion survey of French community pharmacists. Pharmacoepidemiol Drug Saf, 2004; 13: 711-5.

[51] Schrempp S, Ryan-Haddad A, Gait KA. Pharmacist counseling of pregnant or lactating women. J Am Pharm Assoc (Wash), 2001; 41: 887-90.

[52] Lyszkiewicz DA, Gerichhausen S, Bjornsdottir I, Einarson TR, Koren G, Einarson A. Evidence based information on drug use during pregnancy: a survey of community pharmacists in three countries. Pharm World Sci, 2001; 23: 76-81.

[53] Bains S, Kitutu FE, Rahhal A, Abu Samaha R, Wilby KJ, Rowe H. Comparison of pharmacist knowledge, perceptions and training opportunities regarding maternal-fetal medicine in Canada, Qatar and Uganda. Can Pharm J (Ott), 2014; 147: 345-51.

[54] McAuley JW, Casey J, Long L. An evaluation of pharmacists' knowledge of women's issues in epilepsy. Epilepsy Behav, 2009; 14: 243-6.

[55] Hutchinson S, Mitchell K, Hansford D, Stewart D. Community pharmacists' views and experiences of counter-prescribing in pregnancy. International Journal of Pharmacy Practice, 2011; 9: 15-21.

[56] Zehnder S, Beutler M, Bruppacher R, Ehrenhofer T, Hersberger KE. Needs and use of drug information sources in community pharmacies: a questionnaire based survey in German-speaking Switzerland. Pharm World Sci, 2004; 26: 197-202.

[57] Tan MP, Koren G. Teratogen information service for pharmacists: a pilot study. J Popul Ther Clin Pharmacol, 2011; 18: e377-89.

[58] Gatti ME, Jacobson KL, Gazmararian JA, Schmotzer B, Kripalani S. Relationships between beliefs about medications and adherence. Am J Health Syst Pharm, 2009; 66: 657-64.

[59] Mardby AC, Akerlind I, Jorgensen T. Beliefs about medicines and self-reported adherence among pharmacy clients. Patient Educ Couns, 2007; 69: 158-64.

[60] Foot H, La Caze A, Gujral G, Cottrell N. The necessity-concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. Patient Educ Couns, 2016; 99: 706-17.
[61] Widnes SF, Schjott J, Granas AG. Risk perception and medicines information needs in pregnant women with epilepsy--a qualitative study. Seizure, 2012; 21: 597-602.
[62] Horne R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the Necessity-Concerns Framework. PLoS One, 2013; 8: e80633.
[63] Conover EA, Polifka JE. The art and science of teratogen risk communication. Am J Med Genet C Semin Med Genet, 2011; 157c: 227-33.
[64] Van Calsteren K, Gersak K, Sundseth H, Klingmann I, Dewulf L, Van Assche A, Mahmood T. Position statement from the European Board and College of Obstetrics & Gynaecology (EBCOG): The use of medicines during pregnancy - call for action. Eur J Obstet Gynecol Reprod Biol, 2016; 201: 189-91.
[65] Oladejo M, Bewley S. Adherence in pregnancy: a systematic review of the literature. Fetal and Maternal Medicine Review, 2012; 23: 201-229.
[66] Matsui D. Adherence with Drug Therapy in Pregnancy. Obstetrics and Gynecology International, 2012; 2012: 5.
[67] Nguyen TM, La Caze A, Cottrell N. What are validated self-report adherence scales really measuring?: a systematic review. Br J Clin Pharmacol, 2014; 77: 427-45.
[68] Liekens S, Vandael E, Roter D, Larson S, Smits T, Laekeman G, Foulon V. Impact of training on pharmacists' counseling of patients starting antidepressant therapy. Patient Educ Couns, 2014; 94: 110-5.
[69] Watson M, Norris P, Granas A. A systematic review of the use of simulated patients and pharmacy practice research. International Journal of Pharmacy Practice, 2006; 14: 83-93.
[70] Harden RM. What is an OSCE? Med Teach, 1988; 10: 19-22.
[71] Austin Z, O'Byrne C, Pugsley J, Munoz LQ. Development and Validation Processes for an Objective Structured Clinical Examination (OSCE) for Entry-to-Practice Certification in Pharmacy: The Canadian Experience. American Journal of Pharmaceutical Education, 2003; 67: 76.
[72] Sturpe DA. Objective structured clinical examinations in doctor of pharmacy programs in the United States. Am J Pharm Educ, 2010; 74: 148.
[73] Shirwaikar A. Objective structured clinical examination (OSCE) in pharmacy education - a trend. Pharm Pract (Granada), 2015; 13: 627.

Supplementary Material

Overview of the concepts and corresponding search terms for the three search strategies.

	Beliefs about medicines	**Medication adherence**	**Pharmacists' counselling**
Concept 1	Pregnancy; Pregnant Women; Pregnancies, Gestation	Pregnancy; Pregnant Women; Pregnancies, Gestation	Pregnancy; Pregnant Women; Pregnancies, Gestation
Concept 2	Prescription Drugs; Nonprescription Drugs; Pharmaceutical Preparations; Drugs; Medicines; Medication, Medication usage	Prescription Drugs; Nonprescription Drugs; Pharmaceutical Preparations; Drugs; Medicines; Medication, Medication usage	Pharmacist; Pharmacists; Community Pharmacist; Community Pharmacists; Pharmacy; Community Pharmacy Services
Concept 3	Beliefs about medication; Beliefs about medicines; Beliefs about medicines questionnaire; Perception; Risk perception; Health knowledge, attitudes, practice; Attitude to health;	Medication adherence; Medication nonadherence; Medication persistence; Medication compliance; Medication non-compliance; Drug persistence	Counseling; Counselling; Patient Counseling; Role; Education; Pharmacy education; Pharmaceutical education; Education, pharmacy; Education, pharmacy, continuing; Continuing education; Patient simulation