The impact of gender and sex in psoriasis: What to be aware of when treating women with psoriasis

Carole Guillet, MD, Corsin Seeli, MMed, Meienberger Nina, MMed, Lara Valeska Maul, MD, Julia-Tatjana Maul, MD*

ABSTRACT
Background: Psoriasis is a common chronic inflammatory skin disease with an exceptionally high burden for women. Sex-dependent differences in disease manifestation, severity, treatment choices, subjective disease perception, and the impact on quality of life and risk factors are described and comprehensively discussed.

Methods: A literature search was conducted using MEDLINE (PubMed) and the Cochrane Library for systematic reviews to investigate the challenges in treating women with psoriasis.

Results and conclusions: The incidence, prevalence, and manifestation of psoriasis of the skin are similar between different sexes. Genetic and environmental factors such as obesity and metabolic syndrome are risk factors and are not equally relevant or pronounced in women and men. Overall, women have a lower disease severity measured by the Psoriasis Area Severity Index, which is associated with a higher impairment of their life quality measured by the Dermatology Life Quality Index compared with men. In addition, women with psoriasis are more likely to have depression than men. Hormonal factors affect psoriasis, with a correlation of high estrogen levels and improvement of psoriasis. Data regarding differences in prescribing patterns of systemic treatments and the severity of psoriasis are not entirely consistent. Registry studies show that men tend to have more severe psoriasis and, in some cases, are prescribed systemic therapies more frequently. Women tend to respond better to systemic treatments and to experience more adverse events. Treatment options are the same for both sexes, except during pregnancy and lactation. Various treatment options are contraindicated due to fear of fetal or neonate harm and lack of data. Topical steroids can be prescribed with a high degree of safety during pregnancy. For other topical therapies (calcineurin inhibitors and vitamin D analogs), no studies of adverse effects in pregnancy are available, and safety data mainly stem from studies examining effects after systemic administration. Antitumor necrosis factor monoclonal antibodies (except for certolizumab pegol) have been associated with a possible increased risk of preterm birth, low gestational age, and cesarean deliveries. Prospective data on the safety of biologics other than antitumor necrosis factor-alpha antibodies to accurately assess whether novel biologics (eg, anti-interleukin 17, 12/23, 23) can be used for systemic therapy in pregnancy are lacking or currently being conducted.

Keywords: Differences, gender, pregnancy, psoriasis

Introduction
Psoriasis is a chronic, inflammatory skin disease with a prevalence of 1% to 4% in countries with a predominantly Caucasian population.1–5 Sex-dependent differences in epidemiology, disease manifestation, comorbidities, and treatment outcomes were observed in many diseases and are increasingly relevant in medical science.6–10 Sex-dependent differences were reported for psoriasis disease manifestation, severity, treatment choices, subjective disease perception, and the impact on life quality.11,12 Understanding such disparities could improve care in women with psoriasis, yield more effective and satisfactory treatment outcomes, and reduce inequalities in care.

Methods

Objectives
This narrative literature review highlights gender and sex-specific aspects and considerations when treating women with psoriasis of the skin.

Search methods
A literature search was conducted through March 3, 2021, using MEDLINE (PubMed) and the Cochrane Library for systematic reviews. The keywords included “gender, sex, female, male, women, woman, men, man, dermatology, psoriasis, prevalence, incidence, hormones, pregnancy, lactation, transplacental, transplacental transfer, quality of life (QoL), mental health, genetic risk factors, HLA-Cw6, psoriasis susceptibility 1 gene (PSORS1), chromosome 6p21, treatment, biologic treatment, biologics, adalimumab, brodalumab, certolizumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab, apremilast, cyclosporine, neotigason, fumaric acid, fumarate, tacrolimus, calcipotriol, and calcitriol.” Pivotal papers describing novel insights and society guidelines were considered. Additional studies were found using bibliographical information of relevant articles. To obtain a
Implications for patients and their families: What is known about this subject regarding women and their families?
- Women of childbearing age can be affected by psoriasis and need effective treatment in all stages of their lives, including pregnancy and lactation.
- Many treatments are not approved for use during pregnancy and lactation.
- Women with psoriasis have many comorbidities that should be recognized and treated.
- Women have more psoriasis (as measured by DLQI) than men, and prescribing patterns differ between genders.

What is new from this article as messages for women and their families?
- This review offers a concise overview of studies examining differences in psoriasis between men and women regarding disease burden, risk factors and treatment prescription patterns, treatment response, and adverse events.
- Topical steroids can be prescribed with a high degree of safety during pregnancy. In contrast, other topical therapies (calcineurin inhibitors and vitamin D analogs), studies on adverse effects in pregnancy are lacking, and safety data mainly stem from studies assessing effects after systemic administration.
- Safety studies on monoclonal antibodies, especially anti-TNF alpha, are inconsistent and difficult to compare. Recent data from a large population-based registry study showed that anti-TNF alpha agents that can cross the placental barrier could be associated with an increased risk for preterm birth, cesarean section, and small for gestational age.
- Postmarketing data for other biological agents such as anti-IL-17, anti-IL-23, and anti-IL-12/13 monoclonal antibodies are not yet or only partially available, and appropriate studies are now being carried out.

Results
Epidemiology
The mean age of onset of psoriasis is at 33 years. However, it presents at a younger age than in men than in females. In women, psoriasis usually manifests at 16 to 22 years or 55 to 60 years. In men, these 2 peaks for age at onset occur more around 30 to 39 years and 60 to 79 years. This bimodal peak is associated with the 2 different subtypes of psoriasis, type I with onset before the age of 40 years (75% of cases) and type II with onset after 40 years.4,5

In a recent systematic review, 159 studies reporting on the prevalence of psoriasis were identified, some of which compare the prevalence of the disease in women and men.14,15 Some studies included in this systematic review and also a newer study from Denmark with individuals of all ages demonstrated a higher prevalence of psoriasis in females,16-18 and other studies showed the opposite, with the male population having a higher prevalence.19,20 However, in various other studies, the prevalence of psoriasis between the sexes did not differ.1,13,14-21-27

In a Danish cross-sectional study in children with autoimmune diseases, psoriasis prevalence was higher in girls than in boys.18

Studies reporting on the incidence of psoriasis are scarcer and mainly conducted in western or eastern Europe and North America.14 Studies about variations in incidence rates by sex are somewhat contradictory. In some studies, the incidence was higher in women,16,29,30 and some in men.31-32 In one population-based study from the United States, analyzing the incidence of adult-onset psoriasis between 1970 and 2000, the overall incidence of psoriasis in men was higher than in women (85.5 per 100,000 person-years in men vs 73.2 in women). The highest incidence for men was found in their seventh decade of life (115.3/100,000), for women in their sixth (90.7/100,000), in which they also have a higher incidence than men.31 In children, one study from the United States showed a higher incidence rate in girls than in boys who are ≤18 years of age (43.9 vs 37.9/100,000 person-years).32,33

There is no robust evidence that the prevalence and incidence of psoriasis differ between men and women. Quite clearly, other factors, such as genetic predisposition and environmental factors, are more potent risk factors for the development of psoriasis.4

Gender-related risk factors for the development and severity of psoriasis
Genetic factors
Psoriasis is thought to be caused by the interaction of multiple genetic and environmental risk factors.14 Its incidence is higher among first- and second-degree relatives and more concordant among monozygotic than dizygotic twins. Several genomic regions (loci) were identified in linkage studies, with PSORS1 being the most important.14 PSORS1 is located on chromosome 6p21.3 and is an important locus for psoriasis susceptibility. PSORS1 is responsible for approximately 35% to 50% of the heritability of the disease.22 HLA-Cw6 is located on the PSORS1 locus and is an important psoriasis susceptibility allele.26-28 An association of HLA-Cw6 positivity with early-onset psoriasis and a more severe and unstable course was identified.14,29-31

Few studies compared the genetic differences between men and women who have psoriasis. In one study from Iceland, women who were HLA-Cw6-positive (Cw6+) had an earlier disease onset than HLA-Cw6-positive (Cw6+) men and experienced remission of psoriasis during pregnancy more frequently than HLA-Cw6-negative (Cw6–) women.40 A small study showed a positive correlation of female sex with the Cw6+ allele and the CCHCR1+ allele (earlier HCR1). CCHCR1 is a gene on the PSORS1 locus on chromosome 6p21.3. In this study, CCHCR1+ positivity was negatively correlated with disease severity.41

Genetic factors and polymorphisms could modify the disease course, manifestation, and treatment response in patients with psoriasis of the skin. Currently, no genetic testing or biomarkers are being used to assess these factors in clinical practice but could become relevant in the future.42

Other risk factors
Various studies have identified obesity as a risk factor for the development of psoriasis in both women and men. Obesity is associated with a more severe psoriasis phenotype.24-42 Even though psoriasis and body mass index seem to correlate equally with both sexes, psoriasis, and metabolic syndrome (MetS) do not.41 In a large population-based study in Germany (n = 3723), the probability of a psoriasis diagnosis was higher in women with MetS and body mass index ≥30 than in men. Additionally, in women with psoriasis, several cardiometabolic risk factors (waist...
circumference, obesity, elevated triglycerides, elevated blood glucose, diabetes mellitus, metabolic syndrome, intake of antihypertensives, and antidiabetics) were more prevalent than in women who do not have psoriasis—a reverse finding was true for men.46

Contrarily to this, a uniformly higher prevalence of MetS in both men and women with psoriasis was found in a large cross-sectional study (n = 10,521) in Norway.47,48

In the general population, cardiovascular risk factors and metabolic diseases are unevenly distributed between men and women. The mechanisms that explain sex-specific differences in these diseases are not entirely understood but investigated intensively.49,50 Differences in gene expression from sex chromosomes could lead to differences in cardiovascular function.51 However, it is unclear whether and how sex influences psoriasis and cardiovascular disease. Cardiometabolic disease associated with psoriasis and the corresponding sex-specific analysis requires further investigation. It seems feasible to screen psoriasis patients and especially women specifically for cardiometabolic disease, in the short term.

In addition, smoking and alcohol consumption contribute to psoriasis severity, and the association of both factors is higher in men than in women.45,48,52,53 These findings may be partially explained by the higher alcohol consumption and smoking rates observed in men than women.45,53

Clinical aspects, quality of life, and mental health

Disease severity and clinical manifestation

Psoriasis has many different clinical phenotypes.4 No clear evidence regarding differences in psoriasis morphology between sexes exists.54 The question of whether men have more severe psoriasis than women was first investigated in 1945,55 and various studies have found severe forms of psoriasis to be more common in men than in women.58,59 In a large cross-sectional in Sweden (PsoReg, n = 5438 patients with moderate-to-severe psoriasis), men had a higher median Psoriasis Area and Severity Index (PASI) at first presentation than women (7.2 vs 5.4, P < 0.001).57 In addition, certain studies have shown that men are more likely to be prescribed systemic therapies. It has been hypothesized that the reason for this may be the difference in disease severity.60,61

Quality of life and mental health

Psoriasis has adverse effects on QoL, such as the impact of diabetes, ischemic heart disease, and cancer.62 Psoriasis affects QoL to a greater extent in women than in men, despite their lower mean PASI (as measured by the Dermatology Life Quality Index [DLQI]).57 Compared with the general population, psoriasis patients are more likely to be diagnosed with depression,63 and female psoriasis patients are more likely to have depression than males,64-66 which can potentially lead to a lower QoL in women who have psoriasis.64 In a polish cross-sectional study (n = 219), the risk for depression in female psoriasis patients was significantly higher than in males.65 Interestingly, the severity of psoriasis did not correlate with the degree of deterioration in mental health or QoL.64 Factors that could affect QoL in psoriasis patients are the degrees of perceived stigmatization, the burden of disease, and treatment expectations, which were all higher in women.67,68

Identifying depression and factors leading to a deterioration in mental health or QoL in psoriasis patients, especially in women, is essential since psychiatric diseases are associated with poor treatment response, poor treatment adherence, and...
### Table 1

**Summary of evidence related to use of topical, conventional systemic and biologic therapies in pregnant women/women of childbearing potential**

| Route of administration | Drug | Systemic absorption, transplacental transfer | Maternal risk (e.g., preeclampsia, gestational diabetes) | Fetal and neonate risk | References |
|-------------------------|------|---------------------------------------------|----------------------------------------------------------|------------------------|------------|
| Topical                 | Corticosteroids | Possible | Exist with oral use | Conflicting evidence regarding low birth weight if very high cumulative dose applied topically | 108-111 |
|                         | Pimecrolimus, Tacrolimus | Very low risk of systemic absorption due to large molecule size, transplacental transfer upon systemic administration possible | Not investigated upon topical administration | No direct or indirectly harming effects upon topical administration. Toxicities upon systemic administration. | 112-115 |
|                         | Calcipotriol/ Calcitriol | Possible | Not investigated upon topical administration | No teratogenicity in embryo-fetal studies with oral application of calcitriol in rats. Subcutaneous application in rabbits lead both to maternal toxicity and developmental toxicity at very high doses. Skeletal abnormalities associated with systemic use. Use <25–50 g/week for 3–4 weeks according to expert opinion. | 118, 119 |
| Phototherapy            | Narrowband UVB | Not applicable | Folic acid deficiency | Neural tube defects secondary to folic acid deficiency | 123 |
|                         | Cyclosporine | Yes | Hypertension in pregnancy, gestational diabetes mellitus, preeclampsia, infection | Potential risk of low birth weight, no increased risk of congenital malformations or fetal death | 124-129 |
|                         | Certolizumab | Very low level in umbilical cord blood | No | No increased risk of miscarriage, congenital malformation, fetal death, risk of infection in the first year of life, no impairment of development | 126-132 |
|                         | Adalimumab | Yes (presumably) | No signals specific to maternal risk | Conflicting evidence regarding risk for preterm birth, small for gestational age and cesarean delivery | 128,134,140-142 |
|                         | Etanercept | Yes | No signals specific to maternal risk | - Conflicting evidence regarding risk for preterm birth, small for gestational age and cesarean delivery | 131,135,136,140 |
|                         | Infliximab | Yes | No signals specific to maternal risk | - VACTERL-association | 132,133,140 |
|                         | Ustekinumab | Yes | Very limited data | No signals specific to maternal risk | 145,146 |
|                         | Guselkumab | Presumably yes | Very limited data | No signals specific to maternal risk | 148,153 |
|                         | Risankizumab | Presumably yes | Very limited data | Limited data. | 147,149 |
|                         | Tildrakizumab | Presumably yes | Very limited data | No signals specific to maternal risk | 140,153 |
|                         | Ixekizumab | Presumably yes | Very limited data | Limited data. | 140,149 |
|                         | Secukinumab | Presumably yes | Very limited data | No signals specific to maternal risk | 148 |

Table extended and adapted from Yeung et al. [151]

UVB, ultraviolet B.
inferior outcomes and are an additional source of disability and suffering.\(^{69-72}\) Additionally, depression is associated with an elevated risk of stroke, myocardial infarction, and cardiovascular death in patients with psoriasis.\(^2\)

**Effects of female sex hormones on the skin and psoriasis**

Female sex hormones, notably estrogen, can have beneficial effects on skin aging, water-binding capacity, and wound healing.\(^{73-76}\) For example, transdermal estrogen application in perimenopausal women increases skin water-holding capacity potentially by improving stratum corneum barrier function.\(^77\) Beyond that, female sex hormones also affect the disease manifestation and severity of psoriasis. High estrogen levels, as seen in pregnancy, and increased estrogen to progesterone-ratios correlate with improvement of psoriasis; progesterone alone, however, does not affect psoriasis.\(^{78}\) Several studies reported an improvement of psoriasis during pregnancy in about 50% of psoriasis patients, whereas approximately one-quarter experienced worsening during pregnancy, and one-quarter reported no effect.\(^{78-80}\) So far, it is unknown, whether the improvement of psoriasis is driven by increased estrogen levels alone or in combination with elevated cortisol levels.\(^81\)

Sex hormones, however, influence the cytokine imbalances in psoriasis patients. Low estrogen levels are associated with predominantly Th1-cell immune responses and proinflammatory cytokines, whereas high levels of estrogen promote upregulation of Th2 cell-dependent cytokines.\(^82\) Accordingly, estrogens are negative regulators of tumor necrosis factor (TNF), which plays a crucial role in psoriasis pathogenesis. Its production is also increased during the luteal phase of the menstrual cycle when low estrogen levels. This explains the sometimes-observed improvement of psoriasis during the menstrual cycles.\(^82,83\)

**Pregnancy, pregnancy outcomes, and fertility**

Several studies address whether chronic inflammation as in psoriasis- and psoriasis-related comorbidities increase the risk of complications during pregnancy or not.\(^79\) In a systematic review of observational studies assessing adverse pregnancy outcomes in psoriasis, no clear evidence of increased adverse effects could be found in a total of 4756 pregnancies, and no clear stratification of results between mild and moderate/severe disease was made in all included studies.\(^84\) In a population-based cohort study (total: 8097 births in 6103 women with psoriasis and 964 births in 753 women with psoriasis arthritis), an increased risk for hypertension, preclampsia, gestational diabetes, elective, and emergency cesarean delivery was found mainly in women with severe psoriasis.\(^85\) In a longitudinal study (Psoriasis Longitudinal Assessment and Registry) assessing pregnancy outcomes (women with moderate-to-severe psoriasis), 298 pregnancies of 220 women resulted in 244 (81.9%) live births.\(^86\) This study’s pregnancy-related adverse events (congenital disabilities, spontaneous abortion, neonatal problems) were comparable to the general US population. Outcomes in women receiving biologics were like those receiving conventional systemic therapies. However, the annual fertility rate in the study population (women with psoriasis and of childbearing age) was lower than in the general US population in 2018 (18.9 pregnancies vs 59.1 pregnancies in 1000 women of childbearing age).\(^87\) Similarly, in the Spanish Registry of Systemic Treatments in Psoriasis (Biobadaderm), the fertility rate among women of childbearing age with moderate-to-severe psoriasis was lower than that of women of the same age in the general Spanish population.\(^88\)

When counseling psoriasis patients with a desire to have children, one must keep in mind that most studies investigating pregnancy outcomes and fertility were conducted in patients with moderate-to-severe psoriasis. Data regarding the impact of psoriasis on women’s fertility is controversial, especially since most studies do not discriminate between mild- and moderate-to-severe psoriasis. Although psoriasis probably does not directly impact fertility, a systemic inflammatory state as in psoriasis could be responsible for the overall reduction of pregnancies, as observed in the Psoriasis Longitudinal Assessment and Registry and Spanish Registry of Systemic Treatments in Psoriasis (Biobadaderm). Compared with women without psoriasis, women with psoriasis have an elevated risk of comorbidity (eg, metabolic syndrome, diabetes, cardiovascular disease), which could also affect their fertility.\(^87,88\) In a recent Danish cross-sectional study, women with psoriasis had higher odds for having other immune-mediated diseases such as spondylarthritides, Crohn’s disease, and psoriatic arthritis.\(^89\)

In autoimmune disorders, a dysregulated balance of Th17 and regulatory T cells is characteristic and an increase of Th1 and Th17 cells in the pathogenesis of psoriasis is well established.\(^90,91\) This immune dysregulation could affect pregnancy outcomes or fertility. In psoriasis, rheumatoid arthritis, and inflammatory bowel disease, proinflammatory cytokines are elevated in the mother’s serum and umbilical cord.\(^91\) In particular, the cytokine milieu is critical for successful embryo implantation. Proinflammatory cytokines produced by Th1 cells are embryotoxic and can complicate fetoplacental development (Fig. 1). To prevent fetal rejection, the immune system changes during pregnancy; hormonal changes lead to a reduction in the Th1 cell-dependent immune response and enhance the Th2-dependent immune response and increase the regulatory T-cell subset, which might prevent cell-mediated rejection of the fetus.\(^91\) Subsequently, this reduction in proinflammatory Th1 and Th17 cytokines play a role in improving psoriasis during pregnancy.\(^92,93\)

**Treatment, treatment response, side effects, and discontinuation**

Various treatment options are available for the management of psoriasis (Table 1). These can be selected based on disease severity, comorbidities, patient preferences, and expectancies, including topical treatments, phototherapy, photochemotherapy, and systemic agents.\(^95,96\) Usually, the severity of psoriasis is divided into 2 categories: mild psoriasis and moderate-to-severe psoriasis. Mild disease usually requires only topical treatment, whereas additional phototherapy or systemic therapy may be necessary for moderate-to-severe disease.\(^96\) Besides severity, the location of the skin lesions (eg, on hands and feet, on face) and the presence or absence of joint involvement (psoriasis arthritis) play a significant role in the treatment selection. New systemic treatments are very efficacious; however, the cost is also high. Therefore, conventional therapies such as phototherapy and methotrexate still play an important role when treating patients with psoriasis.\(^97\) In principle, all forms of therapy are available independent of sex. However, depending on sex, differences in prescribing patterns were identified in a survey of 1000 dermatologists in the United States. The treatment decision in women was more driven by the safety of the treatment; therefore, women received medications with a lower perceived risk for side effects than men.\(^98\)

Many studies have found differences in the prescription patterns of psoriasis treatments. In a retrospective study in Sweden (n = 326, 51% men), women were less likely to receive phototherapy. They were more likely to receive topical treatments for home administration than men with the same psoriasis disease severity.\(^99\)

In a Swedish population-based cohort study (data from the nationwide quality registry of psoriasis patients, n = 2294, 58.9% men), men were more severely affected by psoriasis and more likely to receive systemic treatment.\(^58\) Contrarily to this, in a Spanish cohort study (n = 2881; 58.3% men), women had a 33% higher chance of being prescribed a modern therapeutic...
effects and treatment discontinuation was higher in women, 103, 315, 59.7% men) showed that women were less satisfied with systemic use. 118,119 Data with humans are not available. Mental toxicity were observed upon subcutaneous administration of tazarotene.107,117,120,121

should be avoided during pregnancy and lactation due to its teratogenic potential.107,117,120,121 Prospective data from the Dutch psoriasis registry (n = 315, 59.7% men) showed that women were less satisfied with biological treatment regarding global satisfaction and side effects and treatment discontinuation was higher in women, whereas, in an open comparator study from the United Kingdom (n = 201, 44.2% men), treatment adherence was higher in women.104

Treatment and safety concerns during pregnancy and quality of evidence of reporting studies

Even though psoriasis improves in approximately 50% of women during pregnancy, effective treatment is needed, especially for moderate-to-severe psoriasis. In the postpartum period, psoriasis usually returns to baseline before conception. 76,40 In usual psoriasis patient care, pregnant psoriasis patients should be treated according to their subjective and objective disease severity. However, various topical and systemic treatments should be avoided due to patient, fetal or neonate risk.103 Since pregnant women are usually excluded from clinical trials, and many discontinue treatment during pregnancy, data on treatment are limited.

Topical treatments

Emollients are safe to use during pregnancy and lactation.106,107 In mild and moderate disease, topical treatment with corticosteroids is possible. However, topical steroids can have systemic effects and side effects in pregnancy.104,108 Several studies have addressed the impact of topical steroids on the fetus and neonate, and data are conflicting.

In a systematic review, a very high cumulatively applied amount of topical corticosteroids during pregnancy was associated with low birth weight.109 However, a recent large-scale, retrospective cohort study from Denmark evaluating 60,498 pregnancies in which topical corticosteroids had been used had refuted this assumption.111 Therefore, potent topical corticosteroids are probably also safe during pregnancy.

Topical use of calcineurin inhibitors (TCI), namely pimecrolimus and tacrolimus, cannot be generally recommended in pregnancy. TCI are very large molecules, and therefore the penetration in the skin and systemic absorption is not very likely if the skin barrier is intact. Nonetheless, studies in humans on adverse pregnancy outcomes after use of TCI do not exist, and toxicity studies stem from systemic application mainly in organ transplant patients.112-113 The use on small surfaces and not directly on the mammary during breastfeeding is probably safe.114,116

Topical vitamin D analogs (calcitriol, calcipotriol) should be used with caution in pregnancy and only if no alternatives exist.115 In animal studies with rabbits, maternal and developmental toxicity were observed upon subcutaneous administration at high doses, and skeletal abnormalities were associated with systemic use.118,119 Data with humans are not available. Coal tar and anthralin should be avoided due to lack of data and mutagenic/carcinogenic potential in animal studies. Tazarotene should be avoided during pregnancy and lactation due to its teratogenic potential.107,117,120,121

In general, the administration of topical drugs is associated with potentially harmful consequences for the unborn child through systemic absorption and transplacental transfer.

For many topical agents, no studies or only animal studies are available regarding their effect upon topical use in pregnancy. Treatment recommendations are primarily based on studies in which these drugs were used orally.

Phototherapy

In moderate-to-severe disease and insufficient topical treatments, phototherapy can be used during pregnancy but some safety concerns exist.122,123 Narrowband ultraviolet B exposure but not ultraviolet A exposure degrades folate in a dose-dependent manner and can therefore only be recommended in pregnancy if an adequate folic acid supply is ensured. Even in women of childbearing age, folic acid substitution during phototherapy with narrowband ultraviolet B should be considered to prevent congenital disabilities in unplanned pregnancies.123

Systemic treatments

Most traditional systemic treatments (methotrexate, retinoids) are contraindicated in pregnancy and women wishing to conceive due to high risks of teratogenicity. Women wanting to conceive should stop acitretin at least 3 years before conception and methotrexate and fumarates at least 6 months before conception.107 Cyclosporine can be prescribed with reservations. Reproductive toxicity has been demonstrated in animal studies in rats and rabbits. However, data on the use of cyclosporine in pregnant women with psoriasis are limited. The data of cyclosporine mainly stem from experience in transplantation medicine. Following transplantation, pregnant women treated with cyclosporine are at increased risk for preterm delivery.124-126 There are a limited number of observations of children up to 7 years of age who were exposed to cyclosporine in utero. Renal function and blood pressure in these children were normal, however, a risk of prematurity and low birth weight was associated.117,120

Concerning the use of biological drugs during pregnancy, postauthorization data are available for adalimumab, certolizumab pegol, etanercept, and infliximab. Only limited data exist for other biologics licensed for the use in psoriasis in women of childbearing age or are currently being collected in prospective studies and registries.122 When clinically needed, certolizumab pegol can be used during pregnancy and lactation in women with moderate-to-severe psoriasis.126 Certolizumab pegol is a pegylated Fc-free anti-TNF-α Fab fragment, which does not actively cross the placental barrier during pregnancy and shows no to minimal transfer from plasma to breast milk during lactation.129,130 In January 2018, European Medicines Agency approved a label change making it the first anti-TNF-α and first biological for potential use in pregnancy and lactation. Unlike certolizumab pegol, other anti-TNF-α monoclonal antibodies were found in umbilical cord blood in varying concentrations.131-133 Various studies, especially from gastroenterology and rheumatology, have investigated whether anti-TNF-α monoclonal antibodies harm pregnancy outcomes ranging from single case reports and small case series134-135 of pregnancies during infliximab or etanercept treatment to extensive retrospective cohort studies136 and prospective (registry) studies133,135 and observational studies.140-142 The generalizability of results is limited due to heterogeneous study designs and variable outcomes and endpoints. A meta-analysis by Komaki comparing 13 different studies showed wide confidence intervals, especially for adverse event outcomes, which reduces the power of these safety studies.143 Nevertheless,
this meta-analysis shows an increased risk for preterm birth (relative risk: 1.36), comparable to the one estimated in a recent registry study from Denmark (relative risk: 1.56). In this study from Denmark comparing >1000 births of anti-TNF-α monoclonal antibody exposed infants with 9399 infants to women treated with nonbiologic systemic treatments (for inflammatory bowel diseases, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and psoriasis), anti-TNF-α monoclonal antibody exposure was also associated with increased risk for emergency cesarean section and small for gestational age.

Overall, anti-TNF-α drugs, except certolizumab pegol, are transmitted placidentally and detected weeks after birth. Adverse outcomes are not impossible and could also result from the increased risk of infection associated with anti-TNF-α therapy during pregnancy, which is also an independent risk for preterm delivery.

Postmarketing data are lacking for newer drugs such as IL-17 monoclonal antibodies and IL-23 p19 monoclonal antibodies. There are very few cases of unplanned pregnancies in premarketing studies, most of which resulted in pregnancy discontinuation. In animal studies, mainly conducted on monkeys, few safety signals concerning fetal risk were observed. More data are now being collected in several prospective registry studies.

In a cohort study in patients with Crohn’s disease, 29 pregnancies during ustekinumab treatment resulted in 26 (90%) live births, 2 (7%) spontaneous abortions, and 1 (3%) elective termination, which is comparable with rates among the general population. A few reports show no increased rate of abortion or congenital malformation for exposure to ixekizumab, secukinumab, or tildrakizumab during premarketing clinical trials. Due to animal studies in cynomolgus monkeys showing a dose-dependent increased risk for abortion and embryofetal death, apremilast is contraindicated during pregnancy.

There are many safe treatment options for pregnant and breastfeeding women with psoriasis, including topical therapies, light therapy, and highly effective systemic therapies such as certolizumab pegol. Clinical trials on the safety of risankizumab (NCT04846959), tildrakizumab (NCT03992729), ustekinumab, and guselkumab (NCT02103361) in pregnancy are ongoing and will give us more information on the safety of these drugs in pregnancy.

**Conclusion**

Gender medicine is an essential and new field of research. For decades, pregnant women have been automatically excluded from clinical trials. Using psoriasis as an example, we have shown in this review that women have more psoriasis than men do, respond differently to treatments, and that differences in prescribing patterns exist. Women with psoriasis have a lower socioeconomic status and higher use of health resources, including prescription analgesics. Regarding the treatment of women of childbearing age, many safe options exist. However, safety concerns exist for novel, biological therapies during pregnancy and lactation. Today, postmarketing studies are lacking for many of these drugs, and pregnancy-specific registries are needed to characterize the effect of psoriasis and its treatment more fully on birth outcomes.

In the future, we believe that therapies will be tailored, for example, the biologic drug may only be selected after a more precise determination of the cytokine profile or, for example, metabolic markers. In this situation, it needs to be explored whether there are differences in disease phenotype between women and men and how this might influence therapy choices. Furthermore, there is a need to examine whether different therapies result in different responses and, if so, whether specific treatments are superior for women than for men or vice versa. These questions could be addressed in prospective registries, and appropriate guidelines could result.

**Author contributions**

- **CG:** Conception and design, acquisition/analysis, and interpretation, drafting of the article, final approval, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **CS, NM:** Conception and design, drafting of the article, final approval, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **JTM, LVM:** Conception and design, data interpretation, critical revision for important intellectual content, final approval, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **JTM:** Conception and design, acquisition/analysis, and data interpretation, drafting of the article, critical revision for important intellectual content, final approval, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Conflicts of interest**

- **CG:** served as advisor and participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Novartis; received a research grant from EAACI (European Academy of Allergy and Clinical Immunology) to perform research outside of the submitted work at the Department of Dermatology of Charité—Universitätsmedizin, Berlin.
- **CS, NM:** None.
- **LVM:** served as advisor or received speaking fees or participated in clinical trials sponsored by Amgen, BMS, Celgene, Eli Lilly, MSD, Novartis, Pierre Fabre, Roche, Sanofi.
- **LVM:** Conception and design, data interpretation, critical revision for important intellectual content, final approval, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Funding**

None.

**Study approval**

N/A.

**References**

1. Armstrong AW, Mehta MD, Schupp CW, Gondo GC, Bell SJ, Griffiths CEM. Psoriasis prevalence in adults in the United States. JAMA Dermatol 2021;157:940–946.
2. Müller D, Augustin M, Banik N, et al. [Memorandum registry for health services research]. Gesundheitswesen 2010;72:824–839.
3. Gottlieb AB, Ryan C, Murase JE. Clinical considerations for the management of psoriasis in women. Int J Womens Dermatol 2019;5:141–150.
4. Griffiths CEM, Armstrong AW, Gadjonsson JE, Barker JWN. Psoriasis. Lancet 2021;397:1301–1315.
5. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet 2007;370:263–271.
6. Blewer AL, McGovern SK, Schmicker RH, et al; Resuscitation Outcomes Consortium (ROC) Investigators. Gender disparities among adult recipients of bystander cardiopulmonary resuscitation in the public. Circ Cardiovasc Qual Outcomes 2018;11:e004710.
7. Corraro S, Santalucia P, Argano C, et al; REPOSI Investigators. Gender-differences in disease distribution and outcome in hospitalized elderly: data from the REPOSI study. Eur J Intern Med 2014;25:617–623.
59. Na SJ, Jo SJ, Youn JL. Clinical study on psoriasis patients for past 30 years (1982-2012) in Seoul National University Hospital Psoriasis Clinic. J Dermatol 2013;40:731–735.
60. Hotard RS, Feldman SR, Fleischer AB Jr. Sex-specific differences in the treatment of severe psoriasis. J Am Acad Dermatol 2000;42:620–623.
61. White D, O’Shea SJ, Rogers S. Do men have more severe psoriasis than women? J Eur Acad Dermatol Venereol 2012;26:126–127.
62. Finlay AY, Kelly SE. Psoriasis—an index of disability. Clin Exp Dermatol 1987;12:8–11.
63. Dowlatshahi EA, Wakkee M, Arends LR, Nijsten T. The prevalence and odds of depressive symptoms and clinical depression in psoriasis patients: a systematic review and meta-analysis. J Invest Dermatol 2014;134:1542–1551.
64. Sampogna F, Chren MM, Melchi GF, Pasquini P, Tabolli S, Abeni D; Italian Multipurpose Psoriasis Research on Vital Experiences (Improve) Study Group. Age, gender, quality of life and psychological distress in patients hospitalized with psoriasis. Br J Dermatol 2006;154:325–331.
65. Finzi A, Colombo D, Caputo A, et al; PSYCHAE Study Group. Psychological distress and coping strategies in patients with psoriasis: the PSYCHAE Study. J Eur Acad Dermatol Venereol 2007;21:1161–1169.
66. Wojtyna E, Łakuta P, Marciniekwicz K, Bergler-Czop B, Brzezińska-Wcisło L. Gender, body image and social support: biopsychosocial deter-minants of depression among patients with psoriasis. Acta Derm Venereol 2017;97:91–97.
67. Hawro M, Maurer M, Weller K, et al. Lesions on the back of hands and female gender predispose to stigmatization in patients with psoriasis. J Am Acad Dermatol 2017;76:648–654.e2.
68. Maur JT, Navarini AA, Sonmer R, et al. Gender and age significantly determine patient needs and treatment goals in psoriasis—a lesson for practice. J Eur Acad Dermatol Venereol 2019;33:700–708.
69. Fortune DG, Richards HL, Kirby B, et al. Psychological distress impairs clearance of psoriasis in patients treated with phototherapy. Arch Dermatol 2003;139:752–756.
70. Renzi C, Picardi A, Abeni D, et al. Association of dissatisfaction with care and psychiatric morbidity with poor treatment compliance. Arch Dermatol 2002;138:337–342.
71. Verhoeven EW, Kruimhaar FW, de Jong EM, Schalkwijk J, van de Water-Haring E. Is it possible to predict responders versus non-responders to phototherapy in patients with severe psoriasis vulgaris? J Am Acad Dermatol 2001;45:50–53.
72. Dunn LB, Damesyn M, Moore AA, Mallbris L, Skov L, Hansen PR. Does estrogen prevent skin aging? Results from the First National Health and Nutrition Examination Survey (NHANES I). Arch Dermatol 1997;133:339–342.
73. Schmidt JF, Binder M, Demschik G, Biegelmayer C, Reiner A. Treatment of skin aging with topical estrogens. Int J Dermatol 1996;35:669–674.
74. Pérard-Branchimon C, Letawe C, Goffin V, Goffin V, Pérard GE. Skin water-holding capacity and transdermal estrogen therapy for menopause: a pilot study. Maturitas 1995;22:151–154.
75. Murase JE, Chan KK, Garite TJ, Cooper DM, Weinstein GD. Hormonal effect on psoriasis in pregnancy and post partum. Arch Dermatol 2000;136:347–350.
76. Kimball AB, Guenterh L, Kalia S, et al. Pregnancy outcomes in women with moderate-to-severe psoriasis: the swiss treatment pathway. Dermatology 2012;235:166–178.
77. Na SJ, Jo SJ, Youn JI. Clinical study on psoriasis patients for past 30 years (1982-2012) in Seoul National University Hospital Psoriasis Clinic. J Dermatol 2013;40:731–735.
78. Kimball AB, Guenther L, Kalia S, et al. Pregnancy outcomes in women with moderate-to-severe psoriasis. J Am Acad Dermatol 2004;50:9–20.
79. Murase JE, Chan KK, Leyden J, et al. Effect of maternal psoriasis on pregnancy and birth outcomes: a population-based cohort study from Denmark and Sweden. Acta Derm Venereol 2018;98:728–734.
80. Gonzalez-Cantu A, Carretero G, Rivera R, et al; BIOBADADERM Study Group. Women with moderate-to-severe psoriasis in Spain (BIOBADADERM registry) show more than a 50% reduction in age-adjusted fertility rate when compared with the general population. Br J Dermatol 2019;181:1085–1087.
81. De Simone C, Calabrese L, Balato A, et al; SIDeMaST “Psoriasis in Women of Childbearing Age” Task Force. Psoriasis and its management in women of childbearing age: tools to increase awareness in dermatologists and patients. G Ital Dermatol Venereol 2020;155:343–440.
82. Oliveira Mde F, Rocha Bde O, Duarte GV. Psoriasis: classical and emerging comorbidities. An Bras Dermatol. 2015;90:9–20.
83. Johansen CB, Egeberg A, Jimenez Solum E, Vittrup I, Skov L, Francis Thomsen S. Comorbidities, socioeconomic status, drug use, and health care for Danish women with psoriasis: a nationwide cross-sectional study. Int J Womens Dermatol 2021;7:246–258.
84. Boehncke WH, Schön MP. Psoriasis. Lancet 2015;386:983–994.
85. Figueiredo AR, Schumacher A. The T helper type 17/regulatory T cell paradigm in pregnancy. Immunology 2016;148:13–21.
86. De Simone C, Caldarola G, Corbeddu M, et al. A possible role of polycystic ovary syndrome for pregnancy complications in women with psoriasis. Drug Dev Res 2014;75(suppl 1):S64–S66.
87. Ruiz V, Manuñezs E, Pugl L. Psoriasis in pregnancy: a review. I. Actas Dermosifiliogr 2014;105:734–743.
88. Saito S, Nakashima A, Shima T, Ito M. Th1/Th2/Th17 and regulatory T-cell paradigm in pregnancy. Immunology 2016;148:13–21.
89. Menter A, Griffiths CE. Current and future management of psoriasis. Lancet 2007;370:767–778.
90. Nast A, Gisondi P, Ormerod AD, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris—Update 2015—Short version—EDF in cooperation with EADV and IPC. J Eur Acad Dermatol Venereol 2015;29:2277–2294.
91. Siband E, Chaimani A, Afach S, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev 2020;1:CD011535.
92. Van J, Abuabara K, Troxel AB, et al. Dermatologist preferences for first-line therapy of moderate to severe psoriasis in healthy adult patients. J Am Acad Dermatol 2012;66:376–386.
93. Nyberg B, Osika I, Evengård B. “The Laundry Bag Project”—unequal distribution of dermatological healthcare resources for male and female psoriatic patients in Sweden. Int J Dermatol 2008;47:144–149.
94. Hernandez-Fernandez CP, Carretero G, Rivera R, et al; the BIOBADADERM Study Group. Effect of sex in systemic psoriasis therapy: differences in prescription, effectiveness and safety in the BIOBADADERM prospective cohort. Acta Derm Venereol 2021;101:adv00354.
95. Maul JT, Augsburger M, Sorbe C, et al. Association of sex and systemic therapy treatment outcomes in psoriasis: a two-country, multicentre, prospective, noninterventional registry study. Br J Dermatol 2021;185:1160–1168.
96. Di Cesare A, Bianchi G, Pescitelli L, et al. Risk of acute infections in psoriatic patients during biologic therapies is linked to gender. J Eur Acad Dermatol Venereol 2019;33:362–364.
97. van der Schoot LS, van den Reek JMPA, Gemoewend MM, et al. Female patients are less satisfied with biological treatment for psoriasis and experience more side-effects than male patients: results from the prospective BioCAPTURE registry. J Eur Acad Dermatol Venereol 2019;33:1913–1920.
98. Zaghloul SS, Goodfield MJ. Objective assessment of compliance with psoriasis treatment. Arch Dermatol 2004;140:408–414.
99. Lam J, Polifka JE, Dohil MA. Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases. J Am Acad Dermatol 2008;59:295–310.
100. Maul JT, Anzengruber F, Conrad C, et al. Topical treatment of psoriasis vulgaris: the swiss treatment pathway. Dermatology 2015;231:166–178.
101. Nast A, Smith C, Spuls PI, et al. EuroGuidErm Guideline on the systemic treatment of Psoriasis vulgaris—Part 2: specific clinical and comorbid situations. J Eur Acad Dermatol Venereol 2021;35:281–317.
102. Bandoli G, Palmsten K, Forbes Smith CJ, Chambers CD. A review of systemic corticosteroids use in pregnancy and the risk of select pregnancy and birth outcomes. Rheum Dis Clin North Am 2017;43:489–502.
103. Dhar S, Seth J, Parikh D. Systemic side-effects of topical cortico- steroids. Indian J Dermatol 2014;59:460–464.
104. Chi CC, Wang SH, Kirtschig G. Safety of topical corticosteroids in pregnancy. JAMA Dermatol 2016;152:934–935.
112. Andersson NW, Skov L, Andersen JT. Evaluation of topical corticosteroid use in pregnancy and risk of newborns being small for gestational age and having low birth weight. JAMA Dermatol 2021;157:788–795.

113. Drzewoski Z, Naya S, Pariser D, et al. Pharmacokinetics of topical calcineurin inhibitors in adult atopic dermatitis: a randomized, investigator-blind comparison. J Am Acad Dermatol 2005;53:602–609.

114. Rubins A, Gutmane R, Valdmare N, Stevenson P, Foster C, Undre N. Pharmacokinetics of 0.1% tacrolimus ointment after first and repeated application to adults with moderate to severe atopic dermatitis. J Invest Dermatol 2005;125:48–51.

115. Undre NA, Moloney FJ, Ahmadi S, Stevenson P, Murphy GM. Skin and systemic pharmacokinetics of tacrolimus following topical application of tacrolimus ointment in adults with moderate to severe atopic dermatitis. Br J Dermatol 2009;160:665–669.

116. Zheng S, Easterling TR, Hayes K, et al. Tacrolimus placentale transfer at delivery and neonatal exposure through breast milk. Br J Clin Pharmacol 2013;76:988–996.

117. Butler DC, Heller MM, Murase JE. Safety of dermatologic medications in pregnancy and lactation: part II. Lactation. J Am Acad Dermatol. 2014;70:417 e1–10; quiz 27.

118. Murase JE, Heller MM, Butler DC. Safety of dermatologic medications in pregnancy and lactation: part I. Pregnancy. J Am Acad Dermatol. 2014;70:401 e15–19.

119. Rademaker M, Agnew K, Andrews M, et al. Psoriasis in those planning a family, pregnant or breast-feeding. The Australasian Psoriasis Collaboration. Australas J Dermatol 2018;59:86–100.

120. Uchiyama H, Suzuki T, Koike Y, et al. [Reproductive and developmental toxicity studies of calcipotriol (MC903): (3)–A teratogenicity study in rabbits by subcutaneous administration]. J Toxicol Sci 1996;21(suppl 2):425–438.

121. Lambert JW, Segaert S, Ghislain PD, et al. Practical recommendations for systemic treatment in psoriasis according to age, pregnancy, metabolic syndrome, mental health, psoriasis subtype and treatment history (BETA-PSO: Belgian Evidence-based Treatment Advice in Psoriasis; part I). J Eur Acad Dermatol Venereol 2020;34:1654–1665.

122. Nast A, Spuls PI, van der Kraaij G, et al. European S3-Guideline on the systemic treatment of psoriasis vulgaris—Update Apremilast and Secukinumab - EDF in cooperation with EADV and IPC. J Eur Acad Dermatol Venereol 2017;31:1951–1963.

123. Villani AP. Le choix thérapeutique: médicaments du psoriasis et grossesse avant, pendant et après la grossesse. Eur J Dermatol 2020;30(S1):3–13.

124. Zhang M, Goyert G, Lim HW. Folate and phototherapy: what should we inform our patients? J Am Acad Dermatol 2017;77:958–964.

125. Bar Oz B, Hackman R, Einarson T, Koren G. Pregnancy outcome after cyclosporine therapy during pregnancy: a meta-analysis. Transplantation 2001;71:1051–1053.

126. Ghanem ME, El-Baghdadi LA, Badawy AM, Sobhe MA, Ghoneim MA. Pregnancy outcome after renal allograft transplantation: 15 years experience. Eur J Obstet Gynecol Reprod Biol 2005;121:178–181.

127. Paziana K, Del Monaco M, Cardonick E, et al. Ciclosporin use during pregnancy and lactation. Br J Clin Pharmacol 2005;53:1255–1258.

128. Natsumi I, Matsukawa Y, Miyagawa K, et al. Successful childbearing in two women with rheumatoid arthritis and a history of miscarriage after etanercept treatment. Rheumatol Int 2013;33:2433–2435.

129. Casanova MJ, Chaparro M, Domènech E, et al. Safety of thiopurines and anti-TNF-α drugs during pregnancy in patients with inflammatory bowel disease. Am J Gastroenterol 2013;108:433–440.

130. de Lima A, Zelnikova Z, van der Ent C, Steegers EA, van der Woude CJ. Tailored anti-TNF therapy during pregnancy in patients with IBD: maternal and fetal safety. Gut 2016;65:1261–1268.

131. Luu M, Benzenine E, Doret M, et al. Continuous Anti-TNF use throughout pregnancy: possible complications for the mother but not for the Fetus. A retrospective cohort on the French National Health Insurance Database (EVASION). Am J Gastroenterol 2018;113:1669–1677.

132. Broms G, Kieler H, Ekholm A, et al. Anti-TNF treatment during pregnancy and birth outcomes: a population-based study from Denmark, Finland, and Sweden. Pharmacoeconom Drug Saf 2020;29:316–327.

133. Diav-Citrin O, Ochteretiansi-Volodarsky A, Shechtman S, Ornoy A. Pregnancy outcome following gestational exposure to TNF-alpha-inhibitors: a prospective, comparative, observational study. Reprod Toxicol 2014;43:78–84.

134. Schnitzler F, Fidder H, Ferrante M, et al. Outcome of pregnancy in women with inflammatory bowel disease treated with antitumor necrosis factor therapy. Inflamm Bowel Dis 2011;17:1846–1854.

135. Komaki F, Komaki Y, Micic D, Ido A, Sakuraba A. Outcome of pregnancy and neonatal complications with anti-tumor necrosis factor-α use in females with immune mediated diseases; a systematic review and meta-analysis. J Matern Neonatal Med 2017;30:38–52.

136. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:175–84.

137. Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. BMJ 2000;320:1708–1712.

138. Wils P, Seksik P, Stefanescu C, et al; PREGNANCY-GETAID study group. Safety of ustekinumab or vedolizumab in pregnant inflammatory bowel disease patients: a multicentre cohort study. Aliment Pharmacol Ther 2021;53:460–470.

139. Haycraft K, DiRuggiero D, Rozzo SJ, Mendelson AM, Bhutani T. Outcomes of pregnancies from the tildrakizumab phase I-III clinical development programme. Br J Dermatol 2020;183:184–186.

140. Warren RB, Reich K, Langley RG, et al. Secukinumab in pregnancy: outcomes in psoriasis, psoriatic arthritis and ankylosing spondylitis from the global safety database. Br J Dermatol 2018;179:1205–1207.

141. Steven F, Beth P, Wen X, et al. Ixekizumab and pregnancy outcome. J Am Acad Dermatol. 2017;76(Supplement 1):AB419.

142. Porter ML, Lockwood SJ, Kimball AB. Update on biologic safety for patients with psoriasis during pregnancy. Int J Womens Dermatol 2017;3:21–25.

143. Yeung J, Gooderham MJ, Grewal P, et al. Management of plaque psoriasis with biologic therapies in women of child-bearing potential consensus paper. J Cutan Med Surg 2020;24(suppl 1):38–45.

144. Porter ML, Lockwood SJ, Kimball AB. Update on biologic safety for patients with psoriasis during pregnancy. Int J Womens Dermatol 2017;3:21–25.

145. Schnitzler F, Fidder H, Ferrante M, et al. Outcome of pregnancy in women with inflammatory bowel disease treated with antitumor necrosis factor therapy. Inflam Bowel Dis 2011;17:1846–1854.

146. Komaki F, Komaki Y, Micic D, Ido A, Sakuraba A. Outcome of pregnancy and neonatal complications with anti-tumor necrosis factor-α use in females with immune mediated diseases; a systematic review and meta-analysis. J Matern Neonatal Med 2017;30:38–52.

147. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:175–84.

148. Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. BMJ 2000;320:1708–1712.

149. Wils P, Seksik P, Stefanescu C, et al; PREGNANCY-GETAID study group. Safety of ustekinumab or vedolizumab in pregnant inflammatory bowel disease patients: a multicentre cohort study. Aliment Pharmacol Ther 2021;53:460–470.

150. Haycraft K, DiRuggiero D, Rozzo SJ, Mendelson AM, Bhutani T. Outcomes of pregnancies from the tildrakizumab phase I-III clinical development programme. Br J Dermatol 2020;183:184–186.

151. Warren RB, Reich K, Langley RG, et al. Secukinumab in pregnancy: outcomes in psoriasis, psoriatic arthritis and ankylosing spondylitis from the global safety database. Br J Dermatol 2018;179:1205–1207.

152. Steven F, Beth P, Wen X, et al. Ixekizumab and pregnancy outcome. J Am Acad Dermatol. 2017;76(Supplement 1):AB419.