

## Review

# Addressing Common Oral Contraceptive Pill Concerns for the Primary Care Provider

Amelia C. Inclan <sup>1</sup>, Danielle Snyder <sup>1</sup>, Sophie G. Tillotson <sup>1</sup>, Katelyn E. Flaherty <sup>1</sup> , Angelica Byrd <sup>1</sup>, Alyssa Pasvantis <sup>1</sup> and Charlotte Chaiklin <sup>2,\*</sup> 

<sup>1</sup> College of Medicine, University of Florida, Gainesville, FL 32610, USA; amelia.inclan@ufl.edu (A.C.I.); daniellesnyder@ufl.edu (D.S.); sophietillotson@ufl.edu (S.G.T.); flahertyk@ufl.edu (K.E.F.); angelica.byrd@ufl.edu (A.B.); alyssa.pasvantis@ufl.edu (A.P.)

<sup>2</sup> Division of General Internal Medicine, Department of Medicine, University of Florida, Gainesville, FL 32610, USA

\* Correspondence: cchaiklin@ufl.edu

## Abstract

Primary care providers are increasingly tasked with providing basic gynecologic care, including contraceptive therapy, to their patients. In the United States, oral contraceptive pills are the most frequently prescribed form of contraception; thus, it is critical that primary care providers are well versed in addressing common patient questions. Well-documented concerns relating to oral contraception initiation include changes in weight, mood, cancer risk, libido, acne, and infertility. Herein, we provide a clinical case example of a patient with these common concerns, review the related evidence, and suggest appropriate counseling with the goal of helping primary care clinicians provide the highest level of evidence-based oral contraceptive care.

**Keywords:** birth control; oral contraceptive pills; patient concerns



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## 1. Introduction

While primary care providers are expected to provide comprehensive care to their patients, including basic gynecologic care, they do not always receive the training necessary to adequately address patient questions and concerns. In the United States, 38.5% of primary care physicians (PCPs) are trained in family medicine, 2% are trained in geriatrics, 21.4% in pediatrics, and 38.1% in internal medicine. While the Accreditation Council for Graduate Medical Education requires at least 100 h or one month of gynecology training during family medicine residency, there are no such requirements for physicians who complete pediatric or internal medicine residency programs [1–3]. In fact, multiple studies have noted this deficit in internal medicine residency curricula [4,5]. This gap in training is notable, as contraception—the deliberate use of a medication, device, or behavior to prevent pregnancy—is a crucial part of routine gynecologic care for patients with childbearing potential [6]. This article is designed to help fill in the gaps in gynecologic training and empower PCPs with the necessary information to effectively prescribe and counsel patients about oral contraceptive therapy.

It is estimated that 99% of patients with childbearing potential who have had sexual intercourse have used some form of contraception in their lifetime [7]. In the United States, oral contraceptive therapy is one of the most used and prescribed forms of contraception [6–8].

There are two types of oral contraceptive pills (OCPs) that PCPs can prescribe: progestin-only pills (POPs), often referred to as the “mini pill,” and combined hormonal

contraceptive (CHC) pills, which contain both an estrogen and progestin component. Several different formulations of POPs are currently available, including norethindrone, drospirenone, and norgestrel. Norgestrel, marketed as the over-the-counter product “Opill,” represents an important advance in contraceptive accessibility, whereas drospirenone-containing POPs are a newer option with comparatively less long-term data available to guide clinical practice [9]. Herein, the term “POPs” will refer specifically to norethindrone formulations, as these remain the most widely studied and commonly prescribed. With perfect use, fewer than 1 in 100 patients will become pregnant within the first year while taking either type of OCP [10–12]. However, with typical use, OCPs are 93% effective, with approximately 7 in 100 patients becoming pregnant within the first year of use [13].

When deciding which type of OCP to prescribe, the PCP must take into consideration the patient’s medical history and current medications in addition to patient preferences. Neither type of OCP should be used in certain medical situations, such as the presence or history of breast cancer, the presence of malignant hepatocellular carcinoma, previous bariatric surgery such as Roux-en-Y gastric bypass or biliopancreatic diversion that resulted in compromised absorption of medications, and the use of certain anticonvulsant and antimicrobial medications [13]. The PCP may choose to prescribe POPs over CHC pills in certain clinical scenarios where CHC pills are contraindicated, including but not limited to the immediate postpartum period, migraine with aura, risk factors for venous thromboembolism (VTE), risk factors for atherosclerotic cardiovascular disease, thrombophilia, diabetes mellitus with nephropathy, retinopathy, neuropathy or other vascular disease, diabetes mellitus of >20 years duration, use of tobacco at age 35 years or older, nephrotic syndrome, end stage renal disease requiring either peritoneal or hemodialysis, sickle cell disease, inflammatory bowel disease with increased risk for VTE, use of lamotrigine therapy, and decompensated cirrhosis [13]. A full list of contraindications to both POPs and CHC pills can be found in Appendix A Tables A1 and A2.

When initiating oral contraceptive therapy, the clinician should educate patients about common side effects of OCPs, measure patient blood pressure, and rule out pregnancy. Common side effects of OCPs include nausea, breast tenderness, and breakthrough bleeding, bleeding outside the expected withdrawal period unrelated to the normal menstrual cycle [14]. CHC pills specifically have been shown to increase blood pressure and risk of cardiovascular events, particularly in patients with a history of hypertension or cardiovascular disease. As such, it is imperative to rule out uncontrolled hypertension prior to initiating CHC therapy [15]. Pregnancy should also be ruled out by obtaining a detailed history. If the patient denies signs or symptoms of pregnancy and started normal menstruation within 7 days, has not had sexual intercourse since last normal menses, has been correctly and consistently using a reliable method of contraception, had a spontaneous or induced abortion within 7 days, is within 4 weeks postpartum, or is exclusively or almost exclusively breastfeeding (defined as  $\geq 85\%$  of feeds), amenorrheic, and < 6 months postpartum, then the healthcare provider can be reasonably certain the patient is not pregnant. Based on clinical judgment a urine pregnancy test may also be considered [13,15]. The importance of strict adherence to oral contraceptive therapy for pregnancy prevention should be emphasized [10,16]. Clarification that OCPs do not protect against sexually transmitted infections should be provided, and continued condom use for this purpose is recommended.

Finally, prior to initiating oral contraceptive therapy, any patient concerns should be addressed, including those relating to common oral contraceptive myths. Despite a lack of evidence directly linking OCP use to significant weight gain, mood changes, overall increased cancer risk, decrease in libido, worsening acne, and infertility, multiple studies have noted patient fears related to these myths at the time of OCP initiation. These same factors are commonly cited as reasons for discontinuation of OCPs [17,18]. As such, PCPs

must be ready and able to discuss these concerns with their patients [17–19]. Below, we provide a patient case illustrating common concerns related to oral contraceptive therapy to help busy PCPs and other healthcare professionals deliver effective and comprehensive contraceptive counseling.

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### Clinical Case

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A 24-year-old woman with a body mass index (BMI) of 36 kg/m<sup>2</sup>, well-controlled major depressive disorder, primary dysmenorrhea, and a history of acne vulgaris presents to a primary care clinic to establish care and discuss starting oral contraceptive therapy. She is a lifetime non-smoker and has no additional past medical history, yet mentions that her mother was recently diagnosed with breast cancer. She is not currently sexually active with her fiancé, but she is hoping to start oral contraceptive therapy before her wedding in a few months. She is concerned that starting OCPs will negatively impact her weight and has heard that OCPs cannot be used safely in overweight patients. She wonders if her current weight will make her ineligible for OCP use and is worried about weight gain due to OCPs. How do you respond to her concerns?

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## 2. Impact on Weight

Patients' weight-related concerns often include the safety of OCP in patients with obesity and the risk of weight gain [20].

POPs and CHC pills are both considered safe contraceptive options for patients with obesity. However, prior to initiation of CHC pills in patients with obesity, careful evaluation for comorbidities is needed as cardiovascular conditions may increase patient risk of major adverse cardiovascular events [10]. Patients also need to be evaluated for their individual risk of venous thromboembolism, as obesity alone has been shown to increase this risk by 2.5 times [21]. A 2016 Cochrane review found no significant association between obesity and lack of efficacy of hormonal contraception [22]. Per the American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 206, patients with obesity can be prescribed hormonal contraceptive therapy without concern for increased contraceptive failure. However, ACOG notes that more research is needed to fully understand the impact of weight on contraceptive efficacy, particularly in patients with class III obesity or a BMI greater than or equal to 40 kg/m<sup>2</sup> [16].

The literature evaluating the impact of POPs on weight regulation is limited. Several studies have investigated the association between weight and non-pill forms of progestin-only contraception, such as the levonorgestrel-releasing intrauterine device (IUD), subdermal implant, and Depot Medroxyprogesterone Acetate (DMPA) injection. A 2016 Cochrane review of twenty-two studies found a mean weight gain of less than 2 kg (4.4 pounds) at 6–12 months with progestin-only contraceptive use. Notably, the two studies included in this review that specifically examined POPs did not demonstrate a similar increase in weight [22]. The marginal weight gain observed in the overall analysis is likely due to the inclusion of progestin injectables such as DMPA, which has been shown to result in a significant increase in weight [22]. Similarly, a 2014 Cochrane review of forty-nine studies comparing CHC pills and weight found no evidence linking CHC pill use to weight change [23]. Subsequent studies investigating the impact of CHC pill use on weight gain, including controlled studies comparing CHC methods to placebo, found no significant changes in weight or body mass index [24–26].

The patient should be reassured that both POP and CHC pills can be safely and effectively used in patients with obesity without significant risk for weight gain (Table 1). In patients without cardiovascular comorbidities, CHCs may be preferred given the possible

decreased risk for weight gain compared to POPs, though the two have yet to be compared directly in the literature.

**Table 1.** Weight Quick Facts.

| Weight                                                                |                                                                                                                                                                                                     |
|-----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>CHC Pills</b><br>No evidence linking CHC pill use to weight change | <b>POPs</b><br>Low-quality data suggesting mean weight gain of less than 2 kg or 4.4 pounds at 6–12 months (marginally higher than average weight gain of 1 kg or 2.2 pounds per year in US adults) |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient is relieved to learn that OCPs can be used safely and effectively in obese patients with minimal impact on weight. She is now wondering about the effects of OCPs on her mood. She reports a three-year history of major depressive disorder in remission on fluoxetine therapy. She has read online that OCPs can worsen depression and may interact with the medications used to treat depression. How do you respond to her concerns? |

3. Mood Disturbances

The patient’s concerns are common, as evidenced by a study of patients with childbearing potential and physicians specializing in gynecology that found that >50% of patients and >40% of physicians believed CHC pills have a deleterious impact on mood [27]. Despite these concerns, no evidence to date has demonstrated a worsening of depressive symptoms with either POPs or CHC pills. In fact, ACOG Practice Bulletin No. 206 states “women with depressive disorders can use all methods of hormonal contraception because depressive symptoms do not appear to worsen with use of any method of hormonal contraception” [16]. This statement is supported by a 2016 systematic review that found no significant worsening of pre-existing depression or bipolar disorder in patients using any form of hormonal contraceptive therapy, including both POPs and CHC pills [28]. Additionally, the use of oral contraceptive therapy has not been shown to significantly affect mood across the menstrual cycle in patients with bipolar disorder [13]. As such, there are no guidelines suggesting discontinuation of OCPs on the basis of mood disturbances, though this occurs frequently in clinical practice.

Oral contraceptive therapy does not appear to interact with the metabolism of selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, sertraline, escitalopram, paroxetine, and citalopram, or serotonin norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine, desvenlafaxine, or duloxetine [16,29]. Patients taking SSRIs or SNRIs can be reassured that the efficacy of their medications for mood disorders should not be impacted. However, patients taking St. John’s wort, an over-the-counter herbal supplement marketed for the treatment of depression, should be advised that this supplement may interact with the metabolism of oral contraceptive therapy and could potentially lead to decreased contraceptive efficacy depending on the dose [29].

Of note, oral contraceptives may improve mood disorders related to the menstrual cycle, such as premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD). According to the American Academy of Family Physicians, there is consistent evidence that oral contraceptives are effective for the treatment of PMS and PMDD [30]. This guidance is supported by a 2023 systematic review that found that CHC pills with drospirenone and ethinylestradiol may improve premenstrual symptoms associated with functional impairments in patients with PMDD [31]. This study and others suggest that the continuous, rather than cyclic, use of CHC pills offers greater benefit in treating symptoms of PMS and PMDD [32].

The patient in our clinical case should be reassured that the use of neither POPs nor CHC pills will negatively impact her depressive symptoms, nor will it alter the efficacy of her fluoxetine therapy (Table 2).

Table 2. Mood Quick Facts.

| Mood Disturbances                                                                                                                                 |                                                                                                              |
|---------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| <b>CHC Pills</b><br>No evidence demonstrating worsening depressive symptoms<br>No interaction with SSRIs or SNRIs<br>May improve symptoms of PMDD | <b>POPs</b><br>No evidence demonstrating worsening depressive symptoms<br>No interaction with SSRIs or SNRIs |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient is pleased to hear that her depression should not be negatively impacted by oral contraceptive therapy but is concerned about her risk of breast cancer with OCP use given her family history. She reports her mother was diagnosed with breast cancer at the age of 56 years old. She denies any additional family history of cancer. How do you counsel this patient? |

4. Cancer Risk

The use of oral contraceptive therapy, specifically CHC, has been shown to slightly increase the risk of invasive breast cancer in average-risk patients [33,34]. In a study of Danish patients using hormonal contraception, there was one case of invasive breast cancer for every 7690 patients [33]. Similarly, prior meta-analyses found the use of CHC pills increases the risk of invasive breast cancer by anywhere from 8 to 24% [35–37]. It is important to note that the increased risk of invasive breast cancer associated with CHC pills has not been consistently observed with progestin-only contraceptive therapy [38]. While POP use does not appear to increase invasive breast cancer risk, the use of a progestin-based IUD has been shown to increase the relative risk of breast cancer to a rate like that seen with CHC pill use [34,38]. Given the small sample sizes of prior studies evaluating POP use and breast cancer risk, in addition to inconsistent results regarding progestin-only contraception, additional research is needed [38].

Both OCPs and POPs have been shown to be associated with increased risk of cervical cancer, particularly with prolonged use [37,39,40]. However, the overall risk of cervical cancer remains relatively low. One large study estimated one additional case of cervical cancer for every 14,700 women using OCPs for one year [39]. This study consisted primarily of individuals not previously vaccinated against the human papillomavirus (HPV). Additionally, other studies have shown that less than 25% of adolescents use dual methods of contraception, indicating decreased condom use among those utilizing OCPs as contraception, potentially increasing exposure to HPV [41]. With the widespread implementation of the HPV vaccine, the hope is that the overall cervical cancer burden in the population will continue to decline. Until further research is available, the impact of contraception on cervical cancer rates in the setting of widespread HPV vaccination remains unclear.

Healthcare providers should recognize that the overwhelming benefits of OCP use often outweigh the increased risks of breast and cervical cancer. The use of OCPs has been shown to be protective against endometrial, ovarian, and colon cancer [37,42]. In one study evaluating OCP use and cancer risk, the absolute decrease in lifetime risk of endometrial, ovarian, and colon cancer for patients who have ever used OCPs versus non-users was 1.77%, 0.54%, and 0.76%, respectively [43]. With all three cancers, the longer the duration of use, the greater the apparent risk reduction [42,43]. Despite the slight increase in invasive breast and cervical cancer, overall cancer risk may be slightly lower in patients using



oral contraceptive therapy compared to non-users given protection against endometrial, ovarian, and colon cancer [43].

Healthcare providers should recognize that the overwhelming benefits of OCP use often outweigh the increased risks of breast and cervical cancer. OCPs should therefore be prescribed without hesitation as long as patients are informed of increased cancer risks.

The patient in our case should be informed that although CHC pill use carries an increased risk of breast cancer and both CHC pills and POP increase the risk of cervical cancer, the benefits of OCP therapy outweigh the risks. The patient should be made aware that both OCP types may decrease her overall cancer risk as they are associated with decreased risk of endometrial, ovarian, and colon cancers (Table 3).

Table 3. Cancer Quick Facts.

| Cancer Risk                                               |                                                           |
|-----------------------------------------------------------|-----------------------------------------------------------|
| <b>CHC Pills</b>                                          | <b>POPs</b>                                               |
| Increased risk of breast cancer                           | Inconsistent data about breast cancer risk                |
| Increased risk of cervical cancer                         | Increased risk of cervical cancer                         |
| Protection against endometrial, ovarian, and colon cancer | Protection against endometrial, ovarian, and colon cancer |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient thanks you for explaining to her the information regarding OCP use and cancer risk, especially in light of her family history. However, before starting contraception she states that she has heard OCPs can cause a significant decrease in libido. She is about to get married and is worried about having a low sex drive with her future husband. What do you tell her? |

5. Libido

Despite up to one in five patients discontinuing contraceptive therapy due to negative sexual side effects, to date there has been conflicting evidence in regard to the impact of oral contraceptive therapy on libido. A systematic review evaluating CHC pill use and sexual desire found that 15% of patients taking CHC pills with low-dose (15 µg) ethinylestradiol reported a decrease in libido, while 85% of patients reported an increase or no change in libido [44]. In this same review, there was no significant difference in libido among patients taking CHC pills with 20–35 µg of esthinyalestradiol [44]. Like the CHC pill, the existing data evaluating the impact of POPs on libido has mixed results, with the majority of patients taking POPs having no contraceptive-related decrease in sexual desire [45,46]. Given the conflicting evidence demonstrating an association between OCP use (both CHC and POPs) and sexual desire, it is recommended that OCP therapy be discontinued if a contraceptive-related decrease in libido is suspected [46].

When counseling the patient in our clinical case, the provider should discuss the conflicting evidence regarding the impact of OCP therapy on libido and explain that existing data suggests low rates of contraceptive-related decrease in libido (Table 4). The patient should be reassured that if contraceptive-related decrease in libido does occur, OCP therapy can be discontinued. However, prior to OCP discontinuation on the basis of decreased libido, the patient and provider should consider the other possible etiologies of decreased libido, such as depression and/or medication side effects as is seen with SSRI and SNRI use [47,48].

Table 4. Libido Quick Facts.

| Libido                                |                                           |
|---------------------------------------|-------------------------------------------|
| CHC Pills                             | POPs                                      |
| Mixed data regarding impact on libido | Mixed data regarding impact on libido     |
| Possible risk of decreased libido     | Majority of patients experience no change |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient understands that there may be a small risk of decreased libido with OCP therapy and still wishes to proceed with OCPs for contraception. She is planning to go to Europe for her honeymoon and would like to not have a menstrual period during her travels if possible. She is worried about the effects of skipping menstruation as her grandmother told her that monthly menstruation is necessary for women to be healthy. What do you tell her? |

6. Need for Menstruation

The misconception that patients with childbearing potential should have a menstrual period each month originated with the initial design of OCPs in the mid-twentieth century. The initial formulation of OCPs consisted of 21 active hormone containing pills followed by a seven-day break or placebo phase to induce monthly withdrawal bleeding and mimic the natural menstrual cycle. The desire to imitate the normal menstrual cycle was driven by the cultural and social pressures of the 1950s, including a strong disapproval of contraceptive use by the Catholic Church, rather than being based in medical necessity [49,50]. More current data suggests a growing acceptance of menstrual suppression, with 53% of individuals with childbearing potential expressing a preference to skip their monthly menstrual period altogether [51]. Although awareness and acceptance of menstrual suppression are increasing, a substantial disparity persists between patients and healthcare providers in their knowledge of the safety and benefits of menstrual suppression using OCPs.

It is important that providers recognize and highlight the distinctions between OCP-induced amenorrhea and pathologic amenorrhea. Pathologic amenorrhea typically results from disruptions in the hypothalamic–pituitary–ovarian (HPO) axis, leading to anovulation. Persistent anovulation poses a significant risk for endometrial hyperplasia from unopposed estrogen stimulating endometrial proliferation in the absence of a progesterone-secreting corpus luteum which places patients at risk of developing endometrial cancer. In contrast, OCP-induced amenorrhea maintains suppression of the HPO axis, resulting in a thin and atrophic endometrium [52]. Therefore, even in the absence of regular menses, the risk of endometrial hyperplasia and subsequent increased risk of endometrial cancer is effectively eliminated with OCP-induced amenorrhea [53].

Patients may be concerned about the impact of OCP-induced menstrual suppression on future fertility [54]. Multiple studies have consistently demonstrated neither significant delay in return to normal menses nor adverse impact on fertility following the cessation of OCP-induced menstrual suppression [53,55].

OCP-induced amenorrhea can provide patients with significant therapeutic and lifestyle benefits, particularly for patients experiencing dysmenorrhea, abnormal uterine bleeding, or disruptive menstrual cycles. Additionally, it has been shown to be beneficial for patients with logistical challenges related to menses such as military personnel, patients with physical or cognitive disabilities, and transgender or gender-diverse individuals [50,56].

OCP-induced amenorrhea can be accomplished with either POPs or CHC pills [50]. In patients seeking amenorrhea with POP use, the healthcare provider can consider higher doses of progestin-only therapy, specifically norethindrone acetate 5 mg daily, as opposed to the typical dosing of 0.35 mg daily. Norethindrone 5 mg has been associated with

higher rates of amenorrhea, with amenorrhea achieved at two years of use in up to 76% of patients. However, it should be noted that norethindrone 5 mg daily dosing is not approved by the United States Food and Drug Administration (FDA) for contraceptive use but can be used off-label for this purpose [50]. It should be noted that higher doses of norethindrone are associated with a dose–response relationship with thrombotic events, so this should be used with caution in high-risk patients [57]. To achieve OCP-induced amenorrhea with CHC pills, the provider should prescribe continuous OCP use, where the active hormone-containing pills are taken continuously. This practice of omitting the placebo pills each month can be performed safely for an indefinite number of consecutive cycles [50]. Continuous use has been shown to result in complete amenorrhea in 79% to 88% of women at 12 months [50]. A 2014 Cochrane review found this to be a safe and effective contraceptive strategy for patients desiring both contraception and menstrual suppression (Table 5) [58].

Table 5. Need for Menstruation Quick Facts.

| Need for Menstruation                                                                                                                                                    |                                                                                                                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>CHC Pills</b><br>No negative impact on health with OCP-induced amenorrhea<br>Higher efficacy in inducing amenorrhea than POPs (when prescribed at contraceptive dose) | <b>POPs</b><br>No negative impact on health with OCP-induced amenorrhea<br>Norethindrone 5 mg may induce amenorrhea but not FDA approved as contraception, however, can be used off-label for this purpose |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient is looking forward to using OCPs to skip her menstrual period during her upcoming honeymoon travels and has a few more questions for you. She states she has a history of acne vulgaris requiring systemic antibiotic therapy in the past and is concerned about the impact of OCPs on her now well controlled acne vulgaris. How do you counsel the patient? |

When counseling the patient in our clinical case, the provider should attempt to emphasize the difference between pathologic and OCP-induced amenorrhea using patient-friendly language to highlight the safety and efficacy of OCP therapy for those seeking menstrual suppression in addition to contraception.

7. Acne

Per the 2024 American Academy of Dermatology (AAD) Guidelines of care for the management of acne vulgaris, there is moderate-certainty evidence that shows combined hormonal contraceptive therapy is effective for the treatment of inflammatory acne in patients with childbearing potential [59]. In fact, there are four combined OCPs approved by the FDA for the treatment of acne vulgaris: ethinyl estradiol/norgestimate, ethinyl estradiol/norethindrone acetate/ferrous fumarate, ethinyl estradiol/drospirenone, and ethinyl estradiol/drospirenone/levomefolate. CHC pills help treat acne due to their antiandrogenic properties. CHC pills decrease ovarian androgen production, reduce 5-alpha-reductase activity, and increase sex hormone-binding globulin which results in decreased circulating free testosterone and subsequently leads to decreased androgen receptor activation. To date, no significant data has demonstrated the superiority of one type of CHC pill over another [59].

In contrast, POPs, specifically norethindrone therapy, have been shown to potentially worsen acne by increasing androgenic activity [59,60]. Progestins are derived from testosterone and exogenous use can stimulate sebaceous glands resulting in increased sebum



production and worsening of acne [59–61]. For this reason, the AAD recommends avoiding POP use in patients concerned about oral contraceptive therapy worsening current or prior acne vulgaris [59]. The patient in our clinical case should be informed about possible worsening of acne vulgaris with POP use. She should also be advised that CHC pills are FDA approved to treat acne vulgaris and, therefore, it is possible her acne may improve with CHC pill use (Table 6).

Table 6. Acne Quick Facts.

| Acne                                                                                                                |                                                              |
|---------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| <b>CHC Pills</b><br>Improve acne<br>FDA approved to treat acne with no pill type shown to be superior to the others | <b>POPs</b><br>Worsen acne via increased androgenic activity |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient in our clinical case thanks you for clarifying the impact of OCPs on acne and is just about ready to make an informed decision as to which type of OCP she wishes to start. Before you send a prescription to her preferred pharmacy, she tells you that she and her fiancé plan to start a family in 1–2 years. She has heard that OCP therapy can cause issues with fertility and wants to know more about this. What do you tell her? |

8. Infertility

While OCP-induced infertility is a commonly cited concern among patients with childbearing potential, there is no substantial evidence to suggest that OCP use leads to long-term infertility [19,62]. Fears regarding OCP-induced infertility stem from reports of high-dose OCPs (specifically the OCPs used in the early years of contraceptive therapy) blocking normal HPO axis function and resulting in long lasting, or even irreversible, infertility [62]. With modern OCPs, the impact on fertility is minimal (Table 7) [62].

Table 7. Infertility Quick Facts.

| Infertility                                                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>CHC Pills and POPs</b><br>Transient delay in return to normal fertility upon cessation<br>Normal pregnancy rates within one year of discontinuation |

| Clinical Case Continued                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The patient in our clinical case thanks you for clarifying the impact of OCPs on acne and The patient thanks you for taking the time to answer all her questions and states she feels much more comfortable starting OCPs. After your discussion, she opts to use CHC pills for contraceptive purposes. Her blood pressure is within normal limits and the point-of-care pregnancy test is negative. You counsel her about possible side effects when initiating OCPs, including nausea, breast tenderness, and breakthrough bleeding. You emphasize that side effects should resolve spontaneously within a few months of use. You send a prescription for drospirenone/ethinylestradiol therapy to her preferred pharmacy and hand her an OCP common concerns quick facts sheet (Figure 1) that covers what was discussed during her appointment today. She uses CHC pills for contraception for the next year without any concerns or complaints. |

In a systematic review and meta-analysis of OCP use (both POP and CHC pills) and fertility, 87% of patients previously taking OCPs were pregnant within one year of stopping contraceptive therapy [62]. The rates of pregnancy at 12 months following OCP discontinuation have been shown to be comparable to rates following discontinuation of IUDs, condoms, and natural family planning, regardless of the type or duration of OCP

use [62–65]. There is mixed data suggesting a transient delay of a few months in returning to normal fertility among patients with childbearing potential who have used modern OCPs [62,65]. This delay following cessation of OCP use is thought to be due to the time required for exogenous hormones to be completely cleared from the body [62].

When counseling the patient in our clinical case about the impact of OCP use on fertility, the healthcare provider should emphasize that modern OCP use does not lead to long lasting infertility. The clinician should acknowledge that OCP use may cause a transient delay in fertility for a few months after discontinuation, but one-year pregnancy rates are comparable to patients previously using IUDs, condoms, and natural family planning.

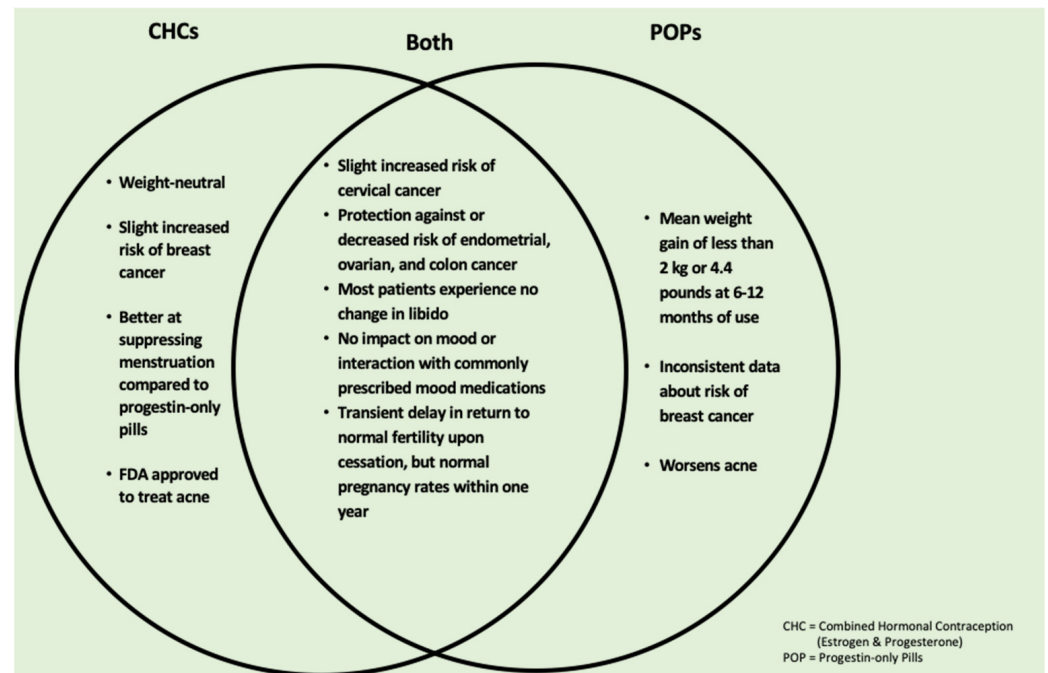


Figure 1. Patient Handout.

## 9. Conclusions

Given that OCPs are the most prescribed form of contraception in the United States, it is important that PCPs are equipped to answer patient concerns with regard to OCPs [6–8]. Common patient concerns include the impact of OCPs on weight gain, mood changes, overall cancer risk, decreased libido, acne, and infertility. While weight gain is a significant concern in patients considering OCPs, there is no evidence linking CHC pills to weight gain. However, low-quality evidence suggests that POPs may be associated with a marginal increase in weight of 2 kg or 4.4 pounds at 6–12 months. OCP use has not been shown to negatively impact mood and, in fact, CHC pills may improve symptoms of PMDD. In terms of cancer risk, both CHC pills and POPs have been shown to increase the risk of cervical cancer. CHC pills increase the risk of breast cancer. There is inconsistent data regarding POPs and increased breast cancer risk. However, both types of OCPs have a protective effect against endometrial, ovarian, and colon cancer and therefore may provide an overall decreased risk of cancer. The impact of either type of OCP on libido is mixed with most patients experiencing no changes in their reported libido. OCPs can safely be used to induce amenorrhea without any negative impact on health. When used for both contraception and medication-induced amenorrhea, CHC pills have been shown to be more effective than POPs. In terms of acne, CHC pills are FDA approved to treat acne while POPs, specifically norethindrone, may worsen acne via androgenic activity. Although CHC pills and POPs may temporarily delay fertility after cessation, fertility rates at 1 year

were not impacted when compared to other methods of contraception, including natural family planning (Table 8). When taken as prescribed, OCPs are an easy and effective way to prevent pregnancy and are safe to use in the vast majority of patients [16]. With this evidence in mind, PCPs can provide the counseling necessary to empower patients to make informed decisions regarding OCP use.

**Table 8.** CHC Pills and POPs.

| Quick Facts Summary                                                                                       |                                                                                                                                                             |                                                                                                                                                                                                       |
|-----------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Myth                                                                                                      | CHC Pills                                                                                                                                                   | POPs                                                                                                                                                                                                  |
| <b>Weight</b><br>“OCPs make you gain weight”                                                              | No evidence linking CHC pill use to weight change                                                                                                           | Low-quality data suggesting a mean weight gain of less than 2 kg or 4.4 pounds at 6–12 months (marginally higher than average weight gain of 1 kg or 2.2 pounds per year in US adults)                |
| <b>Mood Disturbances</b><br>“OCPs make depression worse”                                                  | No evidence demonstrating worsening depressive symptoms<br>No interaction with SSRIs or SNRIs<br>May improve symptoms of PMDD                               | No evidence demonstrating worsening depressive symptoms<br>No interaction with SSRIs or SNRIs                                                                                                         |
| <b>Cancer Risk</b><br>“OCPs cause breast cancer or other cancers of the female organs”                    | Increased risk of breast cancer<br>Increased risk of cervical cancer<br>Protection against endometrial, ovarian, and colon cancer                           | Inconsistent data about breast cancer risk<br>Increased risk of cervical cancer<br>Protection against endometrial, ovarian, and colon cancer                                                          |
| <b>Libido</b><br>“OCPs decrease your libido”                                                              | Mixed data regarding impact on libido<br>Possible risk of decreased libido                                                                                  | Mixed data regarding impact on libido<br>Majority of patients experience no change                                                                                                                    |
| <b>Need for menstruation</b><br>“It isn’t good to just skip your period; you need to have one each month” | No negative impact on health with <i>OCP-induced</i> amenorrhea<br>Higher efficacy in inducing amenorrhea than POPs (when prescribed at contraceptive dose) | No negative impact on health with <i>OCP-induced</i> amenorrhea<br>Norethindrone 5 mg may induce amenorrhea but is not FDA approved as contraception, however, can be used off-label for this purpose |
| <b>Acne</b><br>“OCPs make your skin break out”                                                            | Improve acne<br>FDA approved to treat acne with no pill type shown to be superior to the others                                                             | Worsen acne via increased androgenic activity                                                                                                                                                         |
| <b>Infertility</b><br>“OCPs can affect your long-term fertility”                                          | Transient delay in return to normal fertility upon cessation<br>Normal pregnancy rates within one year of discontinuation                                   |                                                                                                                                                                                                       |

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## Appendix A

**Table A1.** Progestin-Only Pills Contraindications [13].

| Progestin-Only Pills Contraindications                                                   |
|------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• Presence or history of breast cancer</li> </ul> |

**Table A1.** *Cont.*

- 
- Presence of malignant hepatocellular carcinoma
  - Previous bariatric surgery such as Roux-en-Y gastric bypass or biliopancreatic diversion that resulted in compromised absorption of medications
  - Use of certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine) and antimicrobials such as rifampin or rifabutin
  - For the drospirenone formulation only:
    - Current nephrotic syndrome with known hyperkalemia
    - Hemodialysis with known hyperkalemia
    - Peritoneal dialysis with known hyperkalemia
- 

**Table A2.** Combined Hormonal Contraceptive Pills Contraindications [13].

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**Combined Hormonal Contraceptive Pills Contraindications**


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- <21 days postpartum
  - Breastfeeding individuals 21 to <30 days postpartum with or without other risk factors for VTE (age  $\geq$  35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI  $\geq$  30 kg/m<sup>2</sup>, postpartum hemorrhage, post cesarean delivery, preeclampsia, or smoking) or 30–42 days postpartum with risk factors for VTE (see above)
  - Non-breastfeeding individuals 21–42 days postpartum with other risk factors for VTE (see above)
  - Smoking at age 35 years or older
  - Previous bariatric surgery such as Roux-en-Y gastric bypass or biliopancreatic diversion that resulted in compromised absorption of medications
  - Surgery with prolonged immobilization
  - Patients with multiple risk factors for atherosclerotic cardiovascular disease (i.e., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)
  - Hypertension
  - Presence of history of deep vein thrombosis or pulmonary embolism
  - Thrombophilia (factor V Leiden mutation; prothrombin gene mutation; protein S, protein C, and antithrombin deficiencies, or antiphospholipid syndrome)
  - Presence or history of superficial venous thrombosis
  - Presence or history of ischemic heart disease
  - Presence or history of stroke
  - Complicated valvular heart disease (pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis)
  - Peripartum cardiomyopathy
  - Nephrotic syndrome
  - End stage renal disease requiring dialysis (hemodialysis or peritoneal)
  - Positive (or unknown) antiphospholipid antibodies
  - Migraine with aura
  - Multiple sclerosis with prolonged immobility
  - Presence or history of breast cancer
  - Diabetes mellitus with nephropathy, retinopathy, neuropathy, or other vascular disease OR diabetes of >20 years duration
  - Inflammatory bowel disease with increased risk for VTE (those with active or extensive disease, surgery, immobilization, corticosteroid use, vitamin deficiencies, or fluid depletion)
  - Current or medically treated symptomatic gallbladder disease
  - History of cholestasis due to CHC use
  - Initiation of CHC during acute viral hepatitis
  - Decompensated cirrhosis
  - Hepatocellular adenoma
  - Malignant hepatocellular carcinoma
-

Table A2. Cont.

- Sickle cell disease
- Solid organ transplant with graft failure
- Use of certain medications including the HIV medication Fosamprenavir, certain anticonvulsant medications (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine, lamotrigine), and antimicrobials such as rifampin or rifabutin

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