Continuous Versus Cyclical OCP Use in PCOS (CCOUP)

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Continuous versus Cyclical OCP Use in PCOS (CCOUP): A Pilot Study

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This is a clinical research study. Your study doctors, Dr. Heather Huddleston and Dr. Marcelle Cedars from the UCSF Department of Reproductive Endocrinology and Fertility, will explain the study to you. You have been asked to take part in a research study called *Continuous vs. Cyclical OCP Use in PCOS (CCOUP): A Pilot Study* at UCSF which seeks to identify a more effective means of treating elevated testosterone levels, excess body hair growth and acne, seen in Polycystic Ovary Syndrome (PCOS).

Taking part in this study is entirely voluntary. We urge you to discuss any questions about this study with our staff members. Talk to your family and friends about it and take your time to make your decision. If you decide to participate, you must sign this form to show that you want to take part.

Why is this study being done?

You are being asked to participate in this research study because you have been found to have a diagnosis of Polycystic Ovary Syndrome (PCOS) and are recommended to start an oral contraceptive pill/birth control pill (OCP). The purpose of this study is to find out whether one form of an OCP has a better outcome on decreasing testosterone levels, excess hair growth and acne, than another. In particular, we are looking at two different lengths of active hormone pills using the OCP Yasmin (30 mcg Ethinyl estradiol/3mg Drospirenone). The two forms being compared in this study are:

- a 21-day active hormone + 7-day placebo (or inactive) OCP taken monthly for 6 months
  or
- a 168-day active hormone + 0 placebo (or inactive) OCP taken for 6 months straight

Approximately 60 people are expected to take part in this research at the UCSF PCOS Multidisciplinary Clinic in San Francisco, California. Of note, the investigators in this study have no disclosures including financial or proprietary interests. The UCSF Department of Reproductive Endocrinology and Fertility is paying for the conduct of this study.

How many people will take part in this study?

About 60 people are expected to take part in this study.

What will happen if I take part in this research study?

Prior to the start of the study, it is expected that you have been seen and evaluated at the UCSF PCOS Multidisciplinary clinic as a new patient and are now recommended to start an OCP. If you choose to take part in this study, we will ask you to sign this consent form prior to starting medication therapy. Details of procedures and tests in this study are detailed below.

At the start of the study
If you agree to take part in the research, your routine initial pelvic ultrasound as well as skin exam findings completed during your first visit to the clinic will be included as baseline measurements in the study. After which, you will be randomly assigned to one of two study groups. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor your doctor can choose the group you will be in. You will have a 50/50 chance of being placed in the group that receives either 6 months of a monthly OCP (containing 21 days of active hormonal pills followed by 7 days of inactive pills) or a continuous 6-month OCP (with 168 days of active hormone pills, no inactive pills). Lastly, a baseline survey will be sent to you securely through your e-mail for you to fill out.

1 Month into Therapy
At 1 month into starting an OCP we will ask that you come into the PCOS Clinic for blood work. This is for research purposes. The timing of this blood work will depend on when you start your first OCP pack and the dates will be provided to you at the start of the study.

3 Months into Therapy
At 3 months into OCP therapy we will again ask that you come back to the PCOS Clinic, this time for a 30- minute routine follow up visit. At this visit we will check in to see how you are doing on your current therapy. In addition, you will have repeat blood work drawn similar to your 1-month visit (this is standard of care and not solely for research purposes). You will also receive a lab slip to get routine fasting blood work at your local lab as well. In addition to the blood work, you will receive another secure email with a link to some online surveys for you to fill out on your own.

6 Months into Therapy
At 6 months into OCP therapy we will once again ask that you come back for a final follow up study visit (this is not routine but for research purposes). This study visit should last about 30 minutes-1 hour and will include a repeat skin exam, as well as a pelvic ultrasound to look at your ovaries. We will ask that you do not undergo any hair removal procedures (waxing, tweezing, shaving, electrolysis, or use Nair/Veet,) at least 1 week prior to your clinic visit. This is so that we can fully assess your body hair growth while on the OCP therapy. In addition, you will again be expected to get blood work drawn at the PCOS Clinic (for research purposes). The study will conclude with several online surveys that will be emailed securely for you to fill out.

Schedule of Events

Visit	What you do
Enrollment	☐ *Sign Consent Form to participate in study* ☐ *You will be randomized into 1 of 2 treatment groups* *A) **Cyclical OCP Group**: Yasmin 21 days of hormone pills + 7 days of placebo pills taken monthly for 6 months* *B) **Continuous OCP Group**: Yasmin 168 days of hormone pills + 0 days of placebo pills taken continuously for 6 months* ☐ *Complete online survey*
Month 1	☐ *Come to clinic for blood work (for research purposes)*
Month 3	☐ *Come to clinic for a "routine" follow up visit* ☐ *Routine blood work drawn in clinic* ☐ *Fasting blood work to be done at your local lab* ☐ *Complete online surveys*
Month 6	☐ *Come to clinic for a "research" follow up visit* ☐ *Blood work drawn in clinic (for research purpose)* ☐ *Pelvic Ultrasound* ☐ *Skin exam* ☐ *Complete online surveys*

How long will I be in this study?

The study will last approximately 6 months and you will be asked to take the OCP Yasmin throughout this time. Once enrolled, we will ask you to make 3 visits to the UCSF PCOS Clinic and obtain blood work at scheduled time points during the study (3 of which will occur in the PCOS clinic and 1 time at your local lab). Each clinic visit varies in length of time but ranges from 30 minutes-1 hour.

Can I still get medical care within the UCSF PCOS Multidisciplinary clinic if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get at UCSF now or in the future. You may choose to not take part in the study and still request OCP therapy or other individualized therapy whether similar or different to this study. There will be no penalty, and you won't lose any benefits you would receive now or have a right to receive.

Taking part in this research study is up to you and you can change your mind and drop out later. If you decide that you want to drop out, please tell us so that we can make sure that you stop the study safely. We will also talk to you about follow up care, if needed.

The study doctor may also stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow up the study rules or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious and your health care team may give you medicines to help lessen the side effects. Many of the side effects go away after you stop taking the drug, but in some cases, side effects can be serious, long lasting, or may never go away.

Prior to start of therapy, your physician will review your medical chart to make sure you do not have any contraindications to starting OCP therapy that may put you more at risk of developing a drug side effect. However, you should talk to your study doctor about any side effects you experience while taking part in this study. Risks and side effects related to the OCPs/Yasmin are listed below:

- **Medication Side Effects Common to All OCPs:**
  - **Likely**: Premenstrual syndrome (13.2%), headache/migraine (10.7%), breast pain/tenderness/discomfort (8.3%), nausea/vomiting (4.5%), abdominal pain/tenderness/discomfort (2.3%), mood changes (2.3%), vaginal bleeding/spotting.
  - **Less likely**: Gallbladder disease, elevation in blood pressures, benign liver tumors, elevation in cholesterol or triglyceride levels
  - **Rare but serious**: Blood clots in a vein, with possible pain, swelling or redness at the site (risk is greatest during the first year of use and less than the risk associated with pregnancy), hepatocellular carcinoma (a type of cancer). Women over 35 years of old and smoke have an increased risk of serious cardiovascular events from OCP use including heart attack, blood clots or stroke.
- **Medication Side Effects Specific to the OCP Yasmin:**
  - If you are assigned to the continuous OCP treatment group, you are likely to have more irregular bleeding than those randomized to cyclical use.
  - There is a slightly increased risk of Deep Vein Thrombosis (a blood clot in a vein, typically in the thigh or leg) with Yasmin as compared to some other OCPs.
- **Randomization risks**: You will be assigned to a treatment program by chance, and the treatment that you receive may prove to be less effective or to have more side effects than the other study treatment or other available treatments.
- **Blood drawing (venipuncture) risks**: Drawing blood may cause temporary discomfort from the needle stick, bruising, infection and fainting.
- **Pelvic Ultrasound risks**: There can be some discomfort and or pressure experienced with the pelvic ultrasound as this is done vaginally.

- **Surveys/Questionnaires**: You will be asked to complete several questionnaires throughout the study that ask sensitive information regarding your mental health (specifically regarding anxiety and depression). If these questionnaires show that you are at high risk for self-harm, you will be contacted by a physician immediately and evaluated for imminent risk. You may be placed on a medical hold and be taken to the nearest Emergency Room for further evaluation and monitoring. If you are diagnosed with suicidal ideation or intent, this is reportable and will be documented in your medical file as well as in the study file (though study files will not contain your name or any identifying information).
- **Reproductive Risks**: As the drug used in this study is also used as a form of birth control, you should not become pregnant or continue taking this medication if you become pregnant. There also may be other side effects or discomforts that we cannot predict especially to a fetus or embryo. Your doctor will discuss this with you.
- **Unknown Risks**: The experimental treatments may have side effect that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

  For more information about risks and side effects, ask your study doctor.

Are there benefits from taking part in this study?

Possible benefits to you: You may or may not benefit from taking part in this research study. However, there is strong evidence that OCP therapy can help regulate your periods, improve acne, and lower your testosterone level. Potentially you could see improvement in your hormone levels as well as decrease in facial or body hair growth and acne production.

Possible benefits to others: While there are many research studies that have compared various kinds of OCPs, none have looked at the possible benefits of longer active hormone pill preparations in women with PCOS. We hope to learn from you whether there is one form of OCP therapy that should be standardized in treatment. Ultimately, this study could pave the way for further research and potentially help create future guidelines to OCP therapy in women with PCOS.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your PCOS without being in the study
- Taking part in another study
- Getting no treatment

Please talk to your doctor about your choices before deciding if you will take part in this study.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some

information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the University of California
- Representatives of the Food and Drug Administration (FDA)

Of note, a survey regarding your mental health will be sent to you at two-time points during this study. If you are found to be at risk of self-harm, please note that this is a reportable event and may be documented into your medical record. In addition, immediate steps will be taken to ensure your safety by involving your care with a healthcare provider and clinical psychologist.

Are there any costs to me for taking part in this study?

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research.

- You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay.
- There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network.
- Any procedures done only for research will not be charged to you or your insurer.

Will I be paid for taking part in this study?

In return for your time, effort and travel expenses, you will be eligible to receive up to $100 in the form of an Amazon gift card.

- At the end of the 1st clinic visit (Month 1 – blood draw), participants will receive a $25 gift card.
- At the end of the 2nd clinic visit (Month 3 – follow up visit, blood draw and online surveys), participants will receive another $25 gift card.
- At the end of the 3rd and final clinic visit (Month 6 – follow up visit, pelvic ultrasound, skin exam and online surveys), those who have completed all study procedures will receive a $50 Amazon gift card.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctors, Dr. Huddleston or Dr. Cedars, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call her at 415-353-7475.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctors Dr. Heather Huddleston or Dr. Jerrine Morris at (415)-353-7475 Monday – Friday 9:00 AM – 5:00 PM.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker

A Parent or Legal Guardian must sign for participants under 18:
The person being considered for this study is unable to consent for herself because she is a minor. By signing below, you are giving your permission for your child to be included in this study.

Date	Parent or Legal Guardian