Please note: An update has been published for this report. To view the update, please click here

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 3
July 29, 2016

U.S. Medical Eligibility Criteria for Contraceptive Use, 2016

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CONTENTS

Introduction 1
Methods 2
How to Use This Document 3
Keeping Guidance Up to Date 5
References 8
Abbreviations and Acronyms 9
Appendix A: Summary of Changes from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010* 10
Appendix B: Classifications for Intrauterine Devices 18
Appendix C: Classifications for Progestin-Only Contraceptives 35
Appendix D: Classifications for Combined Hormonal Contraceptives 55
Appendix E: Classifications for Barrier Methods 81
Appendix F: Classifications for Fertility Awareness–Based Methods 88
Appendix G: Lactational Amenorrhea Method 90
Appendix H: Coitus Interruptus (Withdrawal) 91
Appendix I: Female and Male Sterilization 92
Appendix J: Classifications for Emergency Contraception 93
Appendix K: Summary of Classifications for Hormonal Contraceptive Methods and Intrauterine Devices 96

Disclosure of Relationship

CDC, our planners, and our content experts wish to disclose they have no financial interest or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters. Planners have reviewed content to ensure there is no bias. This document will not include any discussion of the unlabeled use of a product or a product under investigational use, with the exception that some of the recommendations in this document might be inconsistent with package labeling.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Title]. MMWR Recomm Rep 2016;65(No. RR-#):[inclusive page numbers].

Centers for Disease Control and Prevention
Thomas R. Frieden, MD, MPH, *Director*
Harold W. Jaffe, MD, MA, *Associate Director for Science*
Joanne Cono, MD, ScM, *Director, Office of Science Quality*
Chesley L. Richards, MD, MPH, *Deputy Director for Public Health Scientific Services*
Michael F. Iademarco, MD, MPH, *Director, Center for Surveillance, Epidemiology, and Laboratory Services*

***MMWR* Editorial and Production Staff (Serials)**
Sonja A. Rasmussen, MD, MS, *Editor-in-Chief*
Charlotte K. Kent, PhD, MPH, *Executive Editor*
Christine G. Casey, MD, *Editor*
Teresa F. Rutledge, *Managing Editor*
David C. Johnson, *Lead Technical Writer-Editor*
Catherine B. Lansdowne, MS, *Project Editor*
Martha F. Boyd, *Lead Visual Information Specialist*
Maureen A. Leahy, Julia C. Martinroe,
Stephen R. Spriggs, Moua Yang, Tong Yang,
Visual Information Specialists
Quang M. Doan, MBA, Phyllis H. King, Terraye M. Starr,
Information Technology Specialists

***MMWR* Editorial Board**
Timothy F. Jones, MD, *Chairman*
Matthew L. Boulton, MD, MPH
Virginia A. Caine, MD
Katherine Lyon Daniel, PhD
Jonathan E. Fielding, MD, MPH, MBA
David W. Fleming, MD
William E. Halperin, MD, DrPH, MPH
King K. Holmes, MD, PhD
Robin Ikeda, MD, MPH
Rima F. Khabbaz, MD
Phyllis Meadows, PhD, MSN, RN
Jewel Mullen, MD, MPH, MPA
Jeff Niederdeppe, PhD
Patricia Quinlisk, MD, MPH
Patrick L. Remington, MD, MPH
Carlos Roig, MS, MA
William L. Roper, MD, MPH
William Schaffner, MD

U.S. Medical Eligibility Criteria for Contraceptive Use, 2016

Kathryn M. Curtis, PhD[1]
Naomi K. Tepper, MD[1]
Tara C. Jatlaoui, MD[1]
Erin Berry-Bibee, MD[1,2]
Leah G. Horton, MSPH[1]
Lauren B. Zapata, PhD[1]
Katharine B. Simmons, MD[1,2]
H. Pamela Pagano, MPH[1]
Denise J. Jamieson, MD[1]
Maura K. Whiteman, PhD[1]

[1]*Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC, Atlanta, Georgia*
[2]*Department of Obstetrics and Gynecology, University of North Carolina School of Medicine, Chapel Hill, North Carolina*

Summary

The 2016 U.S. Medical Eligibility Criteria for Contraceptive Use *(U.S. MEC) comprises recommendations for the use of specific contraceptive methods by women and men who have certain characteristics or medical conditions. These recommendations for health care providers were updated by CDC after review of the scientific evidence and consultation with national experts who met in Atlanta, Georgia, during August 26–28, 2015. The information in this report updates the 2010 U.S. MEC* (CDC. U.S. medical eligibility criteria for contraceptive use, 2010. MMWR 2010:59 [No. RR-4]). *Notable updates include the addition of recommendations for women with cystic fibrosis, women with multiple sclerosis, and women receiving certain psychotropic drugs or St. John's wort; revisions to the recommendations for emergency contraception, including the addition of ulipristal acetate; and revisions to the recommendations for postpartum women; women who are breastfeeding; women with known dyslipidemias, migraine headaches, superficial venous disease, gestational trophoblastic disease, sexually transmitted diseases, and human immunodeficiency virus; and women who are receiving antiretroviral therapy. The recommendations in this report are intended to assist health care providers when they counsel women, men, and couples about contraceptive method choice. Although these recommendations are meant to serve as a source of clinical guidance, health care providers should always consider the individual clinical circumstances of each person seeking family planning services. This report is not intended to be a substitute for professional medical advice for individual patients. Persons should seek advice from their health care providers when considering family planning options.*

Introduction

Approximately 45% of all pregnancies that occur in the United States are unintended (*1*), with associated increased risks for adverse maternal and infant health outcomes (*2*) and increased health care costs (*3*). Women, men, and couples have increasing numbers of safe and effective choices for contraceptive methods, including long-acting reversible contraception methods such as intrauterine devices (IUDs) and implants, to reduce the risk for an unintended pregnancy. However, with these expanded options comes the need for evidence-based guidance to help health care providers offer quality family planning care to their patients, including choosing the most appropriate contraceptive method for individual circumstances and using that method correctly, consistently, and continuously to maximize effectiveness.

Corresponding author: Kathryn M. Curtis, PhD, Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC. Telephone: 770-488-5200; E-mail: kmc6@cdc.gov.

In 2010, CDC published the first *U.S. Medical Eligibility Criteria for Contraceptive Use* (U.S. MEC), which provided recommendations on safe use of contraceptive methods for women with various medical conditions and other characteristics (and was adapted from global guidance developed by the World Health Organization [WHO MEC]) (*4*,*5*). U.S. MEC is a companion document to the *U.S. Selected Practice Recommendations for Contraceptive Use* (U.S. SPR), which provides guidance on how to use contraceptive methods safely and effectively once they are deemed to be medically appropriate (*6*). WHO intended for the global guidance to be used by local or national policy makers, family planning program managers, and the scientific community as a reference when they develop family planning guidance at the country or program level. During 2008–2010, CDC participated in a formal process to adapt the global guidance for appropriateness

for use in the United States, which included rigorous identification and critical appraisal of the scientific evidence through systematic reviews, and input from national experts on how to translate that evidence into recommendations for U.S. health care providers (*5*). At that time, CDC committed to keeping this guidance up to date and based on the best available evidence, with full review every few years (*5*).

This document updates CDC's U.S. MEC 2010 (*5*), based on new evidence and input from experts. A summary of changes from U.S. MEC 2010 is provided (Appendix A). Notable updates include the following:

- addition of recommendations for women with cystic fibrosis, women with multiple sclerosis, and women receiving certain psychotropic drugs or St. John's wort
- revisions to the recommendations for emergency contraception, including the addition of ulipristal acetate
- revisions to the recommendations for postpartum women; women who are breastfeeding; women with known dyslipidemias, migraine headaches, superficial venous disease, gestational trophoblastic disease, sexually transmitted diseases (STDs), and human immunodeficiency virus (HIV); and women who are receiving antiretroviral therapy

The goal of these recommendations is to remove unnecessary medical barriers to accessing and using contraception, thereby decreasing the number of unintended pregnancies. These recommendations are meant to serve as a source of clinical guidance for health care providers; health care providers should always consider the individual clinical circumstances of each person seeking family planning services. This report is not intended to be a substitute for professional medical advice for individual patients, who should seek advice from their health care providers when considering family planning options.

Methods

Since publication of U.S. MEC 2010, CDC has monitored the literature for new evidence relevant to the recommendations through the WHO/CDC continuous identification of research evidence (CIRE) system. This system identifies new evidence as it is published and allows WHO and CDC to update systematic reviews and facilitate updates to recommendations as new evidence warrants. Automated searches are run in PubMed weekly, and the results are reviewed. Abstracts that meet specific criteria are added to the web-based CIRE system, which facilitates coordination and peer review of systematic reviews for both WHO and CDC (*7*). In 2014, CDC reviewed all of the existing recommendations in U.S. MEC 2010 for new evidence identified by CIRE that had the potential to lead to a changed recommendation. During August 27–28, 2014, CDC held a meeting in Atlanta, Georgia, of 11 family planning experts and representatives from partner organizations to solicit their input on the scope of and process for updating both U.S. MEC 2010 and U.S. SPR 2013. The participants were experts in family planning and represented various types of health care providers, as well as health care provider organizations. A list of participants is provided at the end of this report. Meeting participants discussed topics to be addressed in the update of U.S. MEC based on new evidence published since 2010 (identified through the CIRE system), topics addressed at a 2014 WHO meeting to update global guidance, and suggestions CDC received from health care providers for the addition of recommendations for women with medical conditions not yet included in U.S. MEC (e.g., from provider feedback through e-mail, public inquiry, and questions received at conferences). CDC identified several topics to consider when updating the guidance, including revision of existing recommendations for certain medical conditions or characteristics (breastfeeding, postpartum, HIV, receiving antiretroviral therapy, obesity, dyslipidemia, increased risk for STDs, superficial venous thrombosis, gestational trophoblastic disease, and migraine headaches), addition of recommendations for new medical conditions (cystic fibrosis, multiple sclerosis, use of certain psychotropic drugs, and St. John's wort), and addition of recommendations for new contraceptive methods (ulipristal acetate for emergency contraception). CDC determined that all other recommendations in U.S. MEC 2010 were up to date and consistent with the existing body of evidence for that recommendation.

In preparation for a subsequent expert meeting held during August 26–28, 2015, to review the scientific evidence for potential recommendations, CDC staff members and other invited authors listed at the end of this report conducted independent systematic reviews for each of the topics being considered. The purpose of these systematic reviews was to identify direct evidence about the safety of contraceptive method use by women with selected conditions (e.g., risk for disease progression or other adverse health effects in women with multiple sclerosis who use combined hormonal contraceptives [CHCs]). Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed for reporting systematic reviews (*8*,*9*), and strength and quality of the evidence were assigned using the system of the U.S. Preventive Services Task Force (*10*). When direct evidence was limited or not available, indirect evidence (e.g., evidence on surrogate outcomes or among healthy women) and theoretical issues were considered and either added to direct evidence within a systematic review or separately compiled for presentation to the meeting participants. Completed systematic

reviews were peer reviewed by two or three experts and then provided to participants before the expert meeting. Reviews are referenced and cited throughout this document; the full reviews appear in the published literature and contain the details of each review, including the systematic review question, literature search protocol, inclusion and exclusion criteria, evidence tables, and quality assessments. CDC staff continued to monitor new evidence identified through the CIRE system during the preparation for the August 2015 meeting.

During August 26–28, 2015, in Atlanta, Georgia, CDC held a meeting with 44 participants who were invited to provide their individual perspectives on the scientific evidence presented and potential recommendations. Twenty-nine of the participants represented a wide range of expertise in family planning provision and research, and included obstetricians/gynecologists, pediatricians, family physicians, nurse practitioners, epidemiologists, and others with research and clinical practice expertise in contraceptive safety, effectiveness, and management; these individuals participated in the entire meeting. Fifteen participants with expertise relevant to specific topics on the meeting agenda provided information and participated in the discussion (e.g., an expert in cystic fibrosis was asked to provide general information about the condition and to assist in interpreting the evidence and any theoretical concerns on the use of contraceptive methods in women with the condition); these participants provided input only during the session for which their topics were discussed. Lists of participants and any potential conflicts of interest are provided at the end of this report. During the meeting, the evidence from the systematic review for each topic was presented, including direct evidence and any indirect evidence or theoretical concerns. Participants provided their perspectives on using the evidence to develop recommendations that would meet the needs of U.S. health care providers. After the meeting, CDC determined the recommendations in this report, taking into consideration the perspectives provided by the meeting participants. Feedback also was received from three external reviewers, composed of health care providers and researchers who had not participated in the update meetings. These reviewers were asked to provide comments on the accuracy, feasibility, and clarity of the recommendations. Areas of research that need additional investigation also were considered during the meeting (*11*).

How to Use This Document

These recommendations are intended to help health care providers determine the safe use of contraceptive methods among women and men with various characteristics and medical conditions. Providers also can use the information in these recommendations when consulting with women, men, and couples about their selection of contraceptive methods. The tables in this document include recommendations for the use of contraceptive methods by women and men with particular characteristics or medical conditions. Each condition is defined as representing either an individual's characteristics (e.g., age or history of pregnancy) or a known preexisting medical or pathologic condition (e.g., diabetes or hypertension). The recommendations refer to contraceptive methods being used for contraceptive purposes; the recommendations do not consider the use of contraceptive methods for treatment of medical conditions because the eligibility criteria in these situations might differ. The conditions affecting eligibility for the use of each contraceptive method are classified into one of four categories (Box 1).

Using the Categories in Practice

Health care providers can use the eligibility categories when assessing the safety of contraceptive method use for women and men with specific medical conditions or characteristics. Category 1 comprises conditions for which no restrictions exist for use of the contraceptive method. Classification of a method/condition as category 2 indicates the method generally can be used, although careful follow-up might be required. For a method/condition classified as category 3, use of that method usually is not recommended unless other more appropriate methods are not available or acceptable. The severity of the condition and the availability, practicality, and acceptability of alternative methods should be considered, and careful follow-up is required. Hence, provision of a contraceptive method to a woman with a condition classified as category 3 requires careful clinical judgement and access to clinical services. Category 4 comprises conditions that represent an unacceptable health risk if the method is used. For example, a smoker aged <35 years generally can use combined oral contraceptives (COCs) (category 2). However, for a woman

BOX 1. Categories of medical eligibility criteria for contraceptive use

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

aged ≥35 years who smokes <15 cigarettes per day, the use of COCs usually is not recommended unless other methods are not available or acceptable to her (category 3). A woman aged ≥35 years who smokes ≥15 cigarettes per day should not use COCs because of unacceptable health risks, primarily the risk for myocardial infarction and stroke (category 4). The programmatic implications of these categories might depend on the circumstances of particular professional or service organizations. For example, in some settings, a category 3 might mean that a special consultation is warranted.

The recommendations address medical eligibility criteria for the initiation and continued use of all methods evaluated. The issue of continuation criteria is clinically relevant whenever a medical condition develops or worsens during use of a contraceptive method. When the categories differ for initiation and continuation, these differences are noted in the Initiation and Continuation columns. When initiation and continuation are not indicated, the category is the same for initiation and continuation of use.

On the basis of this classification system, the eligibility criteria for initiating and continuing use of a specific contraceptive method are presented in tables (Appendices A–K). In these tables, the first column indicates the condition. Several conditions are divided into subconditions to differentiate between varying types or severity of the condition. The second column classifies the condition for initiation or continuation (or both) into category 1, 2, 3, or 4. For certain conditions, the numeric classification does not adequately capture the recommendation; in these cases, the third column clarifies the numeric category. These clarifications were determined during the discussions of the scientific evidence and are considered a necessary element of the recommendation. The third column also summarizes the evidence for the recommendation if evidence exists. The recommendations for which no evidence is cited are based on expert opinion from either the WHO or U.S. expert meeting in which these recommendations were developed, and might be based on evidence from sources other than systematic reviews. For certain recommendations, additional comments appear in the third column and generally come from the WHO meeting or the U.S. meeting.

Recommendations for Use of Contraceptive Methods

The classifications for whether women with certain medical conditions or characteristics can use specific contraceptive methods are provided for intrauterine contraception, including the copper-containing IUD and levonorgestrel-releasing IUDs (Appendix B); progestin-only contraceptives (POCs), including etonogestrel implants, depot medroxyprogesterone acetate injections, and progestin-only pills (Appendix C); CHCs, including low-dose (containing ≤35 μg ethinyl estradiol) COCs, combined hormonal patch, and combined vaginal ring (Appendix D); barrier contraceptive methods, including male and female condoms, spermicides, diaphragm with spermicide, and cervical cap (Appendix E); fertility awareness–based methods (Appendix F); lactational amenorrhea method (Appendix G); coitus interruptus (Appendix H); female and male sterilization (Appendix I); and emergency contraception, including emergency use of the copper-containing IUD and emergency contraceptive pills (Appendix J). A table at the end of this report summarizes the classifications for the hormonal and intrauterine methods (Appendix K).

Contraceptive Method Choice

Many elements need to be considered by women, men, or couples at any given point in their lifetimes when choosing the most appropriate contraceptive method. These elements include safety, effectiveness, availability (including accessibility and affordability), and acceptability. The guidance in this report focuses primarily on the safety of a given contraceptive method for a person with a particular characteristic or medical condition. Therefore, the classification of category 1 means that the method can be used in that circumstance with no restrictions with regard to safety but does not necessarily imply that the method is the best choice for that person; other factors, such as effectiveness, availability, and acceptability, might play an important role in determining the most appropriate choice. Voluntary informed choice of contraceptive methods is an essential guiding principle, and contraceptive counseling, when applicable, might be an important contributor to the successful use of contraceptive methods.

In choosing a method of contraception, dual protection from the simultaneous risk for HIV and other STDs also should be considered. Although hormonal contraceptives and IUDs are highly effective at preventing pregnancy, they do not protect against STDs, including HIV. Consistent and correct use of the male latex condom reduces the risk for HIV infection and other STDs, including chlamydial infection, gonococcal infection, and trichomoniasis (*12*). Although evidence is limited, use of female condoms can provide protection from acquisition and transmission of STDs (*12*). All patients, regardless of contraceptive choice, should be counseled about the use of condoms and the risk for STDs, including HIV infection (*12*). Additional information about prevention and treatment of STDs is available from the CDC *Sexually Transmitted Diseases Treatment Guidelines* (http://www.cdc.gov/std/treatment) (*12*).

Contraceptive Method Effectiveness

Contraceptive method effectiveness is critical for minimizing the risk for an unintended pregnancy, particularly among women for whom an unintended pregnancy would pose additional health risks. The effectiveness of contraceptive methods depends both on the inherent effectiveness of the method itself and on how consistently and correctly it is used (Figure). Methods that depend on consistent and correct use have a wide range of effectiveness. IUDs and implants are considered long-acting, reversible contraception (LARC); these methods are highly effective because they do not depend on regular compliance from the user. LARC methods are appropriate for most women, including adolescents and nulliparous women. All women should be counseled about the full range and effectiveness of contraceptive options for which they are medically eligible so that they can identify the optimal method.

Unintended Pregnancy and Increased Health Risk

For women with conditions that might make pregnancy an unacceptable health risk, long-acting, highly effective contraceptive methods might be the best choice to avoid unintended pregnancy (Figure). Women with these conditions should be advised that sole use of barrier methods for contraception and behavior-based methods of contraception might not be the most appropriate choice because of their relatively higher typical-use rates of failure (Figure). Conditions included in U.S. MEC that are associated with increased risk for adverse health events as a result of pregnancy are identified throughout the document (Box 2). Some of the medical conditions included in U.S. MEC recommendations are treated with teratogenic drugs. While the woman's medical condition may not affect her eligibility to use certain contraceptive methods, women using teratogenic drugs are at increased risk for poor pregnancy outcomes; long-acting, highly effective contraceptive methods might be the best option to avoid unintended pregnancy or delay pregnancy until teratogenic drugs are no longer needed.

BOX 2. Conditions associated with increased risk for adverse health events as a result of pregnancy*

- Breast cancer
- Complicated valvular heart disease
- Cystic fibrosis
- Diabetes: insulin dependent; with nephropathy, retinopathy, or neuropathy or other vascular disease; or of >20 years' duration
- Endometrial or ovarian cancer
- Epilepsy
- Hypertension (systolic ≥160 mm Hg or diastolic ≥100 mm Hg)
- History of bariatric surgery within the past 2 years
- HIV: not clinically well or not receiving antiretroviral therapy
- Ischemic heart disease
- Gestational trophoblastic disease
- Hepatocellular adenoma and malignant liver tumors (hepatoma)
- Peripartum cardiomyopathy
- Schistosomiasis with fibrosis of the liver
- Severe (decompensated) cirrhosis
- Sickle cell disease
- Solid organ transplantation within the past 2 years
- Stroke
- Systemic lupus erythematosus
- Thrombogenic mutations
- Tuberculosis

* Long-acting, highly effective contraceptive methods might be the best choice for women with conditions that are associated with increased risk for adverse health events as a result of pregnancy. These women should be advised that sole use of barrier methods for contraception and behavior-based methods of contraception might not be the most appropriate choice because of their relatively higher typical-use rates of failure.

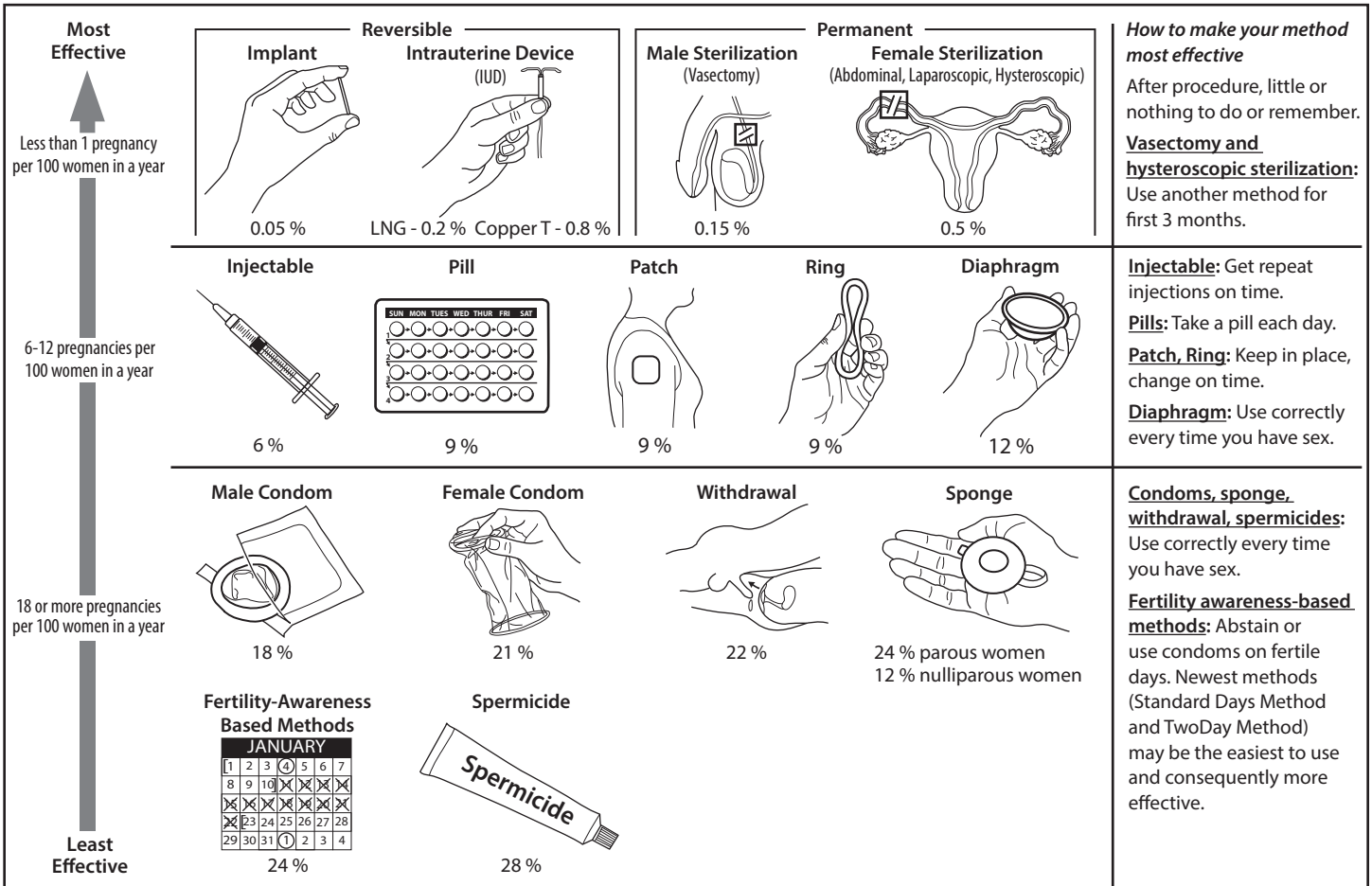
Keeping Guidance Up to Date

Updating the evidence-based recommendations as new scientific evidence becomes available is a challenge. CDC will continue to work with WHO to identify and assess new relevant evidence as it becomes available and to determine whether changes in the recommendations are warranted (*7*). In most cases, U.S. MEC follows the WHO guidance updates, which typically occur every 5 years (or sooner if warranted by new data). However, CDC will review all WHO updates for their application in the United States. CDC also will identify and assess any new literature for the recommendations and medical conditions that are not included in the WHO guidance. CDC will completely review U.S. MEC every 5 years as well. Updates to the guidance will appear on the CDC U.S. MEC website (http://www.cdc.gov/reproductivehealth/UnintendedPregnancy/USMEC.htm).

Acknowledgments

This report is based, in part, on the work of the Promoting Family Planning Team, Department of Reproductive Health and Research, World Health Organization, and its development of *Medical Eligibility Criteria for Contraceptive Use, 5th edition*.

FIGURE. Effectiveness of family planning methods*



CONDOMS SHOULD ALWAYS BE USED TO REDUCE THE RISK OF SEXUALLY TRANSMITTED INFECTIONS.

Other Methods of Contraception

Lactational Amenorrhea Method: LAM is a highly effective, *temporary* method of contraception.

Emergency Contraception: Emergency contraceptive pills or a copper IUD after unprotected intercourse substantially reduces risk of pregnancy.

Sources: Adapted from World Health Organization (WHO) Department of Reproductive Health and Research, Johns Hopkins Bloomberg School of Public Health/ Center for Communication Programs (CCP). Knowledge for health project. Family planning: a global handbook for providers (2011 update). Baltimore, MD; Geneva, Switzerland: CCP and WHO; 2011; and Trussell J. Contraceptive failure in the United States. Contraception 2011;83:397–404.

* The percentages indicate the number out of every 100 women who experienced an unintended pregnancy within the first year of typical use of each contraceptive method.

U.S. Medical Eligibility Criteria for Contraceptive Use Participants

CDC Guideline Development Group for *U.S. Medical Eligibility Criteria for Contraceptive Use* and *U.S. Selected Practice Recommendations for Contraceptive Use*

Kathryn M. Curtis, PhD (Chair), Erin Berry-Bibee, MD, Suzanne G. Folger, PhD, Leah G. Horton, MSPH, Denise J. Jamieson, MD, Tara C. Jatlaoui, MD, Polly A. Marchbanks, PhD, H. Pamela Pagano, MPH, Halley E.M. Riley, MPH, Mirelys Rodriguez, Katharine B. Simmons, MD, Naomi K. Tepper, MD, Maura K. Whiteman, PhD, Lauren B. Zapata, PhD, CDC, Atlanta, Georgia.

Invited Meeting Participants, August 27–28, 2014, Atlanta, Georgia

Herbert Peterson, MD, University of North Carolina, Chapel Hill, North Carolina (Chair); Gale Burstein, MD, Erie County Department of Health, Buffalo, New York; Alison Edelman, MD, Oregon Health and Science University, Portland, Oregon; Eve Espey, MD, University of New Mexico, Albuquerque, New Mexico; Emily Godfrey, MD, University of Washington, Seattle, Washington; Andrew Kaunitz, MD, University of Florida, Jacksonville, Florida; Susan Moskosky, MS, U.S. Department of Health and Human Services, Rockville, Maryland; Kavita Nanda, MD, FHI360 and American College of Obstetricians and Gynecologists, Durham, North Carolina; Deborah Nucatola, MD, Planned Parenthood Federation of America, New York, New York; Michael Policar, MD, University of California, San Francisco, California; Carolyn Westhoff, MD, Columbia University, New York, New York.

Systematic Review Presenters and Authors, Meeting, August 26–28, 2015, Atlanta, Georgia

Erin Berry-Bibee, MD, Kathryn M. Curtis, PhD, Leah G. Horton, MSPH, Denise J. Jamieson, MD, Tara C. Jatlaoui, MD, Polly A. Marchbanks PhD, Titilope Oduyebo, MD, Pamela Pagano, MPH, Halley E.M. Riley, MPH, Katharine B. Simmons, MD, Naomi K. Tepper, MD, Maura K. Whiteman, PhD, Lauren B. Zapata, PhD, CDC, Atlanta, Georgia; Monica Dragoman, MD, Mary E. Gaffield, PhD, Sharon J. Phillips, MD, Marleen Temmerman, MD, World Health Organization, Geneva, Switzerland; Andra James, MD, Duke University Medical Center, Durham, North Carolina; Nathalie Kapp, MD, HRA Pharma, Paris, France; Kavita Nanda, MD, FHI360, Durham, North Carolina; Seth Walker, MD, Emory University, Atlanta, Georgia.

Invited Meeting Participants, August 26–28, 2015, Atlanta, Georgia

Herbert Peterson, MD, University of North Carolina, Chapel Hill, North Carolina (Chair); Rebecca Allen, MD, American Society for Reproductive Medicine and Women and Infants Hospital, Providence, Rhode Island; Jean Anderson, MD, Johns Hopkins University, Baltimore, Maryland; Abbey Berenson, MD, University of Texas Medical Branch, Galveston, Texas; Amanda Black, MD, University of Ottawa, Ontario, Canada; Cora Collette Breuner, MD, American Academy of Pediatrics and Seattle Children's Hospital, Seattle, Washington; Gale Burstein MD, Erie County Department of Health, Buffalo, New York; Anne Calhoun, MD, University of North Carolina, Chapel Hill, North Carolina; Nahida Chakhtoura, MD, National Institutes of Health, Rockville, Maryland; Alicia Christy, MD, National Institutes of Health, Rockville, Maryland; Mitchell D. Creinin, MD, University of California, Davis, California; Linda Dominguez, Southwest Women's Health, Albuquerque, New Mexico; Alison Edelman, MD, Oregon Health and Science University, Portland, Oregon; Eve Espey, MD, University of New Mexico, Albuquerque, New Mexico; Emily Godfrey, MD, University of Washington, Seattle, Washington; Marji Gold, MD, Albert Einstein College of Medicine, Bronx, New York; Donald Goldstein, MD, Harvard Medical School, Boston, Massachusetts; Robert Hatcher, MD, Emory University, Atlanta, Georgia; Mark Hathaway, MD, JHPIEGO and Unity Healthcare, Washington, DC; Stephen Heartwell, MD, Susan Thompson Buffett Foundation, Omaha, Nebraska; Paula Hillard, MD, Stanford University, Palo Alto, California; Maria Houtchens, MD, Harvard Medical School, Boston, Massachusetts; Andra James, MD, Duke University Medical Center, Durham, North Carolina; Andrew Kaunitz, MD, University of Florida, Jacksonville, Florida; Myong-Jin Kim, Pharm-D, Food and Drug Administration, Rockville, Maryland; Barbara Konkle, MD, Bloodworks Northwest, Seattle, Washington; Tobias Kurth, MD, INSERM, Bordeaux, France; Miriam Labbok, MD, Academy of Breastfeeding Medicine and University of North Carolina, Chapel Hill, North Carolina; Reagan McDonald-Mosley, MD, Planned Parenthood Federation of America, New York, New York; Joan Meek, MD, American Academy of Pediatrics and Florida State University College of Medicine, Orlando, Florida; Mark Mirochnick, MD, Boston University, Boston, Massachusetts; Susan Moskosky, MS, U.S. Department of Health and Human Services, Rockville, Maryland; Kavita Nanda, MD, FHI360, Durham, North Carolina; Jeffrey Peipert, MD, Washington University, St. Louis, Missouri; Michael Policar, MD, University of California, San Francisco, California; Sarah Prager, MD, University of Washington, Seattle Washington; David Soper, MD, Medical University of South Carolina, Charleston, South Carolina; Lisa Soule, MD, Food and Drug Administration, Rockville, Maryland; Alison Stuebe, MD, American College of Obstetricians and Gynecologist and University of North Carolina, Chapel Hill, North Carolina; James Trussell, PhD, Princeton University, Princeton, New Jersey; Seth Walker, MD, Emory University, Atlanta, Georgia; Nanette Wenger, MD, Emory University, Atlanta, Georgia; Carolyn Westhoff, MD, Columbia University, New York, New York; Christopher Zahn, MD, American College of Obstetricians and Gynecologists, Washington, DC.

CDC Attendees

Wanda D. Barfield, MD, Peter Briss, MD, W. Craig Hooper, PhD, Jill Huppert, MD, Caroline King, PhD, Michele Mandel, Titilope Oduyebo, MD, Cria Perrine, MD, Sam Posner, PhD.

External Reviewers

Abigail R.A. Aiken, PhD, Princeton University, Princeton, New Jersey; Linda Burdette, PA-C, Premier Women's Health of Yakima, Yakima, Washington; Mimi Zieman, MD, Planned Parenthood Southeast, Atlanta, Georgia.

Conflicts of Interest for Invited Meeting Participants, August 26–28, 2015, Atlanta, Georgia

Rebecca Allen, Nexplanon trainer for Merck and Liletta trainer for Actavis, consultant, advisory board and education grant from Bayer; Mitchell D. Creinin, Nexplanon trainer for Merck, litigation consultant for Bayer, advisory board for Merck and Teva Pharmaceutical Industries, Ltd., consultant for Lemonaid – PolkaDoc app, research support to University of California, Davis from Medicines360, Contramed, Merck, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and Society of Family Planning; Linda Dominguez, speaker for Bayer, Merck, and Actavis; Alison Edelman, royalties from Up to Date, Inc., consultant for Genzyme, grant support from the National Institutes of Health and the Gates Foundation, travel funds from the World Health Organization, grant support and honorarium from Society of Family Planning, honorarium and travel funds from Contemporary Forum, trainer for Merck, consultant for Gynuity Health Projects, honorarium from CDC, Projects In Knowledge, and American Congress of Obstetricians and Gynecologists, advisory board for Agile Therapeutics; Eve Espey, travel funds from the American Congress of Obstetricians and Gynecologists, Society for Family Planning, and U.S. Food and Drug Administration, Reproductive and Drug Advisory Committee for U.S. Food and Drug Administration, travel funds and honoraria from Wayne State University, Telluride Conference, New Mexico Department of Health Clinician Conference, Planned Parenthood National Medical Conference and Society of Family Planning, British Columbia Contraception Access Research Team Conference, and American Congress of Obstetricians and Gynecologists annual meeting; Emily Godfrey, research funding from Bayer Women's Health, Prima-Temp, and Teva Pharmaceutical Industries, Ltd., trainer for Merck and Upstream USA, grant reviewer for Fellowship of Family Planning and Society of Family Planning Research Fund; Mark Hathaway, Liletta trainer and speaker for Actavis and Medicines360, Nexplanon trainer for Merck, advisory board for Contramed and Afaxys Pharmaceuticals; Paula Hillard, consultant for American Civil Liberties Union, Advanced Health Media, CMEology, National Sleep Foundation, and Planned Parenthood Federation of America, honoraria from National Sleep Foundation, Dignity Health, CMEology, Advance Health Media, and Medscape, editorial board for Advanstar–Contemporary OB/GYN, board examiner for the American Board of Obstetrics and Gynecology, contract reviewer for the U.S. Department of Health and Human Services, editorial board for EBSCO–PEMSoft, Nexplanon trainer for Merck, scientific advisor to Proctor and Gamble, publication royalties from Wiley Blackwell Publishing; Andrew Kaunitz, advisory board participant of Allergan, Bayer, Merck, and Pfizer, clinical trial funding to University of Florida from Agile Therapeutics, Bayer, Merck; Mark Mirochnick, data and safety monitoring board for Merck and ViiV Healthcare, advisory board for Merck; Jeffrey Peipert, research funding from Bayer and Teva Pharmaceutical Industries, Ltd., advisory board for Perrigo; Michael Policar, litigation consultant for Bayer; James Trussell, advisory board for Merck and Teva Pharmaceutical Industries, Ltd., consultant for Bayer; Nanette Wenger, research grants from Alnylam Pharmaceuticals, Gilead Sciences, National Heart, Lung, and Blood Institute, Pfizer, and Society for Women's Health Research, consultant for Amgen, AstraZeneca, Gilead Sciences and Merck; Carolyn Westhoff, data and safety monitoring board for Merck and Bayer, advisory board for Agile Therapeutics, MicroChips Biotech, and Actavis, research support to Columbia University from Medicines360, León Farma, and ContraMed.

Handling Conflicts of Interest

To promote transparency, all participants were asked to disclose any potential conflicts of interest to CDC prior to the expert meeting and to report any potential conflicts of interest during the introductory portion of the expert meeting. All potential conflicts of interest are listed above. No participants were excluded from discussion based on potential conflicts of interest. CDC staff who ultimately decided and developed these recommendations have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters relevant to these recommendations.

References

1. Finer LB, Zolna MR. Declines in unintended pregnancy in the United States, 2008–2011. N Engl J Med 2016;374:843–52.http://dx.doi.org/10.1056/NEJMsa1506575
2. Gipson JD, Koenig MA, Hindin MJ. The effects of unintended pregnancy on infant, child, and parental health: a review of the literature. Stud Fam Plann 2008;39:18–38. http://dx.doi.org/10.1111/j.1728-4465.2008.00148.x
3. Sonfield A, Kost K. Public costs from unintended pregnancies and the role of public insurance programs in paying for pregnancy-related care: national and state estimates for 2010. New York: Guttmacher Institute; 2015.
4. World Health Organization. Medical eligibility criteria for contraceptive use. 4th ed. Geneva, Switzerland: World Health Organization; 2009.
5. CDC. U.S. medical eligibility criteria for contraceptive use, 2010. MMWR Recomm Rep 2010;59(No. RR-4).
6. Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. selected practice recommendations for contraceptive use, 2016. MMWR Recomm Rep 2016;65(No. RR-4).
7. Mohllajee AP, Curtis KM, Flanagan RG, Rinehart W, Gaffield ML, Peterson HB. Keeping up with evidence a new system for WHO's evidence-based family planning guidance. Am J Prev Med 2005;28:483–90.http://dx.doi.org/10.1016/j.amepre.2005.02.008
8. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 2009;62:e1–34. http://dx.doi.org/10.1016/j.jclinepi.2009.06.006
9. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg 2010;8:336–41. http://dx.doi.org/10.1016/j.ijsu.2010.02.007
10. Harris RP, Helfand M, Woolf SH, et al; Methods Work Group, Third US Preventive Services Task Force. Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med 2001;20(Suppl):21–35. http://dx.doi.org/10.1016/S0749-3797(01)00261-6
11. Horton L, Folger SG, Berry-Bibee E, Jatlaoui TC, Tepper NK, Curtis KM. Research gaps from evidence-based contraception guidance: the U.S. Medical Eligibility Criteria for Contraceptive Use, 2016, and the U.S. Selected Practice Recommendations for Contraceptive Use, 2016. Contraception. In press 2016.
12. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(No. RR-3).

Abbreviations and Acronyms

ARV = antiretroviral [therapy]
BMD = bone mineral density
BMI = body mass index
CHC = combined hormonal contraceptive
COC = combined oral contraceptive
Cu-IUD = copper-containing intrauterine device
DMPA = depot medroxyprogesterone acetate
DVT = deep venous thrombosis
ECP = emergency contraceptive pills
FAB = fertility awareness–based [methods]
hCG = human chorionic gonadotropin
HDL = high-density lipoprotein
HIV = human immunodeficiency virus
IBD = inflammatory bowel disease
IUD = intrauterine device
LARC = long-acting reversible contraception
LDL = low-density lipoprotein
LNG = levonorgestrel
LNG-IUD = levonorgestrel-releasing intrauterine device
NET-EN = norethisterone enantate
NNRTI = nonnucleoside reverse transcriptase inhibitor
NRTI = nucleoside reverse transcriptase inhibitor
PE = pulmonary embolism
PID = pelvic inflammatory disease
POC = progestin-only contraceptive
POP = progestin-only pill
SLE = systemic lupus erythematosus
SSRI = selective serotonin reuptake inhibitors
STD = sexually transmitted disease
UPA = ulipristal acetate
U.S. MEC = U.S. Medical Eligibility Criteria for Contraceptive Use
U.S. SPR = U.S. Selected Practice Recommendations for Contraceptive Use
VTE = venous thromboembolism

Appendix A

Summary of Changes from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010*

The classification additions, deletions, and modifications from the 2010 *U.S. Medical Eligibility Criteria for Contraceptive Use* (U.S. MEC) are summarized in the following tables (Box A1) (Tables A1 and A2). For conditions for which classifications changed for one or more contraceptive methods or the condition description underwent a major modification, the changes or modifications are in bold italics (Tables A1 and A2). Conditions that do not appear in this table remain unchanged from the 2010 U.S. MEC.

BOX A1. Categories for classifying intrauterine devices and hormonal contraceptives

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

TABLE A1. Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs	Clarification
Breastfeeding							
a. <21 days postpartum	—	—	2	2	2	***4***	Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*1*).
b. 21 to <30 days postpartum							
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	—	—	***2***	***2***	***2***	***3***	Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*1*). ***CHCs: For women with other risk factors for VTE, these risk factors might increase the classification to a category 4.***
ii. Without other risk factors for VTE	—	—	***2***	***2***	***2***	***3***	Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*1*).
c. 30–42 days postpartum							
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	—	—	***1***	***1***	***1***	***3***	Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*1*). ***CHCs: For women with other risk factors for VTE, these risk factors might increase the classification to a category 4.***
ii. Without other risk factors for VTE	—	—	***1***	***1***	***1***	***2***	Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*1*).
d. >42 days postpartum	—	—	***1***	***1***	***1***	***2***	Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*1*).

See table footnotes on page 16.

TABLE A1. (*Continued*) Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs	Clarification
Postpartum (nonbreastfeeding women)							
a. <21 days postpartum	—	—	1	1	1	***4***	—
b. 21–42 days postpartum							
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	—	—	***1***	***1***	***1***	***3***	***CHCs: For women with other risk factors for VTE, these risk factors might increase the classification to a category 4.***
ii. Without other risk factors for VTE	—	—	***1***	***1***	***1***	***2***	—
c. >42 days postpartum	—	—	***1***	***1***	***1***	***1***	—
Postpartum (including cesarean delivery)							
a. <10 minutes after delivery of the placenta							***IUDs: Insertion of IUDs among postpartum women is safe and does not appear to increase health risks associated with IUD use such as infection. Higher rates of expulsion during the postpartum period should be considered as they relate to effectiveness, along with patient access to interval placement (i.e., not related to pregnancy) when expulsion rates are lower.*** ***Breastfeeding: Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (1).***
i. Breastfeeding	***1***	***2***	—	—	—	—	
ii. Nonbreastfeeding	***1***	***1***	—	—	—	—	
b. 10 minutes after delivery of the placenta to <4 weeks (breastfeeding or nonbreastfeeding)	2	2	—	—	—	—	***IUDs: Insertion of IUDs among postpartum women is safe and does not appear to increase health risks associated with IUD use such as infection. Higher rates of expulsion during the postpartum period should be considered as they relate to effectiveness, along with patient access to interval placement (i.e., not related to pregnancy) when expulsion rates are lower.*** ***Breastfeeding: Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (1).***
c. ≥4 weeks (breastfeeding or nonbreastfeeding)	1	1	—	—	—	—	***IUDs: Insertion of IUDs among postpartum women is safe and does not appear to increase health risks associated with IUD use such as infection. Higher rates of expulsion during the postpartum period should be considered as they relate to effectiveness, along with patient access to interval placement (i.e., not related to pregnancy) when expulsion rates are lower.*** ***Breastfeeding: Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (1).***
d. Postpartum sepsis	4	4	—	—	—	—	—

See table footnotes on page 16.

TABLE A1. (*Continued*) Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs	Clarification
Multiple risk factors for atherosclerotic cardiovascular disease (e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	1	2	2	3	2	3/4	**Implants, DMPA, POP:** When multiple major risk factors exist, risk for cardiovascular disease might increase substantially. Certain POCs might increase the risk for thrombosis, although this increase is substantially less than with COCs. The effects of DMPA might persist for some time after discontinuation. **CHCs:** When a woman has multiple major risk factors, any of which alone would substantially increase her risk for cardiovascular disease, use of CHCs might increase her risk to an unacceptable level. However, a simple addition of categories for multiple risk factors is not intended; for example, a combination of two category 2 risk factors might not necessarily warrant a higher category. **Implants, DMPA, POP, CHCs:** The recommendations apply to known preexisting medical conditions or characteristics. Few if any screening tests are needed before initiation of contraception. See the *U.S. Selected Practice Recommendations for Contraceptive Use* (http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usspr.htm)
Superficial venous disorders							
a. Varicose veins	1	1	1	1	1	1	—
b. Superficial venous thrombosis (acute or history)	1	1	1	1	1	***3***	***CHCs: Superficial venous thrombosis might be associated with an increased risk for VTE. If a woman has risk factors for concurrent DVT (e.g., known thrombophilia or cancer) or has current or history of DVT, see recommendations for DVT/PE. Superficial venous thrombosis associated with a peripheral intravenous catheter is less likely to be associated with additional thrombosis and use of CHCs may be considered.***
Headaches							
a. Nonmigraine (mild or severe)	1	1	1	1	1	***1***	**CHCs:** Classification depends on accurate diagnosis of those severe headaches that are migraines and those headaches that are not, as well as diagnosis of ever experiencing aura. Aura is a specific focal neurologic symptom. For more information about headache classification see *The International Headache Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf). Any new headaches or marked changes in headaches should be evaluated.
b. Migraine							
i. Without aura (This category of migraine includes menstrual migraine.)	1	***1***	***1***	***1***	***1***	***2***	**CHCs:** Classification depends on accurate diagnosis of those severe headaches that are migraines and those headaches that are not, as well as diagnosis of ever experiencing aura. Aura is a specific focal neurologic symptom. For more information about headache classification see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf). Any new headaches or marked changes in headaches should be evaluated. **CHCs:** Classification is for women without any other risk factors for stroke (e.g., age, hypertension, and smoking).
ii. With aura	1	***1***	***1***	***1***	***1***	4	
Multiple sclerosis							
a. With prolonged immobility	***1***	***1***	***1***	***2***	***1***	***3***	—
b. Without prolonged immobility	***1***	***1***	***1***	***2***	***1***	***1***	—
Gestational trophoblastic disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).							***For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.***
a. Suspected gestational trophoblastic disease (immediate postevacuation)							***For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.***
i. Uterine size first trimester	***1***	***1***	***1***	***1***	***1***	***1***	
ii. Uterine size second trimester	***2***	***2***	***1***	***1***	***1***	***1***	

See table footnotes on page 16.

TABLE A1. (*Continued*) Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs	Clarification
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)	Initiation	Continuation	Initiation	Continuation					
i. Undetectable/nonpregnant β-hCG levels	***1***	***1***	***1***	***1***	***1***	***1***	***1***	***1***	***For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.***
ii. Decreasing β-hCG levels	***2***	***1***	***2***	***1***	***1***	***1***	***1***	***1***	***For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.***
									IUD: For women at higher risk for disease progression, the benefits of effective contraception must be weighed against the potential need for early IUD removal.
iii. Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	***2***	***1***	***2***	***1***	***1***	***1***	***1***	***1***	***For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.***
iv. Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	***4***	***2***	***4***	***2***	***1***	***1***	***1***	***1***	***For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.***
Sexually transmitted diseases	Initiation	Continuation	Initiation	Continuation					
a. Current purulent cervicitis or chlamydial infection or gonococcal infection	4	2	4	2	1	1	1	1	**IUD continuation:** Treat the STD using appropriate antibiotics. The IUD usually does not need to be removed if the woman wants to continue using it. Continued use of an IUD depends on the woman's informed choice and her current risk factors for STDs and PID.
b. Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	2	2	2	2	1	1	1	1	—
c. Other factors related to STDs	***2***	***2***	***2***	***2***	1	1	1	1	***IUD initiation: Most women do not require additional STD screening at the time of IUD insertion. If a woman with risk factors for STDs has not been screened for gonorrhea and chlamydia according to CDC STD treatment guidelines (2), screening may be performed at the time of IUD insertion and insertion should not be delayed.***
High risk for HIV	Initiation 2	Continuation 2	Initiation 2	Continuation 2	1	1	1	1	***DMPA: Some studies suggest that women using progestin-only injectable contraception might be at increased risk for HIV acquisition; other studies do not show this association. CDC reviewed all available evidence and agreed that the data were not sufficiently conclusive to change current guidance. However, because of the inconclusive nature of the body of evidence on possible increased risk for HIV acquisition, women using progestin-only injectable contraception should be strongly advised to also always use condoms (male or female) and take other HIV preventive measures. Expansion of contraceptive method mix and further research on the relationship between hormonal contraception and HIV infection are essential. These recommendations will be continually reviewed in light of new evidence.***
HIV infection ***For women with HIV infection who are not clinically well or not receiving ARV therapy, this condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).***	—	—	—	—	1	1	1	1	**Implants, DMPA, POP, CHCs:** Drug interactions might exist between hormonal contraceptives and ARV drugs; see Drug Interactions section.
a. Clinically well receiving ARV therapy	***1***	***1***	***1***	***1***	—	—	—	—	—
b. Not clinically well or not receiving ARV therapy	***2***	***1***	***2***	***1***	—	—	—	—	—

See table footnotes on page 16.

TABLE A1. (*Continued*) Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs	Clarification
Cystic fibrosis *This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).*	*1*		*1*		*1*	*2*	*1*	*1*	***Persons with cystic fibrosis are at increased risk for diabetes, liver disease, gallbladder disease, and VTE (particularly related to use of central venous catheters) and are frequently prescribed antibiotics. Categories assigned to such conditions in U.S. MEC should be the same for women with cystic fibrosis who have these conditions. For cystic fibrosis, classifications are based on the assumption that no other conditions are present; these classifications must be modified in the presence of such conditions.*** ***Implants, DMPA, POP, CHCs: Certain drugs to treat cystic fibrosis (e.g., lumacaftor) might reduce effectiveness of hormonal contraceptives, including oral, injectable, transdermal, and implantable contraceptives.***
Antiretroviral therapy	Initiation	Continuation	Initiation	Continuation					**IUD:** No known interaction exists between ARV therapy and IUD use. However, IUD insertion is classified as category 2 if the woman is not clinically well or not receiving ARV therapy. Otherwise, both insertion and continuation are classified as category 1 (see HIV Infection section).
a. Nucleoside reverse transcriptase inhibitors (NRTIs)									
i. Abacavir (ABC)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
ii. Tenofovir (TDF)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
iii. Zidovudine (AZT)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
iv. Lamivudine (3TC)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
v. Didanosine (DDI)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
vi. Emtricitabine (FTC)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
vii. Stavudine (D4T)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
b. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)									
i. Efavirenz (EFV)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	***Implants, DMPA, POP, CHCs: Evidence suggests drug interactions between efavirenz and certain hormonal contraceptives. These interactions might reduce the effectiveness of the hormonal contraceptive.***
ii. Etravirine (ETR)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
iii. Nevirapine (NVP)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
iv. Rilpivirine (RPV)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
c. Ritonavir-boosted protease inhibitors									
i. Ritonavir-boosted atazanavir (ATV/r)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	***Implants, DMPA, POP: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.*** ***CHCs: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive.***
ii. Ritonavir-boosted darunavir (DRV/r)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	***Implants, DMPA, POP: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.*** ***CHCs: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive.***

See table footnotes on page 16.

TABLE A1. (*Continued*) Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs	Clarification
iii. Ritonavir-boosted fosamprenavir (FPV/r)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	*Implants, DMPA, POP: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.* *CHCs: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive.*
iv. Ritonavir-boosted lopinavir (LPV/r)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
v. Ritonavir-boosted saquinavir (SQV/r)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	*Implants, DMPA, POP: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.* *CHCs: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive.*
vi. Ritonavir-boosted tipranavir (TPV/r)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	*Implants, DMPA, POP: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.* *CHCs: Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive.*
d. Protease inhibitors without ritonavir									
i. Atazanavir (ATV)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*2*	*CHCs: Theoretical concern exists that increased levels of ethinyl estradiol because of interactions with ATV might increase the risk for adverse events.*
ii. Fosamprenavir (FPV)	*1/2*	*1*	*1/2*	*1*	*2*	*2*	*2*	*3*	*Implants, DMPA, POP: Theoretical concern exists that interactions between FPV and hormonal contraceptives leading to decreased levels of FPV might diminish effectiveness of the antiretroviral drug. The drug interaction likely involves CYP3A4 pathways; POCs have less effect on CYP3A4 enzymes than CHCs.* *CHCs: Concern exists that interactions between FPV and hormonal contraceptives leading to decreased levels of FPV might diminish effectiveness of the antiretroviral drug.*
iii. Indinavir (IDV)	*1/2*	*1*	*1/2*	*1*	*1*	*1*	*1*	*1*	—
iv. Nelfinavir (NFV)	*1/2*	*1*	*1/2*	*1*	*2*	*1*	*2*	*2*	*Implants, DMPA, POP: Theoretically, drug interactions might occur between certain protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA. Concern exists that interactions between NFV and POCs might decrease NFV levels.* *CHCs: Evidence suggests drug interactions between certain protease inhibitors and certain hormonal contraceptives. These interactions might reduce the effectiveness of the hormonal contraceptive.*

See table footnotes on page 16.

TABLE A1. (*Continued*) Summary of changes in classifications from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs	Clarification
e. CCR5 co-receptor antagonists									
i. Maraviroc (MVC)	***1/2***	***1***	***1/2***	***1***	***1***	***1***	***1***	***1***	—
f. HIV integrase strand transfer inhibitors									
i. Raltegravir (RAL)	***1/2***	***1***	***1/2***	***1***	***1***	***1***	***1***	***1***	—
ii. Dolutegravir (DTG)	***1/2***	***1***	***1/2***	***1***	***1***	***1***	***1***	***1***	—
iii. Elvitegravir (EVG)	***1/2***	***1***	***1/2***	***1***	***1***	***1***	***1***	***1***	—
g. Fusion inhibitors									
i. Enfuvirtide	***1/2***	***1***	***1/2***	***1***	***1***	***1***	***1***	***1***	—
Psychotropic medications									
a. SSRIs		***1***		***1***	***1***	***1***	***1***	***1***	—
St. John's wort		***1***		***1***	***2***	***1***	***2***	***2***	—

Abbreviations: ARV = antiretroviral; BMI = body mass index; CHC = combined hormonal contraceptive; COC = combined oral contraceptive; Cu-IUD = copper-containing intrauterine device; DMPA = depot medroxyprogesterone acetate; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; HDL = high-density lipoprotein; HIV = human immunodeficiency virus; LDL = low-density lipoprotein; LNG-IUD = levonorgestrel-releasing intrauterine device; PE = pulmonary embolism; PID = pelvic inflammatory disease; POC = progestin-only contraceptive; POP = progestin-only pill; SSRI = selective serotonin uptake inhibitor; STD = sexually transmitted disease; VTE = venous thromboembolism.

* For conditions for which classification changed for one or more contraceptive methods or the condition description underwent a major modification, the changes or modifications are in bold italics.

TABLE A2. Summary of changes for emergency contraception from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010

Condition	Category				Clarification
	Cu-IUD	UPA	LNG	COC	
Pregnancy	4	***NA***	NA	NA	***IUD: The IUD is not indicated during pregnancy and should not be used because of the risk for serious pelvic infection and septic spontaneous abortion.*** ***ECPs: Although this method is not indicated for a woman with a known or suspected pregnancy, no harm to the woman, the course of her pregnancy, or the fetus if ECPs are inadvertently used is known to exist.***
Breastfeeding	***1***	***1***	1	1	***UPA: Breastfeeding is not recommended for 24 hours after taking UPA because it is excreted in breast milk with highest concentrations in the first 24 hours, and maximum maternal serum levels are reached 1-3 hours after administration. Mean UPA concentrations in breast milk decrease markedly from 0 to 24–48 hours and then slowly decrease over 5 days (3). Breast milk should be expressed and discarded for 24 hours after taking UPA.***
Past ectopic pregnancy	***1***	***1***	1	1	—
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	***1***	***1***	1	1	—
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	***1***	***1***	1	1	—
History of severe cardiovascular disease (ischemic heart disease, cerebrovascular attack, or other thromboembolic conditions) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	***1***	***2***	2	2	—
Rheumatoid arthritis					
a. Receiving immunosuppressive therapy	***2***	***1***	1	1	—
b. Not receiving immunosuppressive therapy	***1***	***1***	1	1	—
Migraine	***1***	***1***	***1***	2	—
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	***1***	***1***	1	1	—
Severe liver disease (including jaundice) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	***1***	***2***	2	2	—

See table footnotes on page 17.

TABLE A2. (*Continued*) Summary of changes for emergency contraception from *U.S. Medical Eligibility Criteria for Contraceptive Use, 2010**

Condition	Category				Clarification
	Cu-IUD	UPA	LNG	COC	
Solid organ transplantation This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Complicated: graft failure (acute or chronic), rejection, or cardiac allograft vasculopathy	***3***	***1***	1	1	—
b. Uncomplicated	***2***	***1***	1	1	—
Repeated ECP use	***1***	***1***	1	1	**ECPs:** Recurrent ECP use is an indication that the woman requires further counseling about other contraceptive options. Frequently repeated ECP use might be harmful for women with conditions classified as 2, 3, or 4 for CHC or POC use.
Sexual assault	***2***	***1***	1	1	***IUD: Women who have experienced sexual assault are at increased risk for STDs. According to CDC STD treatment guidelines, routine presumptive treatment of chlamydia, gonorrhea, and trichomonas is recommended after sexual assault (2). Women with current purulent cervicitis or chlamydial infection or gonococcal infection should not undergo IUD insertion (category 4).***
Obesity (BMI ≥30 kg/m^2)	***1***	***2***	***2***	***2***	***ECPs: ECPs might be less effective among women with BMI ≥30 kg/m^2 than among women with BMI <25 kg/m^2. Despite this, no safety concerns exist.***
CYP3A4 inducers (e.g., bosentan, carbamazepine, felbamate, griseofulvin, oxcarbazepine, phenytoin, rifampin, St. John's wort, topiramate, efavirenz, and lumacaftor)	***1***	***2***	***2***	***2***	***ECPs: Strong CYP3A4 inducers might reduce the effectiveness of ECPs.***

Abbreviations: BMI = body mass index; CHC = combined hormonal contraceptive; COC = combined oral contraceptive; Cu-IUD = copper-containing intrauterine device; ECP = emergency contraceptive pill; IUD = intrauterine device; LNG = levonorgestrel; NA = not applicable; POC = progestin-only contraceptive; STD = sexually transmitted disease; UPA = ulipristal acetate.
* For conditions for which classification changed for one or more contraceptive methods or the condition description underwent a major modification, the changes or modifications are in bold italics.

References

1. US Department of Health and Human Services. Healthy people 2020: maternal, infant, and child health objectives. Washington, DC: US Department of Health and Human Services; 2015. http://www.healthypeople.gov/2020/topics-objectives/topic/maternal-infant-and-child-health/objectives
2. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(No. RR-03).
3. Watson Pharmaceuticals. Ella [Prescribing information]. Morristown, NJ; 2010. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022474s000lbl.pdf

Appendix B

Classifications for Intrauterine Devices

Classifications for intrauterine devices (IUDs) are for the copper-containing IUD and levonorgestrel-releasing IUD (containing a total of either 13.5 mg or 52 mg levonorgestrel) (Box B1) (Table B1). IUDs do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

BOX B1. Categories for classifying intrauterine devices

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

TABLE B1. Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category		Clarifications/Evidence/Comments
	Cu-IUD	LNG-IUD	
Personal Characteristics and Reproductive History			
Pregnancy	4	4	**Clarification:** The IUD is not indicated during pregnancy and should not be used because of the risk for serious pelvic infection and septic spontaneous abortion.
Age			
a. Menarche to <20 years	2	2	**Comment:** Concern exists both about the risk for expulsion from nulliparity and for STDs from sexual behavior in younger age groups.
b. ≥20 years	1	1	—
Parity			
a. Nulliparous	2	2	**Evidence:** Data conflict about whether IUD use is associated with infertility among nulliparous women, although well-conducted studies suggest no increased risk (*1–9*).
b. Parous	1	1	—
Postpartum (including cesarean delivery)			
a. <10 minutes after delivery of the placenta			**Clarification:** Insertion of IUDs among postpartum women is safe and does not appear to increase health risks associated with IUD use such as infection. Higher rates of expulsion during the postpartum period should be considered as they relate to effectiveness, along with patient access to interval placement (i.e., not related to pregnancy) when expulsion rates are lower.
i. Breastfeeding	1	2	**Clarification (breastfeeding):** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*10*).
ii. Nonbreastfeeding	1	1	**Evidence:** Studies suggest that immediate postplacental (<10 minutes) and early postpartum (10 minutes up until 72 hours) placement of Cu-IUDs and LNG-IUDs is associated with increased risk for expulsion compared with interval placement (i.e., not related to pregnancy). Early postpartum placement has similar or increased risk for expulsion compared with immediate postplacental placement. Although immediate postplacental placement at the time of cesarean delivery might have increased risk for expulsion compared with interval placement, risk appears lower than that for placement at the time of vaginal delivery. Evidence for infection, perforation, and removals for pain or bleeding are limited; however, these events are rare (*11–62*).
			Evidence (breastfeeding): Two randomized controlled trials found conflicting results on breastfeeding outcomes when LNG-IUDs were initiated immediately postpartum compared with 6–8 weeks postpartum. Initiation of LNG-IUDs immediately postpartum had no other harmful effect on infant health, growth, or development (*63*,*64*). Breastfeeding women using IUDs do not have an increased risk for certain IUD-related adverse events including expulsion, infection, pain, or bleeding compared with nonbreastfeeding women. The risk for perforation is increased independently among breastfeeding women and among women ≤36 weeks postpartum, compared with non-postpartum women; however, the absolute risk for perforation remains low (*11–62*,*65*).
			Comment (breastfeeding): Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category		Clarifications/Evidence/Comments
	Cu-IUD	LNG-IUD	
b. 10 minutes after delivery of the placenta to <4 weeks (breastfeeding or nonbreastfeeding)	2	2	**Clarification:** Insertion of IUDs among postpartum women is safe and does not appear to increase health risks associated with IUD use such as infection. Higher rates of expulsion during the postpartum period should be considered as they relate to effectiveness, along with patient access to interval placement (i.e., not related to pregnancy) when expulsion rates are lower. **Clarification (breastfeeding):** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*10*). **Evidence:** Studies suggest that immediate postplacental (<10 minutes) and early postpartum (10 minutes up until 72 hours) placement of Cu-IUDs and LNG-IUDs is associated with increased risk for expulsion compared with interval placement (i.e., not related to pregnancy). Early postpartum placement has similar or increased risk for expulsion compared with immediate postplacental placement. Although immediate postplacental placement at the time of cesarean delivery might have increased risk for expulsion compared with interval placement, risk appears lower than that for placement at the time of vaginal delivery. Evidence for infection, perforation, and removals for pain or bleeding are limited; however, these events are rare (*11*–*62*). **Evidence (breastfeeding):** Two randomized controlled trials found conflicting results on breastfeeding outcomes when LNG-IUDs were initiated immediately postpartum compared with 6–8 weeks postpartum. Initiation of LNG-IUDs immediately postpartum had no other harmful effect on infant health, growth, or development (*63*,*64*). Breastfeeding women using IUDs do not have an increased risk for certain IUD-related adverse events including expulsion, infection, pain, or bleeding compared with nonbreastfeeding women. The risk for perforation is increased independently among breastfeeding women and among women ≤36 weeks postpartum, compared with non-postpartum women; however, the absolute risk for perforation remains low (*11*–*62*,*65*). **Comment (breastfeeding):** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
c. ≥4 weeks (breastfeeding or nonbreastfeeding)	1	1	**Clarification:** Insertion of IUDs among postpartum women is safe and does not appear to increase health risks associated with IUD use such as infection. Higher rates of expulsion during the postpartum period should be considered as they relate to effectiveness, along with patient access to interval placement (i.e., not related to pregnancy) when expulsion rates are lower. **Clarification (breastfeeding):** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*10*). **Evidence (breastfeeding):** Initiation of LNG-IUDs at 4 weeks postpartum or later demonstrated no detrimental effect on breastfeeding outcomes and no harmful effect on infant health, growth, or development (*63*,*64*). Breastfeeding women using IUDs do not have an increased risk for certain IUD-related adverse events including expulsion, infection, pain, or bleeding compared with nonbreastfeeding women. The risk for perforation is increased independently among breastfeeding women and among women ≤36 weeks postpartum, compared with non-postpartum women; however, the absolute risk for perforation remains low (*11*–*62*,*65*). **Comment (breastfeeding):** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
d. Postpartum sepsis	4	4	**Comment:** Theoretical concern exists that postpartum insertion of an IUD in a women with recent chorioamnionitis or current endometritis might be associated with increased complications.

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category		Clarifications/Evidence/Comments
	Cu-IUD	LNG-IUD	
Postabortion			
a. First trimester	1	1	**Clarification:** IUDs can be inserted immediately after spontaneous or induced abortion. **Evidence:** Risk for complications from immediate versus delayed insertion of an IUD after abortion did not differ. Expulsion was greater when an IUD was inserted after a second trimester abortion than when inserted after a first trimester abortion. Safety or expulsion for postabortion insertion of an LNG-IUD did not differ from that of a Cu-IUD (*66*).
b. Second trimester	2	2	
c. Immediate postseptic abortion	4	4	**Comment:** Insertion of an IUD might substantially worsen the condition.
Past ectopic pregnancy	1	1	**Comment:** The absolute risk for ectopic pregnancy is extremely low because of the high effectiveness of IUDs. However, when a woman becomes pregnant during IUD use, the relative likelihood of ectopic pregnancy increases substantially.
History of pelvic surgery (see Postpartum [Including Cesarean Delivery] section)	1	1	—
Smoking			
a. Age <35 years	1	1	—
b. Age ≥35 years			
i. <15 cigarettes per day	1	1	—
ii. ≥15 cigarettes per day	1	1	—
Obesity			
a. BMI ≥30 kg/m^2	1	1	—
b. Menarche to <18 years and BMI ≥30 kg/m^2	1	1	—
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).			
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	1	1	—
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	1	1	—
Cardiovascular Disease			
Multiple risk factors for atherosclerotic cardiovascular disease (e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	1	2	—
Hypertension Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg are associated with increased risk for adverse health events as a result of pregnancy (Box 2).			
a. Adequately controlled hypertension	1	1	**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive.
b. Elevated blood pressure levels (properly taken measurements)			**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Comment:** Theoretical concern exists about the effect of LNG on lipids. Use of Cu-IUDs has no restrictions.
i. Systolic 140–159 mm Hg or diastolic 90–99 mm Hg	1	1	
ii. Systolic ≥160 mm Hg or diastolic ≥100 mm Hg	1	2	

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category		Clarifications/Evidence/Comments
	Cu-IUD	LNG-IUD	
c. Vascular disease	1	2	**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors for cardiovascular disease exist. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Comment:** Theoretical concern exists about the effect of LNG on lipids. Use of Cu-IUDs has no restrictions
History of high blood pressure during pregnancy (when current blood pressure is measurable and normal)	1	1	—
Deep venous thrombosis/ Pulmonary embolism			
a. History of DVT/PE, not receiving anticoagulant therapy			
i. Higher risk for recurrent DVT/PE (one or more risk factors) • History of estrogen-associated DVT/PE • Pregnancy-associated DVT/PE • Idiopathic DVT/PE • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	1	2	—
ii. Lower risk for recurrent DVT/PE (no risk factors)	1	2	—
b. Acute DVT/PE	2	2	**Evidence:** No direct evidence exists on the use of POCs among women with acute DVT/PE. Although findings on the risk for venous thrombosis with the use of POCs in otherwise healthy women are inconsistent, any small increased risk is substantially less than that with COCs (*67–69*).
c. DVT/PE and established anticoagulant therapy for at least 3 months			**Evidence:** No direct evidence exists on the use of POCs among women with acute DVT/PE. Although findings on the risk for venous thrombosis with the use of POCs in otherwise healthy women are inconsistent, any small increased risk is substantially less than that with COCs (*67–69*). **Evidence:** Limited evidence indicates that insertion of the LNG-IUD does not pose major bleeding risks in women receiving chronic anticoagulant therapy (*70–73*). **Comment:** The LNG-IUD might be a useful treatment for menorrhagia in women receiving long-term anticoagulation therapy.
i. Higher risk for recurrent DVT/PE (one or more risk factors) • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	2	2	—
ii. Lower risk for recurrent DVT/PE (no risk factors)	2	2	—
d. Family history (first-degree relatives)	1	1	—
e. Major surgery			
i. With prolonged immobilization	1	2	—
ii. Without prolonged immobilization	1	1	—
f. Minor surgery without immobilization	1	1	

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
Known thrombogenic mutations (e.g., factor V Leiden; prothrombin mutation; and protein S, protein C, and antithrombin deficiencies) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		2		**Clarification:** Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.
Superficial venous disorders					
a. Varicose veins	1		1		—
b. Superficial venous thrombosis (acute or history)	1		1		—
Current and history of ischemic heart disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		Initiation 2	Continuation 3	**Comment:** Theoretical concern exists about the effect of LNG on lipids. Use of Cu-IUDs has no restrictions.
Stroke (history of cerebrovascular accident) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		2		**Comment:** Theoretical concern exists about the effect of LNG on lipids. Use of Cu-IUDs has no restrictions.
Valvular heart disease Complicated valvular heart disease is a condition associated with increased risk for adverse health events as a result of pregnancy (Box 2).					**Comment**: According to the American Heart Association, administration of prophylactic antibiotics solely to prevent endocarditis is not recommended for patients who undergo genitourinary tract procedures, including insertion or removal of IUDs (*74*).
a. Uncomplicated	1		1		
b. Complicated (pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis)	1		1		
Peripartum cardiomyopathy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					**Evidence:** No direct evidence exists on the safety of IUDs among women with peripartum cardiomyopathy. Limited indirect evidence from noncomparative studies did not demonstrate any cases of arrhythmia or infective endocarditis in women with cardiac disease who used IUDs (*75*).
a. Normal or mildly impaired cardiac function (New York Heart Association Functional Class I or II: patients with no limitation of activities or patients with slight, mild limitation of activity) (*76*)					**Comment:** IUD insertion might induce cardiac arrhythmias in healthy women; women with peripartum cardiomyopathy have a high incidence of cardiac arrhythmias.
i. <6 months	2		2		
ii. ≥6 months	2		2		
b. Moderately or severely impaired cardiac function (New York Heart Association Functional Class III or IV: patients with marked limitation of activity or patients who should be at complete rest) (*76*)	2		2		
Rheumatic Diseases					
Systemic lupus erythematosus This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation	Continuation			
a. Positive (or unknown) antiphospholipid antibodies	1	1	3		**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*73*,*77*–*94*).
					Evidence: Antiphospholipid antibodies are associated with a higher risk for both arterial and venous thrombosis (*95*,*96*)

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
b. Severe thrombocytopenia	3	2	2		**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*73*,*77*–*94*). **Clarification:** Severe thrombocytopenia increases the risk for bleeding. The category should be assessed according to the severity of thrombocytopenia and its clinical manifestations. In women with very severe thrombocytopenia who are at risk for spontaneous bleeding, consultation with a specialist and certain pretreatments might be warranted. **Evidence:** The LNG-IUD might be a useful treatment for menorrhagia in women with severe thrombocytopenia (*73*).
c. Immunosuppressive therapy	2	1	2		**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*73*,*77*–*94*).
d. None of the above	1	1	2		**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*73*,*77*–*94*).
Rheumatoid arthritis	Initiation	Continuation	Initiation	Continuation	
a. Receiving immunosuppressive therapy	2	1	2	1	—
b. Not receiving immunosuppressive therapy	1		1		—
Neurologic Conditions					
Headaches					
a. Nonmigraine (mild or severe)	1		1		—
b. Migraine					
i. Without aura (This category of migraine includes menstrual migraine.)	1		1		**Evidence:** No studies directly examined the risk for stroke among women with migraine using LNG-IUDs (*97*). Limited evidence demonstrated that women using LNG-IUDs do not have an increased risk for ischemic stroke compared with women not using hormonal contraceptives (*98*). **Comment:** Menstrual migraine is a subtype of migraine without aura. For more information see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf).
ii. With aura	1		1		
Epilepsy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		1		—
Multiple sclerosis					
a. With prolonged immobility	1		1		—
b. Without prolonged immobility	1		1		—
Depressive Disorders					
Depressive disorders	1		1		**Clarification**: If a woman is receiving psychotropic medications or St. John's wort, see Drug Interactions section. **Evidence:** The frequency of psychiatric hospitalizations for women with bipolar disorder or depression did not significantly differ among women using DMPA, LNG-IUD, Cu-IUD, or sterilization (*99*).

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
Reproductive Tract Infections and Disorders					
Vaginal bleeding patterns			Initiation	Continuation	
a. Irregular pattern without heavy bleeding	1		1	1	—
b. Heavy or prolonged bleeding (includes regular and irregular patterns)	2		1	2	**Clarification:** Unusually heavy bleeding should raise suspicion of a serious underlying condition. **Evidence:** Evidence from studies examining the treatment effects of the LNG-IUD among women with heavy or prolonged bleeding reported no increase in adverse effects and found the LNG-IUD to be beneficial in treating menorrhagia (*100–107*).
Unexplained vaginal bleeding (suspicious for serious condition) before evaluation	Initiation 4	Continuation 2	Initiation 4	Continuation 2	**Clarification:** If pregnancy or an underlying pathological condition (e.g., pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation. The IUD does not need to be removed before evaluation.
Endometriosis	2		1		**Evidence:** LNG-IUD use among women with endometriosis decreased dysmenorrhea, pelvic pain, and dyspareunia (*108–112*).
Benign ovarian tumors (including cysts)	1		1		—
Severe dysmenorrhea	2		1		**Comment:** Dysmenorrhea might intensify with Cu-IUD use. LNG-IUD use has been associated with reduction of dysmenorrhea.
Gestational trophoblastic disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Suspected gestational trophoblastic disease (immediate postevacuation)					**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.
i. Uterine size first trimester	1		1		
ii. Uterine size second trimester	2		2		**Evidence:** Limited evidence suggests that women using an IUD after uterine evacuation for a molar pregnancy are not at greater risk for postmolar trophoblastic disease than are women using other methods of contraception (*113*). **Comment:** The risk for expulsion immediately postevacuation for gestational trophoblastic disease is unknown. Expulsion is greater after IUD insertion immediately postevacuation for a spontaneous or induced abortion in the second trimester compared with IUD insertion after a first trimester abortion.
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)	Initiation	Continuation	Initiation	Continuation	
i. Undetectable/nonpregnant β-hCG levels	1	1	1	1	**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance. **Evidence:** Limited evidence suggests that women using an IUD after uterine evacuation for a molar pregnancy are not at greater risk for postmolar trophoblastic disease than are women using other methods of contraception (*113*). **Comment:** Once β-hCG levels have decreased to nonpregnant levels, the risk for disease progression is likely to be very low.
ii. Decreasing β-hCG levels	2	1	2	1	**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance. **Clarification:** For women at higher risk for disease progression, the benefits of effective contraception must be weighed against the potential need for early IUD removal. **Evidence:** Limited evidence suggests that women using an IUD after uterine evacuation for a molar pregnancy are not at greater risk for postmolar trophoblastic disease than are women using other methods of contraception (*113*).

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
iii. Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	2	1	2	1	**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance. **Evidence:** Limited evidence suggests that women using an IUD after uterine evacuation for a molar pregnancy are not at greater risk for postmolar trophoblastic disease than are women using other methods of contraception (*113*).
iv. Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	4	2	4	2	**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance. **Evidence:** Limited evidence suggests that women using an IUD after uterine evacuation for a molar pregnancy are not at greater risk for postmolar trophoblastic disease than are women using other methods of contraception (*113*). **Comment:** For women with suspected or confirmed intrauterine disease, an IUD should not be inserted because of theoretical risk for perforation, infection, and hemorrhage. For women who already have an IUD in place, individual circumstance along with the benefits of effective contraception must be weighed against theoretical risks of either removal or continuation of the IUD.
Cervical ectropion	1		1		—
Cervical intraepithelial neoplasia	1		2		**Comment:** Theoretical concern exists that LNG-IUDs might enhance progression of cervical intraepithelial neoplasia.
Cervical cancer (awaiting treatment)	Initiation 4	Continuation 2	Initiation 4	Continuation 2	**Comment:** Concern exists about the increased risk for infection and bleeding at insertion. The IUD most likely will need to be removed at the time of treatment but until then, the woman is at risk for pregnancy.
Breast disease Breast cancer is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Undiagnosed mass	1		2		—
b. Benign breast disease	1		1		—
c. Family history of cancer	1		1		—
d. Breast cancer					**Comment:** Breast cancer is a hormonally sensitive tumor. Concerns about progression of the disease might be less with LNG-IUDs than with COCs or higher-dose POCs.
i. Current	1		4		
ii. Past and no evidence of current disease for 5 years	1		3		
Endometrial hyperplasia	1		1		**Evidence:** Among women with endometrial hyperplasia, no adverse health events occurred with LNG-IUD use; most women experienced disease regression (*114*).
Endometrial cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation 4	Continuation 2	Initiation 4	Continuation 2	**Comment:** Concern exists about the increased risk for infection, perforation, and bleeding at insertion. The IUD most likely will need to be removed at the time of treatment, but until then, the woman is at risk for pregnancy.
Ovarian cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		1		**Comment:** Women with ovarian cancer who undergo fertility-sparing treatment and need contraception may use an IUD.
Uterine fibroids	2		2		**Evidence:** Among women with uterine fibroids using an LNG-IUD, most experienced improvements in serum levels of hemoglobin, hematocrit, and ferritin and in menstrual blood loss (*115*). Rates of LNG-IUD expulsion were higher in women with uterine fibroids (11%) than in women without fibroids (0%–3%); these findings were either not statistically significant or significance testing was not conducted (*115*). Rates of expulsion found in noncomparative studies ranged from 0%–20% (*115*). **Comment:** Women with heavy or prolonged bleeding should be assigned the category for that condition.

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
Anatomical abnormalities					
a. Distorted uterine cavity (any congenital or acquired uterine abnormality distorting the uterine cavity in a manner that is incompatible with IUD insertion)	4		4		**Comment:** An anatomical abnormality that distorts the uterine cavity might preclude proper IUD placement.
b. Other abnormalities (including cervical stenosis or cervical lacerations) not distorting the uterine cavity or interfering with IUD insertion	2		2		—
Pelvic inflammatory disease	Initiation	Continuation	Initiation	Continuation	
a. Past PID					**Comment:** IUDs do not protect against STDs, including HIV, or PID. In women at low risk for STDs, IUD insertion poses little risk for PID.
i. With subsequent pregnancy	1	1	1	1	
ii. Without subsequent pregnancy	2	2	2	2	
b. Current PID	4	2	4	2	**Clarification (continuation):** Treat the PID using appropriate antibiotics. The IUD usually does not need to be removed if the woman wants to continue using it. Continued use of an IUD depends on the woman's informed choice and her current risk factors for STDs and PID. **Evidence:** Among IUD users treated for PID, clinical course did not differ regardless of whether the IUD was removed or left in place (*116*).
Sexually transmitted diseases	Initiation	Continuation	Initiation	Continuation	
a. Current purulent cervicitis or chlamydial infection or gonococcal infection	4	2	4	2	**Clarification (continuation):** Treat the STD using appropriate antibiotics. The IUD usually does not need to be removed if the woman wants to continue using it. Continued use of an IUD depends on the woman's informed choice and her current risk factors for STDs and PID. **Evidence:** Among women who had an IUD inserted, the absolute risk for subsequent PID was low among women with STD at the time of insertion but greater than among women with no STD at the time of IUD insertion (*117–123*).
b. Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	2	2	2	2	—
c. Other factors related to STDs	2	2	2	2	**Clarification (initiation):** Most women do not require additional STD screening at the time of IUD insertion. If a woman with risk factors for STDs has not been screened for gonorrhea and chlamydia according to CDC STD treatment guidelines (*124*), screening may be performed at the time of IUD insertion and insertion should not be delayed. **Evidence:** Women who undergo same-day STD screening and IUD insertion have low incidence rates of PID. Algorithms for predicting PID among women with risk factors for STDs have poor predictive value. Risk for PID among women with risk factors for STDs is low (*125*).
HIV					
High risk for HIV	Initiation	Continuation	Initiation	Continuation	**Evidence:** Among women at risk for HIV, Cu-IUD use did not increase risk for HIV acquisition (*126–136*).
	2	2	2	2	
HIV infection For women with HIV infection who are not clinically well or not receiving ARV therapy, this condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					**Evidence:** Among IUD users, limited evidence shows a low risk for PID among HIV-infected women using IUDs and no higher risk for pelvic infectious complications in HIV-infected than in HIV-noninfected women or among women with varying degrees of HIV severity. IUD use did not adversely affect progression of HIV during 6–45 months of follow-up or when compared with hormonal contraceptive use among HIV-infected women. Furthermore, IUD use among HIV-infected women was not associated with increased risk for transmission to sex partners or with increased genital viral shedding (*137*).
a. Clinically well receiving ARV therapy	1	1	1	1	
b. Not clinically well or not receiving ARV therapy	2	1	2	1	

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
Other Infections					
Schistosomiasis					
Schistosomiasis with fibrosis of the liver is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Uncomplicated	1		1		—
b. Fibrosis of the liver (if severe, see Cirrhosis section)	1		1		—
Tuberculosis	Initiation	Continuation	Initiation	Continuation	
This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Nonpelvic	1	1	1	1	—
b. Pelvic	4	3	4	3	**Comment:** Insertion of an IUD might substantially worsen the condition.
Malaria	1		1		—
Endocrine Conditions					
Diabetes					
Insulin-dependent diabetes; diabetes with nephropathy, retinopathy, or neuropathy; diabetes with other vascular disease; or diabetes of >20 years' duration are associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. History of gestational disease	1		1		—
b. Nonvascular disease					**Evidence:** Limited evidence on the use of the LNG-IUD among women with insulin-dependent or non–insulin-dependent diabetes suggests that these methods have little effect on short-term or long-term diabetes control (e.g., glycosylated hemoglobin levels), hemostatic markers, or lipid profile (*138*,*139*).
i. Non-insulin dependent	1		2		
ii. Insulin dependent	1		2		
c. Nephropathy, retinopathy, or neuropathy	1		2		—
d. Other vascular disease or diabetes of >20 years' duration	1		2		—
Thyroid disorders					
a. Simple goiter	1		1		—
b. Hyperthyroid	1		1		—
c. Hypothyroid	1		1		—
Gastrointestinal Conditions					
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	1		1		**Evidence:** Although two case reports described three women with IBD who experienced exacerbation of disease 5 days–25 months after LNG-IUD insertion, no comparative studies have examined the safety of IUD use among women with IBD (*140*).
Gallbladder disease					
a. Symptomatic					
i. Treated by cholecystectomy	1		2		—
ii. Medically treated	1		2		—
iii. Current	1		2		—
b. Asymptomatic	1		2		—
History of cholestasis					
a. Pregnancy related	1		1		—
b. Past COC related	1		2		**Comment:** Concern exists that history of COC related cholestasis might predict subsequent cholestasis with LNG use. Whether risk exists with use of LNG-IUD is unclear.
Viral hepatitis					
a. Acute or flare	1		1		—
b. Carrier	1		1		—
c. Chronic	1		1		—
Cirrhosis					
Severe cirrhosis is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Mild (compensated)	1		1		—
b. Severe (decompensated)	1		3		—

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
Liver tumors Hepatocellular adenoma and malignant liver tumors are associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Benign					
i. Focal nodular hyperplasia	1		2		—
ii. Hepatocellular adenoma	1		3		**Comment:** No evidence is available about hormonal contraceptive use in women with hepatocellular adenoma. COC use in healthy women is associated with development and growth of hepatocellular adenoma; whether other hormonal contraceptives have similar effects is not known.
b. Malignant (hepatoma)	1		3		—
Respiratory Conditions					
Cystic fibrosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		1		**Clarification:** Persons with cystic fibrosis are at increased risk for diabetes, liver disease, gallbladder disease, and VTE (particularly related to use of central venous catheters) and are frequently prescribed antibiotics. Categories assigned to such conditions in U.S. MEC should be the same for women with cystic fibrosis who have these conditions. For cystic fibrosis, classifications are based on the assumption that no other conditions are present; these classifications must be modified in the presence of such conditions.
Anemias					
Thalassemia	2		1		**Comment:** Concern exists about an increased risk for blood loss with Cu-IUDs.
Sickle cell disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	2		1		**Comment:** Concern exists about an increased risk for blood loss with Cu-IUDs.
Iron deficiency anemia	2		1		**Comment:** Concern exists about an increased risk for blood loss with Cu-IUDs.
Solid Organ Transplantation					
Solid organ transplantation This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation	Continuation	Initiation	Continuation	**Evidence:** No comparative studies have examined IUD use among transplant patients. Four case reports of transplant patients using IUDs provided inconsistent results, including beneficial effects and contraceptive failures (*141*).
a. Complicated: graft failure (acute or chronic), rejection, or cardiac allograft vasculopathy	3	2	3	2	
b. Uncomplicated	2	2	2	2	
Drug Interactions					
Antiretroviral therapy	Initiation	Continuation	Initiation	Continuation	**Clarification:** No known interaction exists between ARV therapy and IUD use. However, IUD insertion is classified as category 2 if the woman is not clinically well or not receiving ARV therapy. Otherwise, both insertion and continuation are classified as category 1 (see HIV Infection section).
a. Nucleoside reverse transcriptase inhibitors (NRTIs)					
i. Abacavir (ABC)	1/2	1	1/2	1	—
ii. Tenofovir (TDF)	1/2	1	1/2	1	—
iii. Zidovudine (AZT)	1/2	1	1/2	1	—
iv. Lamivudine (3TC)	1/2	1	1/2	1	—
v. Didanosine (DDI)	1/2	1	1/2	1	—
vi. Emtricitabine (FTC)	1/2	1	1/2	1	—
vii. Stavudine (D4T)	1/2	1	1/2	1	—
b. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)					
i. Efavirenz (EFV)	1/2	1	1/2	1	—
ii. Etravirine (ETR)	1/2	1	1/2	1	—
iii. Nevirapine (NVP)	1/2	1	1/2	1	—
iv. Rilpivirine (RPV)	1/2	1	1/2	1	—
c. Ritonavir-boosted protease inhibitors					
i. Ritonavir-boosted atazanavir (ATV/r)	1/2	1	1/2	1	—
ii. Ritonavir-boosted darunavir (DRV/r)	1/2	1	1/2	1	—

See table footnotes on page 30.

TABLE B1. (*Continued*) Classifications for intrauterine devices, including the copper-containing intrauterine device and levonorgestrel-releasing intrauterine device

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD		LNG-IUD		
iii. Ritonavir-boosted fosamprenavir (FPV/r)	1/2	1	1/2	1	—
iv. Ritonavir-boosted lopinavir (LPV/r)	1/2	1	1/2	1	—
v. Ritonavir-boosted saquinavir (SQV/r)	1/2	1	1/2	1	—
vi. Ritonavir-boosted tipranavir (TPV/r)	1/2	1	1/2	1	—
d. Protease inhibitors without ritonavir					
i. Atazanavir (ATV)	1/2	1	1/2	1	—
ii. Fosamprenavir (FPV)	1/2	1	1/2	1	—
iii. Indinavir (IDV)	1/2	1	1/2	1	—
iv. Nelfinavir (NFV)	1/2	1	1/2	1	—
e. CCR5 co-receptor antagonists					
i. Maraviroc (MVC)	1/2	1	1/2	1	—
f. HIV integrase strand transfer inhibitors					
i. Raltegravir (RAL)	1/2	1	1/2	1	—
ii. Dolutegravir (DTG)	1/2	1	1/2	1	—
iii. Elvitegravir (EVG)	1/2	1	1/2	1	—
g. Fusion inhibitors					
i. Enfuvirtide	1/2	1	1/2	1	—
Anticonvulsant therapy					
a. Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, and oxcarbazepine)	1		1		**Evidence:** Limited evidence suggests use of certain anticonvulsants does not interfere with the contraceptive effectiveness of the LNG-IUD (*142*).
b. Lamotrigine	1		1		**Evidence:** No drug interactions have been reported among women with epilepsy who are receiving lamotrigine and using the LNG-IUD (*143*).
Antimicrobial therapy					
a. Broad-spectrum antibiotics	1		1		—
b. Antifungals	1		1		—
c. Antiparasitics	1		1		—
d. Rifampin or rifabutin therapy	1		1		**Evidence:** One cross-sectional survey found that rifabutin had no impact on the effectiveness of the LNG-IUD (*142*).
Psychotropic medications					**Comment:** For many common psychotropic agents, limited or no theoretical concern exists for clinically significant drug interactions when co-administered with hormonal contraceptives. However, either no or very limited data exist examining potential interactions for these classes of medications.
a. SSRIs	1		1		—
St. John's wort	1		1		—

Abbreviations: ARV = antiretroviral; BMI = body mass index; COC = combined oral contraceptive; Cu-IUD = copper-containing IUD; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; HDL = high-density lipoprotein; HIV = human immunodeficiency virus; IBD = inflammatory bowel disease; IUD = intrauterine device; LDL = low-density lipoprotein; LNG = levonorgestrel; LNG-IUD = levonorgestrel-releasing IUD; PE = pulmonary embolism; PID = pelvic inflammatory disease; POC = progestin-only contraceptive; SLE = systemic lupus erythematosus; SSRI = selective serotonin reuptake inhibitor; STD = sexually transmitted disease; VTE = venous thromboembolism.

References

1. Cramer DW, Schiff I, Schoenbaum SC, et al. Tubal infertility and the intrauterine device. N Engl J Med 1985;312:941–7. http://dx.doi.org/10.1056/NEJM198504113121502
2. Daling JR, Weiss NS, Metch BJ, et al. Primary tubal infertility in relation to the use of an intrauterine device. N Engl J Med 1985;312:937–41. http://dx.doi.org/10.1056/NEJM198504113121501
3. Daling JR, Weiss NS, Voigt LF, McKnight B, Moore DE. The intrauterine device and primary tubal infertility. N Engl J Med 1992;326:203–4. http://dx.doi.org/10.1056/NEJM199201163260314
4. Delbarge W, Bátár I, Bafort M, et al. Return to fertility in nulliparous and parous women after removal of the GyneFix intrauterine contraceptive system. Eur J Contracept Reprod Health Care 2002;7:24–30. http://dx.doi.org/10.1080/ejc.7.1.24.30
5. Doll H, Vessey M, Painter R. Return of fertility in nulliparous women after discontinuation of the intrauterine device: comparison with women discontinuing other methods of contraception. BJOG 2001;108:304–14. http://dx.doi.org/10.1111/j.1471-0528.2001.00075.x
6. Hubacher D, Lara-Ricalde R, Taylor DJ, Guerra-Infante F, Guzmán-Rodríguez R. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. N Engl J Med 2001;345:561–7. http://dx.doi.org/10.1056/NEJMoa010438
7. Skjeldestad FE, Bratt H. Return of fertility after use of IUDs (Nova-T, MLCu250 and MLCu375). Adv Contracept 1987;3:139–45. http://dx.doi.org/10.1007/BF01890702
8. Urbach DR, Marrett LD, Kung R, Cohen MM. Association of perforation of the appendix with female tubal infertility. Am J Epidemiol 2001;153:566–71. http://dx.doi.org/10.1093/aje/153.6.566
9. Wilson JC. A prospective New Zealand study of fertility after removal of copper intrauterine contraceptive devices for conception and because of complications: a four-year study. Am J Obstet Gynecol 1989;160:391–6. http://dx.doi.org/10.1016/0002-9378(89)90455-9
10. US Department of Health and Human Services. Healthy people 2020: Maternal, infant, and child health objectives. Washington, DC: US Department of Health and Human Services; 2015. http://www.healthypeople.gov/2020/topics-objectives/topic/maternal-infant-and-child-health/objectives

11. Annus J, Brat T, Diethelm MP, et al.; World Health Organization Special. Comparative multicentre trial of three IUDs inserted immediately following delivery of the placenta. Contraception 1980;22:9–18.http://dx.doi.org/10.1016/0010-7824(80)90112-2
12. Apelo RA, Waszak CS. Postpartum IUD insertions in Manila, Philippines. Adv Contracept 1985;1:319–28.
13. Baldwin MK, Edelman AB, Lim JY, Nichols MD, Bednarek PH, Jensen JT. Intrauterine device placement at 3 versus 6weeks postpartum: a randomized trial. Contraception 2016;93:356–63.http://dx.doi.org/10.1016/j.contraception.2015.12.006
14. Bonilla Rosales F, Aguilar Zamudio ME, Cázares Montero ML, Hernández Ortiz ME, Luna Ruiz MA. [Factors for expulsion of intrauterine device Tcu380A applied immediately postpartum and after a delayed period]. Rev Med Inst Mex Seguro Soc 2005;43:5–10.
15. Braniff K, Gomez E, Muller R. A randomised clinical trial to assess satisfaction with the levonorgestrel- releasing intrauterine system inserted at caesarean section compared to postpartum placement. Aust N Z J Obstet Gynaecol 2015;55:279–83.http://dx.doi.org/10.1111/ajo.12335
16. Bryant AG, Kamanga G, Stuart GS, Haddad LB, Meguid T, Mhango C. Immediate postpartum versus 6-week postpartum intrauterine device insertion: a feasibility study of a randomized controlled trial. Afr J Reprod Health 2013;17:72–9.
17. Caliskan E, Ozturk N, Dilbaz BO, Dilbaz S. Analysis of risk factors associated with uterine perforation by intrauterine devices. Eur J Contracep Reprod 2003;8:150–5.
18. Çelen S, Möröy P, Sucak A, Aktulay A, Danişman N. Clinical outcomes of early postplacental insertion of intrauterine contraceptive devices. Contraception 2004;69:279–82.http://dx.doi.org/10.1016/j.contraception.2003.12.004
19. Çelen Ş, Sucak A, Yıldız Y, Danışman N. Immediate postplacental insertion of an intrauterine contraceptive device during cesarean section. Contraception 2011;84:240–3.http://dx.doi.org/10.1016/j.contraception.2011.01.006
20. Chen BA, Reeves MF, Hayes JL, Hohmann HL, Perriera LK, Creinin MD. Postplacental or delayed insertion of the levonorgestrel intrauterine device after vaginal delivery: a randomized controlled trial. Obstet Gynecol 2010;116:1079–87.http://dx.doi.org/10.1097/AOG.0b013e3181f73fac
21. Chen JH, Wu SC, Shao WQ, et al. The comparative trial of TCu 380A IUD and progesterone-releasing vaginal ring used by lactating women. Contraception 1998;57:371–9.http://dx.doi.org/10.1016/S0010-7824(98)00043-2
22. Cohen R, Sheeder J, Arango N, Teal SB, Tocce K. Twelve-month contraceptive continuation and repeat pregnancy among young mothers choosing postdelivery contraceptive implants or postplacental intrauterine devices. Contraception 2016;93:178–83.http://dx.doi.org/10.1016/j.contraception.2015.10.001
23. Dahlke JD, Terpstra ER, Ramseyer AM, Busch JM, Rieg T, Magann EF. Postpartum insertion of levonorgestrel—intrauterine system at three time periods: a prospective randomized pilot study. Contraception 2011;84:244–8.http://dx.doi.org/10.1016/j.contraception.2011.01.007
24. Dias T, Abeykoon S, Kumarasiri S, Gunawardena C, Padeniya T, D'Antonio F. Use of ultrasound in predicting success of intrauterine contraceptive device insertion immediately after delivery. Ultrasound Obstet Gynecol 2015;46:104–8.
25. Elsedeek MS. Puerperal and menstrual bleeding patterns with different types of contraceptive device fitted during elective cesarean delivery. Int J Gynaecol Obstet 2012;116:31–4.http://dx.doi.org/10.1016/j.ijgo.2011.07.036
26. Elsedeek MS. Five-year follow-up of two types of contraceptive device fitted during elective cesarean delivery. Int J Gynaecol Obstet 2015;130:179–82.http://dx.doi.org/10.1016/j.ijgo.2015.02.031
27. El-Shafei MM, Mashali A, Hassan EO, El-Boghdad L, El-Lakkany N. Postpartum and postabortion intrauterine device insertion unmet needs of safe reproductive health: three years experience of Mansoura University Hospital. J Egypt Soc Obstet Gynecol 2000;26:253–62.
28. Eroğlu K, Akkuzu G, Vural G, et al. Comparison of efficacy and complications of IUD insertion in immediate postplacental/early postpartum period with interval period: 1 year follow-up. Contraception 2006;74:376–81.http://dx.doi.org/10.1016/j.contraception.2006.07.003
29. Gueye M, Gaye YF, Diouf AA, et al. Trancesarean intra-uterine device. Pilot study performed at Dakar teaching hospital. [French]. J Gynecol Obstet Biol Reprod (Paris) 2013;42:585–90.http://dx.doi.org/10.1016/j.jgyn.2013.06.003
30. Gupta S, Malik S, Sinha R, Shyamsunder S, Mittal MK. Association of the Position of the Copper T 380A as Determined by the Ultrasonography Following its Insertion in the Immediate Postpartum Period with the Subsequent Complications: An Observational Study. J Obstet Gynaecol India 2014;64:349–53.http://dx.doi.org/10.1007/s13224-014-0532-5
31. Hagbard L, Ingemanson CA, Sorbe B. Early postpartum insertion of copper IUD. Contraception 1978;17:355–63.http://dx.doi.org/10.1016/0010-7824(78)90081-1
32. Hayes JL, Cwiak C, Goedken P, Zieman M. A pilot clinical trial of ultrasound-guided postplacental insertion of a levonorgestrel intrauterine device. Contraception 2007;76:292–6.http://dx.doi.org/10.1016/j.contraception.2007.06.003
33. Jatlaoui TC, Marcus M, Jamieson DJ, Goedken P, Cwiak C. Postplacental intrauterine device insertion at a teaching hospital. Contraception 2014;89:528–33.http://dx.doi.org/10.1016/j.contraception.2013.10.008
34. Kumar S, Sethi R, Balasubramaniam S, et al. Women's experience with postpartum intrauterine contraceptive device use in India. Reprod Health 2014;11:32.http://dx.doi.org/10.1186/1742-4755-11-32
35. Laes E, Lehtovirta P, Weintraub D, Pyörälä T, Luukkainen T. Early puerperal insertions of copper-T-200. Contraception 1975;11:289–95.http://dx.doi.org/10.1016/0010-7824(75)90037-2
36. Lara Ricalde R, Menocal Tobías G, Ramos Pérez C, Velázquez Ramírez N. [Random comparative study between intrauterine device Multiload Cu375 and TCu 380a inserted in the postpartum period]. Ginecol Obstet Mex 2006;74:306–11.
37. Lavin P, Bravo C, Waszak C. Comparison of T Cu 200 and Progestasert IUDs. Contracept Deliv Syst 1983;4:143–7.
38. Lavin P, Waszak C, Bravo C. Preliminary report on a postpartum CuT 200 study, Santiago, Chile. Int J Gynaecol Obstet 1983;21:71–5.http://dx.doi.org/10.1016/0020-7292(83)90073-5
39. Lester F, Kakaire O, Byamugisha J, et al. Intracesarean insertion of the Copper T380A versus 6 weeks postcesarean: a randomized clinical trial. Contraception 2015;91:198–203.http://dx.doi.org/10.1016/j.contraception.2014.12.002
40. Letti Müller AL, Lopes Ramos JG, Martins-Costa SH, et al. Transvaginal ultrasonographic assessment of the expulsion rate of intrauterine devices inserted in the immediate postpartum period: a pilot study. Contraception 2005;72:192–5.http://dx.doi.org/10.1016/j.contraception.2005.03.014
41. Levi E, Cantillo E, Ades V, Banks E, Murthy A. Immediate postplacental IUD insertion at cesarean delivery: a prospective cohort study. Contraception 2012;86:102–5.http://dx.doi.org/10.1016/j.contraception.2011.11.019
42. Levi EE, Stuart GS, Zerden ML, Garrett JM, Bryant AG. Intrauterine device placement during cesarean delivery and continued use 6 months postpartum: a randomized controlled trial. Obstet Gynecol 2015;126:5–11.http://dx.doi.org/10.1097/AOG.0000000000000882
43. Mishra S. Evaluation of Safety, Efficacy, and Expulsion of Post-Placental and Intra-Cesarean Insertion of Intrauterine Contraceptive Devices (PPIUCD). J Obstet Gynaecol India 2014;64:337–43.http://dx.doi.org/10.1007/s13224-014-0550-3
44. Morrison C, Waszak C, Katz K, Diabaté F, Mate EM. Clinical outcomes of two early postpartum IUD insertion programs in Africa. Contraception 1996;53:17–21.http://dx.doi.org/10.1016/0010-7824(95)00254-5
45. Nelson AL, Chen S, Eden R. Intraoperative placement of the Copper T-380 intrauterine devices in women undergoing elective cesarean delivery: a pilot study. Contraception 2009;80:81–3.http://dx.doi.org/10.1016/j.contraception.2009.01.014

46. Newton J, Harper M, Chan KK. Immediate post-placental insertion of intrauterine contraceptive devices. Lancet 1977;310:272–4.http://dx.doi.org/10.1016/S0140-6736(77)90955-2
47. Prema K, Gayathri TL, Philips FS. Comparative study of early postpartum, postabortal and interval insertion of Cu T 200 mm2 device. J Obstet Gynaecol India 1978;28:946–8.
48. Puzey M. Mirena at caesarean section. Eur J Contracep Reprod 2005;10:164–7.
49. Ragab A, Hamed HO, Alsammani MA, et al. Expulsion of Nova-T380, Multiload 375, and Copper-T380A contraceptive devices inserted during cesarean delivery. Int J Gynaecol Obstet 2015;130:174–8.http://dx.doi.org/10.1016/j.ijgo.2015.03.025
50. Shukla M, Qureshi S; Chandrawati. Post-placental intrauterine device insertion—a five year experience at a tertiary care centre in north India. Indian J Med Res 2012;136:432–5.
51. Singal S, Bharti R, Dewan R, et al. Clinical Outcome of Postplacental Copper T 380A Insertion in Women Delivering by Caesarean Section. J Clin Diagn Res 2014;8:OC01–04.
52. Stuart GS, Bryant AG, O'Neill E, Doherty IA. Feasibility of postpartum placement of the levonorgestrel intrauterine system more than 6 h after vaginal birth. Contraception 2012;85:359–62.http://dx.doi.org/10.1016/j.contraception.2011.08.005
53. Stuart GS, Lesko CR, Stuebe AM, Bryant AG, Levi EE, Danvers AI. A randomized trial of levonorgestrel intrauterine system insertion 6 to 48 h compared to 6 weeks after vaginal delivery; lessons learned. Contraception 2015;91:284–8.http://dx.doi.org/10.1016/j.contraception.2014.12.009
54. Thiery M, Van Kets H, Van der Pas H. Immediate post-placental IUD insertion: the expulsion problem. Contraception 1985;31:331–49.http://dx.doi.org/10.1016/0010-7824(85)90002-2
55. Van Der Pas MT, Delbeke L, Van Dets H. Comparative performance of two copper-wired IUDs (ML Cu 250 and T Cu 200: immediate postpartum and interval insertion. Contracept Deliv Syst 1980;1:27–35.
56. Welkovic S, Costa LO, Faúndes A, de Alencar Ximenes R, Costa CF. Post-partum bleeding and infection after post-placental IUD insertion. Contraception 2001;63:155–8.http://dx.doi.org/10.1016/S0010-7824(01)00180-9
57. Whitaker AK, Endres LK, Mistretta SQ, Gilliam ML. Postplacental insertion of the levonorgestrel intrauterine device after cesarean delivery vs. delayed insertion: a randomized controlled trial. Contraception 2014;89:534–9.http://dx.doi.org/10.1016/j.contraception.2013.12.007
58. Woo CJ, Alamgir H, Potter JE. Women's experiences after Planned Parenthood's exclusion from a family planning program in Texas. Contraception 2016;93:298–302.http://dx.doi.org/10.1016/j.contraception.2015.12.004
59. Wu SC; Research Group on Failure Causes and Prevention Measures of Intrauterine Device. [Efficacy of intrauterine device TCu380A when inserted in four different periods]. Zhonghua Fu Chan Ke Za Zhi 2009;44:431–5.
60. Xu J, Yang X, Gu X, et al. Comparison between two techniques used in immediate postplacental insertion of TCu 380A intrauterine device: 36-month follow-up. Reprod Contracept 1999;10:156–62.
61. Xu J, Zhuang L, Yu G. [Comparison of two techniques used in immediate postplacental insertion of TCu 380A intrauterine device: 12 month follow-up of 910 cases]. Zhonghua Fu Chan Ke Za Zhi 1997;32:354–7.
62. Xu JX, Rivera R, Dunson TR, et al. A comparative study of two techniques used in immediate postplacental insertion (IPPI) of the Copper T-380A IUD in Shanghai, People's Republic of China. Contraception 1996;54:33–8.http://dx.doi.org/10.1016/0010-7824(96)00117-5
63. Braniff K, Gomez E, Muller R. A randomised clinical trial to assess satisfaction with the levonorgestrel- releasing intrauterine system inserted at caesarean section compared to postpartum placement. Aust N Z J Obstet Gynaecol 2015;55:279–83. http://dx.doi.org/10.1111/ajo.12335
64. Phillips SJ, Tepper NK, Kapp N, Nanda K, Temmerman M, Curtis KM. Progestogen-only contraceptive use among breastfeeding women: a systematic review. Contraception 2015;S0010-7824(15)00585-5.
65. Berry-Bibee E, Tepper N, Jatlaoui T, Whiteman M, Jamieson D, Curtis K. The safety of intrauterine devices in breastfeeding women: a systematic review. Contraception. In press 2016.
66. Steenland MW, Tepper NK, Curtis KM, Kapp N. Intrauterine contraceptive insertion postabortion: a systematic review. Contraception 2011;84:447–64. http://dx.doi.org/10.1016/j.contraception.2011.03.007
67. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. Contraception 1998;57:315–24. http://dx.doi.org/10.1016/S0010-7824(98)00041-9.
68. Heinemann LA, Assmann A, DoMinh T, Garbe E. Oral progestogen-only contraceptives and cardiovascular risk: results from the Transnational Study on Oral Contraceptives and the Health of Young Women. Eur J Contracept Reprod Health Care 1999;4:67–73. http://dx.doi.org/10.3109/13625189909064007
69. Vasilakis C, Jick H, del Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestagens alone. Lancet 1999;354:1610–1. http://dx.doi.org/10.1016/S0140-6736(99)04394-9
70. Kingman CE, Kadir RA, Lee CA, Economides DL. The use of levonorgestrel-releasing intrauterine system for treatment of menorrhagia in women with inherited bleeding disorders. BJOG 2004;111:1425–8. http://dx.doi.org/10.1111/j.1471-0528.2004.00305.x
71. Lukes AS, Reardon B, Arepally G. Use of the levonorgestrel-releasing intrauterine system in women with hemostatic disorders. Fertil Steril 2008;90:673–7. http://dx.doi.org/10.1016/j.fertnstert.2007.07.1315
72. Pisoni CN, Cuadrado MJ, Khamashta MA, Hunt BJ. Treatment of menorrhagia associated with oral anticoagulation: efficacy and safety of the levonorgestrel releasing intrauterine device (Mirena coil). Lupus 2006;15:877–80. http://dx.doi.org/10.1177/0961203306071706
73. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. Am J Obstet Gynecol 2005;193:1361–3. http://dx.doi.org/10.1016/j.ajog.2005.05.002
74. Wilson W, Taubert KA, Gewitz M, et al; American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee; American Heart Association Council on Cardiovascular Disease in the Young; American Heart Association Council on Clinical Cardiology; American Heart Association Council on Cardiovascular Surgery and Anesthesia; Quality of Care and Outcomes Research Interdisciplinary Working Group. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007;116:1736–54. http://dx.doi.org/10.1161/CIRCULATIONAHA.106.183095
75. Tepper NK, Paulen ME, Marchbanks PA, Curtis KM. Safety of contraceptive use among women with peripartum cardiomyopathy: a systematic review. Contraception 2010;82:95–101. http://dx.doi.org/10.1016/j.contraception.2010.02.004
76. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Little, Brown and Co; 1994.
77. Bernatsky S, Clarke A, Ramsey-Goldman R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford) 2004;43:1178–81. http://dx.doi.org/10.1093/rheumatology/keh282
78. Bernatsky S, Ramsey-Goldman R, Gordon C, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford) 2004;43:1386–9. http://dx.doi.org/10.1093/rheumatology/keh331
79. Chopra N, Koren S, Greer WL, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. J Rheumatol 2002;29:1683–8.

80. Esdaile JM, Abrahamowicz M, Grodzicky T, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum 2001;44:2331–7. http://dx.doi.org/10.1002/1529-0131(200110)44:10<2331::AID-ART395≥3.0.CO;2-I
81. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. Br J Rheumatol 1993;32:227–30. http://dx.doi.org/10.1093/rheumatology/32.3.227
82. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol 1997;145:408–15. http://dx.doi.org/10.1093/oxfordjournals.aje.a009122
83. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephritis in systemic lupus erythematosus. Ann Rheum Dis 1993;52:720–4. http://dx.doi.org/10.1136/ard.52.10.720
84. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Ann Rheum Dis 1992;51:56–60. http://dx.doi.org/10.1136/ard.51.1.56
85. Mintz G, Gutiérrez G, Delezé M, Rodríguez E. Contraception with progestagens in systemic lupus erythematosus. Contraception 1984;30:29–38. http://dx.doi.org/10.1016/0010-7824(84)90076-3
86. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res 1995;8:137–45. http://dx.doi.org/10.1002/art.1790080305
87. Petri M. Lupus in Baltimore: evidence-based 'clinical pearls' from the Hopkins Lupus Cohort. Lupus 2005;14:970–3. http://dx.doi.org/10.1191/0961203305lu2230xx
88. Sánchez-Guerrero J, Uribe AG, Jiménez-Santana L, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. N Engl J Med 2005;353:2539–49. http://dx.doi.org/10.1056/NEJMoa050817
89. Sarabi ZS, Chang E, Bobba R, et al. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Rheum 2005;53:609–12. http://dx.doi.org/10.1002/art.21314
90. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. J Rheumatol 2002;29:2531–6.
91. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, Ogryzlo MA. The bimodal mortality pattern of systemic lupus erythematosus. Am J Med 1976;60:221–5. http://dx.doi.org/10.1016/0002-9343(76)90431-9
92. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scand J Rheumatol 1991;20:427–33. http://dx.doi.org/10.3109/03009749109096822
93. Jungers P, Dougados M, Pélissier C, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis Rheum 1982;25:618–23. http://dx.doi.org/10.1002/art.1780250603
94. Petri M, Kim MY, Kalunian KC, et al; OC-SELENA Trial. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med 2005;353:2550–8. http://dx.doi.org/10.1056/NEJMoa051135
95. Choojitarom K, Verasertniyom O, Totemchokchyakarn K, Nantiruj K, Sumethkul V, Janwityanujit S. Lupus nephritis and Raynaud's phenomenon are significant risk factors for vascular thrombosis in SLE patients with positive antiphospholipid antibodies. Clin Rheumatol 2008;27:345–51. http://dx.doi.org/10.1007/s10067-007-0721-z
96. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus—a meta-analysis. Lupus 1997;6:467–73. http://dx.doi.org/10.1177/096120339700600510
97. Tepper NK, Whiteman MK, Zapata LB, Marchbanks PA, Curtis KM. Safety of hormonal contraceptives among women with migraine: a systematic review. Contraception 2016. Epub May 3, 2016. http:// dx.doi.org/10.1016/j.contraception.2016.04.016
98. Tepper NK, Whiteman MK, Marchbanks PA, James AH, Curtis KM. Progestin-only contraception and thromboembolism: a systematic review. Contraception 2016. Epub May 3, 2016. http://dx.doi.org/10.1016/j.contraception.2016.04.014
99. Pagano HP, Zapata LB, Berry-Bibee EN, Nanda K, Curtis KM. Safety of hormonal contraception and intrauterine devices among women with depressive and bipolar disorders: a systematic review. Contraception 2016. Epub June 27, 2016. http://dx.doi.org/10.1016/j.contraception.2016.06.012
100. Barrington JW, Arunkalaivanan AS, Abdel-Fattah M. Comparison between the levonorgestrel intrauterine system (LNG-IUS) and thermal balloon ablation in the treatment of menorrhagia. Eur J Obstet Gynecol Reprod Biol 2003;108:72–4. http://dx.doi.org/10.1016/S0301-2115(02)00408-6
101. Gupta B, Mittal S, Misra R, Deka D, Dadhwal V. Levonorgestrel-releasing intrauterine system vs. transcervical endometrial resection for dysfunctional uterine bleeding. Int J Gynaecol Obstet 2006;95:261–6. http://dx.doi.org/10.1016/j.ijgo.2006.07.004
102. Hurskainen R, Teperi J, Rissanen P, et al. Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial.[see comment]. Lancet 2001;357:273–7. http://dx.doi.org/10.1016/S0140-6736(00)03615-1
103. Istre O, Trolle B. Treatment of menorrhagia with the levonorgestrel intrauterine system versus endometrial resection. Fertil Steril 2001;76:304–9. http://dx.doi.org/10.1016/S0015-0282(01)01909-4
104. Koh SC, Singh K. The effect of levonorgestrel-releasing intrauterine system use on menstrual blood loss and the hemostatic, fibrinolytic/inhibitor systems in women with menorrhagia. J Thromb Haemost 2007;5:133–8. http://dx.doi.org/10.1111/j.1538-7836.2006.02243.x
105. Lethaby AE, Cooke I, Rees M. Progesterone/progestogen releasing intrauterine systems versus either placebo or any other medication for heavy menstrual bleeding. Cochrane Database Syst Rev 2000;(2):CD002126.
106. Magalhães J, Aldrighi JM, de Lima GR. Uterine volume and menstrual patterns in users of the levonorgestrel-releasing intrauterine system with idiopathic menorrhagia or menorrhagia due to leiomyomas. Contraception 2007;75:193–8. http://dx.doi.org/10.1016/j.contraception.2006.11.004
107. Stewart A, Cummins C, Gold L, Jordan R, Phillips W. The effectiveness of the levonorgestrel-releasing intrauterine system in menorrhagia: a systematic review. BJOG 2001;108:74–86. http://dx.doi.org/10.1111/j.1471-0528.2001.00020.x
108. Fedele L, Bianchi S, Zanconato G, Portuese A, Raffaelli R. Use of a levonorgestrel-releasing intrauterine device in the treatment of rectovaginal endometriosis. Fertil Steril 2001;75:485–8. http://dx.doi.org/10.1016/S0015-0282(00)01759-3
109. Lockhat FBE, Emembolu J, Konje JC. The effect of a levonorgestrel intrauterine system (LNG-IUS) on symptomatic endometriosis. Fertil Steril 2002;77(Suppl 1):S24. http://dx.doi.org/10.1016/S0015-0282(01)03086-2
110. Petta CA, Ferriani RA, Abrao MS, et al. Randomized clinical trial of a levonorgestrel-releasing intrauterine system and a depot GnRH analogue for the treatment of chronic pelvic pain in women with endometriosis. Hum Reprod 2005;20:1993–8. http://dx.doi.org/10.1093/humrep/deh869
111. Vercellini P, Aimi G, Panazza S, De Giorgi O, Pesole A, Crosignani PG. A levonorgestrel-releasing intrauterine system for the treatment of dysmenorrhea associated with endometriosis: a pilot study. Fertil Steril 1999;72:505–8. http://dx.doi.org/10.1016/S0015-0282(99)00291-5
112. Vercellini P, Frontino G, De Giorgi O, Aimi G, Zaina B, Crosignani PG. Comparison of a levonorgestrel-releasing intrauterine device versus expectant management after conservative surgery for symptomatic endometriosis: a pilot study. Fertil Steril 2003;80:305–9. http://dx.doi.org/10.1016/S0015-0282(03)00608-3
113. Gaffield ME, Kapp N, Curtis KM. Combined oral contraceptive and intrauterine device use among women with gestational trophoblastic disease. Contraception 2009;80:363–71. http://dx.doi.org/10.1016/j.contraception.2009.03.022

114. Whiteman MK, Zapata LB, Tepper NK, Marchbanks PA, Curtis KM. Use of contraceptive methods among women with endometrial hyperplasia: a systematic review. Contraception 2010;82:56–63. http://dx.doi.org/10.1016/j.contraception.2010.02.005
115. Zapata LB, Whiteman MK, Tepper NK, Jamieson DJ, Marchbanks PA, Curtis KM. Intrauterine device use among women with uterine fibroids: a systematic review. Contraception 2010;82:41–55. http://dx.doi.org/10.1016/j.contraception.2010.02.011
116. Tepper NK, Steenland MW, Gaffield ME, Marchbanks PA, Curtis KM. Retention of intrauterine devices in women who acquire pelvic inflammatory disease: a systematic review. Contraception 2013;87:655–60. http://dx.doi.org/10.1016/j.contraception.2012.08.011
117. Faúndes A, Telles E, Cristofoletti ML, Faúndes D, Castro S, Hardy E. The risk of inadvertent intrauterine device insertion in women carriers of endocervical Chlamydia trachomatis. Contraception 1998;58:105–9. http://dx.doi.org/10.1016/S0010-7824(98)00064-X
118. Ferraz do Lago R, Simões JA, Bahamondes L, Camargo RP, Perrotti M, Monteiro I. Follow-up of users of intrauterine device with and without bacterial vaginosis and other cervicovaginal infections. Contraception 2003;68:105–9. http://dx.doi.org/10.1016/S0010-7824(03)00109-4
119. Morrison CS, Sekadde-Kigondu C, Miller WC, Weiner DH, Sinei SK. Use of sexually transmitted disease risk assessment algorithms for selection of intrauterine device candidates. Contraception 1999;59:97–106. http://dx.doi.org/10.1016/S0010-7824(99)00006-2
120. Pap-Akeson M, Solheim F, Thorbert G, Akerlund M. Genital tract infections associated with the intrauterine contraceptive device can be reduced by inserting the threads into the uterine cavity. Br J Obstet Gynaecol 1992;99:676–9. http://dx.doi.org/10.1111/j.1471-0528.1992.tb13854.x
121. Sinei SK, Schulz KFLP, Lamptey PR, et al. Preventing IUCD-related pelvic infection: the efficacy of prophylactic doxycycline at insertion. Br J Obstet Gynaecol 1990;97:412–9. http://dx.doi.org/10.1111/j.1471-0528.1990.tb01828.x
122. Skjeldestad FE, Halvorsen LE, Kahn H, Nordbø SA, Saake K. IUD users in Norway are at low risk for genital C. trachomatis infection. Contraception 1996;54:209–12. http://dx.doi.org/10.1016/S0010-7824(96)00190-4
123. Walsh TL, Bernstein GS, Grimes DA, Frezieres R, Bernstein L, Coulson AH; IUD Study Group. Effect of prophylactic antibiotics on morbidity associated with IUD insertion: results of a pilot randomized controlled trial. Contraception 1994;50:319–27. http://dx.doi.org/10.1016/0010-7824(94)90019-1
124. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(No. RR-03).
125. Jatlaoui TC, Simmons KB, Curtis KM. The safety of intrauterine contraception initiation among women with current asymptomatic cervical infections or at increased risk of sexually transmitted infections. Contraception 2016. Epub June 1, 2016. http://dx.doi.org/10.1016/j.contraception.2016.05.013
126. Carael M, Van de Perre PH, Lepage PH, et al. Human immunodeficiency virus transmission among heterosexual couples in Central Africa. AIDS 1988;2:201–5.
127. European Study Group on Heterosexual Transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. BMJ 1992;304:809–13. http://dx.doi.org/10.1136/bmj.304.6830.809
128. Kapiga SH, Lyamuya EF, Lwihula GK, Hunter DJ. The incidence of HIV infection among women using family planning methods in Dar es Salaam, Tanzania. AIDS 1998;12:75–84. http://dx.doi.org/10.1097/00002030-199801000-00009.
129. Kapiga SH, Shao JF, Lwihula GK, Hunter DJ. Risk factors for HIV infection among women in Dar-es-Salaam, Tanzania. J Acquir Immune Defic Syndr 1994;7:301–9.
130. Mann JM, Nzilambi N, Piot P, et al. HIV infection and associated risk factors in female prostitutes in Kinshasa, Zaire. AIDS 1988;2:249–54. http://dx.doi.org/10.1097/00002030-198808000-00002
131. Martin HL Jr, Nyange PM, Richardson BA, et al. Hormonal contraception, sexually transmitted diseases, and risk of heterosexual transmission of human immunodeficiency virus type 1. J Infect Dis 1998;178:1053–9. http://dx.doi.org/10.1086/515654
132. Mali JK, Hunter DJ, Maggwa BN, Tukei PM. Contraceptive use and the risk of HIV infection in Nairobi, Kenya. Int J Gynaecol Obstet 1995;48:61–7. http://dx.doi.org/10.1016/0020-7292(94)02214-3
133. Nicolosi A, Corrêa Leite ML, Musicco M, Arici C, Gavazzeni G, Lazzarin A; Italian Study Group on HIV Heterosexual Transmission. The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: a study of 730 stable couples. [comment]. Epidemiology 1994;5:570–5. http://dx.doi.org/10.1097/00001648-199411000-00003
134. Plourde PJ, Plummer FA, Pepin J, et al. Human immunodeficiency virus type 1 infection in women attending a sexually transmitted diseases clinic in Kenya.[comment]. J Infect Dis 1992;166:86–92. http://dx.doi.org/10.1093/infdis/166.1.86
135. Sinei SK, Fortney JA, Kigondu CS, et al. Contraceptive use and HIV infection in Kenyan family planning clinic attenders. Int J STD AIDS 1996;7:65–70. http://dx.doi.org/10.1258/0956462961917104
136. Spence MR, Robbins SM, Polansky M, Schable CA. Seroprevalence of human immunodeficiency virus type I (HIV-1) antibodies in a family-planning population. Sex Transm Dis 1991;18:143–5. http://dx.doi.org/10.1097/00007435-199107000-00003
137. Tepper NK, Curtis KM, Nanda K, Jamieson DJ. Safety of intrauterine devices among women with HIV: a systematic review. Contraception 2016. Epub June 22, 2016. http://dx.doi.org/0.1016/j.contraception.2016.06.011
138. Grigoryan OR, Grodnitskaya EE, Andreeva EN, Shestakova MV, Melnichenko GA, Dedov II. Contraception in perimenopausal women with diabetes mellitus. Gynecol Endocrinol 2006;22:198–206. http://dx.doi.org/10.1080/09513590600624317
139. Rogovskaya S, Rivera R, Grimes DA, et al. Effect of a levonorgestrel intrauterine system on women with type 1 diabetes: a randomized trial. Obstet Gynecol 2005;105:811–5. http://dx.doi.org/10.1097/01.AOG.0000156301.11939.56
140. Zapata LB, Paulen ME, Cansino C, Marchbanks PA, Curtis KM. Contraceptive use among women with inflammatory bowel disease: a systematic review. Contraception 2010;82:72–85. http://dx.doi.org/10.1016/j.contraception.2010.02.012
141. Paulen ME, Folger SG, Curtis KM, Jamieson DJ. Contraceptive use among solid organ transplant patients: a systematic review. Contraception 2010;82:102–12. http://dx.doi.org/10.1016/j.contraception.2010.02.007
142. Bounds W, Guillebaud J. Observational series on women using the contraceptive Mirena concurrently with anti-epileptic and other enzyme-inducing drugs. J Fam Plann Reprod Health Care 2002;28:78–80. http://dx.doi.org/10.1783/147118902101195992
143. Reimers A, Helde G, Brodtkorb E. Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Epilepsia 2005;46:1414–7. http://dx.doi.org/10.1111/j.1528-1167.2005.10105.x

Appendix C

Classifications for Progestin-Only Contraceptives

Classifications for progestin-only contraceptives (POCs) include those for progestin-only implants, depot medroxyprogesterone acetate (DMPA; 150 mg intramuscularly or 104 mg subcutaneously), and progestin-only pills (POPs) (Box C1) (Table C1). POCs do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

BOX C1. Categories for classifying progestin-only contraceptives

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

TABLE C1. Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Personal Characteristics and Reproductive History				
Pregnancy	NA	NA	NA	**Clarification:** Use of POCs is not required. No known harm to the woman, the course of her pregnancy, or the fetus occurs if POCs are inadvertently used during pregnancy. However, the relation between DMPA use during pregnancy and its effects on the fetus remains unclear.
Age				**Evidence:** Most studies have found that women lose BMD during DMPA use but recover BMD after discontinuation. Limited evidence shows a weak association with fracture. However, one large study suggests that women who choose DMPA might be at higher risk for fracture before initiation (*1*). It is unclear whether adult women with long durations of DMPA use can regain BMD to baseline levels before entering menopause and whether adolescents can reach peak bone mass after discontinuation of DMPA. The relationship between these changes in BMD during the reproductive years and future fracture risk is unknown. Studies generally find no effect of POCs other than DMPA on BMD *(1–48)*.
a. Menarche to <18 years	1	2	1	
b. 18–45 years	1	1	1	
c. >45 years	1	2	1	
Parity				
a. Nulliparous	1	1	1	—
b. Parous	1	1	1	—
Breastfeeding				
a. <21 days postpartum	2	2	2	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*49*). **Evidence:** Two small, randomized controlled trials found no adverse impact on breastfeeding with initiation of etonogestrel implants within 48 hours postpartum. Other studies found that initiation of POPs, injectables, and implants at ≤6 weeks postpartum compared with nonhormonal use had no detrimental effect on breastfeeding outcomes or infant health, growth, and development in the first year postpartum. In general, these studies are of poor quality, lack standard definitions of breastfeeding or outcome measures, and have not included premature or ill infants (*50*,*51*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, and certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
b. 21 to <30 days postpartum				**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*49*).
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	2	2	2	**Evidence:** Two small, randomized controlled trials found no adverse impact on breastfeeding with initiation of etonogestrel implants within 48 hours postpartum. Other studies found that initiation of POPs, injectables, and implants at ≤6 weeks postpartum compared with nonhormonal use had no detrimental effect on breastfeeding outcomes or infant health, growth, and development in the first year postpartum. In general, these studies are of poor quality, lack standard definitions of breastfeeding or outcome measures, and have not included premature or ill infants (*50*,*51*).
ii. Without other risk factors for VTE	2	2	2	**Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, and certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
c. 30–42 days postpartum				**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*49*).
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	1	1	1	**Evidence:** Two small, randomized controlled trials found no adverse impact on breastfeeding with initiation of etonogestrel implants within 48 hours postpartum. Other studies found that initiation of POPs, injectables, and implants at ≤6 weeks postpartum compared with nonhormonal use had no detrimental effect on breastfeeding outcomes or infant health, growth, and development in the first year postpartum. In general, these studies are of poor quality, lack standard definitions of breastfeeding or outcome measures, and have not included premature or ill infants (*50*,*51*).
ii. Without other risk factors for VTE	1	1	1	**Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, and certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
d. >42 days postpartum	1	1	1	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*49*).
				Evidence: Overall, studies found that initiation of POPs, injectables, and implants at >6 weeks postpartum compared with nonhormonal use had no detrimental effect on breastfeeding outcomes or infant health, growth, and development in the first year postpartum. In general, these studies are of poor quality, lack standard definitions of breastfeeding or outcome measures, and have not included premature or ill infants (*51*).
				Comment: Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, and certain perinatal complications and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Postpartum (nonbreastfeeding women)				
a. <21 days postpartum	1	1	1	—
b. 21–42 days postpartum				
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	1	1	1	—
ii. Without other risk factors for VTE	1	1	1	—
c. >42 days postpartum	1	1	1	—
Postabortion				
a. First trimester	1	1	1	**Clarification:** POCs may be started immediately postabortion. **Evidence:** Limited evidence suggests that no adverse side effects occur when implants (Norplant) or progestin-only injectables (NET-EN) are initiated after first trimester abortion (*52–55*).
b. Second trimester	1	1	1	**Clarification:** POCs may be started immediately postabortion.
c. Immediate postseptic abortion	1	1	1	**Clarification:** POCs may be started immediately postabortion.
Past ectopic pregnancy	1	1	2	**Comment:** POP users have a higher absolute rate of ectopic pregnancy than do users of other POCs but still lower than women using no method.
History of pelvic surgery	1	1	1	—
Smoking				
a. Age <35 years	1	1	1	—
b. Age ≥35 years				
i. <15 cigarettes per day	1	1	1	—
ii. ≥15 cigarettes per day	1	1	1	—
Obesity				—
a. BMI ≥30 kg/m^2	1	1	1	—
b. Menarche to <18 years and BMI ≥30 kg/m^2	1	2	1	**Evidence:** Among adult women, generally no association has been found between baseline weight and weight gain among DMPA users compared with nonusers. Evidence is mixed for adolescent DMPA users, with some studies observing greater weight gain among obese compared with normal weight users but other studies showing no association; methodologic differences across studies might account for the differences in findings. Data on other POC methods and other adverse outcomes including weight gain are limited (*56–73*).
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	1	1	1	**Evidence:** Limited evidence demonstrated no substantial decrease in effectiveness of oral contraceptives among women who underwent laparoscopic placement of an adjustable gastric band (*74*).
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	1	1	3	**Evidence:** Limited evidence demonstrated no substantial decrease in effectiveness of oral contraceptives among women who underwent a biliopancreatic diversion; however, evidence from pharmacokinetic studies suggested conflicting results regarding oral contraceptive effectiveness among women who underwent a jejunoileal bypass (*74*). **Comment:** Bariatric surgical procedures involving a malabsorptive component have the potential to decrease oral contraceptive effectiveness, perhaps further decreased by postoperative complications such as long-term diarrhea, vomiting, or both.

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Cardiovascular Disease				
Multiple risk factors for atherosclerotic cardiovascular disease (e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	2	3	2	**Clarification:** When multiple major risk factors exist, risk for cardiovascular disease might increase substantially. Certain POCs might increase the risk for thrombosis, although this increase is substantially less than with COCs. The effects of DMPA might persist for some time after discontinuation. **Clarification:** The recommendations apply to known preexisting medical conditions or characteristics. Few if any screening tests are needed before initiation of contraception. See the *U.S. Selected Practice Recommendations for Contraceptive Use* (http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usspr.htm).
Hypertension Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg are associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Adequately controlled hypertension	1	2	1	**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors exist for cardiovascular disease. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Clarification:** Women adequately treated for hypertension are at lower risk for acute myocardial infarction and stroke than are untreated women. Although no data exist, POC users with adequately controlled and monitored hypertension should be at lower risk for acute myocardial infarction and stroke than are untreated hypertensive POC users.
b. Elevated blood pressure levels (properly taken measurements)				**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors exist for cardiovascular disease. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Evidence:** Limited evidence suggests that among women with hypertension, those who used POPs or progestin-only injectables had a small increased risk for cardiovascular events compared with women who did not use these methods (*75*).
i. Systolic 140–159 mm Hg or diastolic 90–99 mm Hg	1	2	1	
ii. Systolic ≥160 mm Hg or diastolic ≥100 mm Hg	2	3	2	
c. Vascular disease	2	3	2	**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors exist for cardiovascular disease. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Comment:** Concern exists about hypoestrogenic effects and reduced HDL levels, particularly among users of DMPA. However, little concern exists about these effects with regard to POPs. The effects of DMPA might persist for some time after discontinuation.
History of high blood pressure during pregnancy (when current blood pressure is measurable and normal)	1	1	1	—
Deep venous thrombosis/Pulmonary embolism				
a. History of DVT/PE, not receiving anticoagulant therapy				

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
i. Higher risk for recurrent DVT/PE (one or more risk factors) • History of estrogen-associated DVT/PE • Pregnancy-associated DVT/PE • Idiopathic DVT/PE • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	2	2	2	—
ii. Lower risk for recurrent DVT/PE (no risk factors)	2	2	2	—
b. Acute DVT/PE	2	2	2	**Evidence:** No direct evidence exists on use of POCs among women with acute DVT/PE. Although findings on the risk for venous thrombosis with use of POCs in otherwise healthy women is inconsistent, any small increased risk is substantially less than that with COCs (*75–77*).
c. DVT/PE and established anticoagulant therapy for at least 3 months				**Evidence:** No direct evidence exists on use of POCs among women with DVT/PE receiving anticoagulant therapy. Although findings on the risk for venous thrombosis with use of POCs is inconsistent in otherwise healthy women, any small increased risk is substantially less than that with COCs (*75–77*). Limited evidence indicates that intramuscular injections of DMPA in women receiving chronic anticoagulation therapy does not pose a significant risk for hematoma at the injection site or increase the risk for heavy or irregular vaginal bleeding (*78*).
i. Higher risk for recurrent DVT/PE (one or more risk factors) • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	2	2	2	
ii. Lower risk for recurrent DVT/PE (no risk factors)	2	2	2	
d. Family history (first-degree relatives)	1	1	1	—
e. Major surgery				
i. With prolonged immobilization	2	2	2	—
ii. Without prolonged immobilization	1	1	1	—
f. Minor surgery without immobilization	1	1	1	—
Known thrombogenic mutations (e.g., factor V Leiden; prothrombin mutation; and protein S, protein C, and antithrombin deficiencies) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	2	2	2	**Clarification:** Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.
Superficial venous disorders				
a. Varicose veins	1	1	1	—
b. Superficial venous thrombosis (acute or history)	1	1	1	—
Current and history of ischemic heart disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation 2 Continuation 3	3	Initiation 2 Continuation 3	**Comment:** Concern exists about hypoestrogenic effects and reduced HDL levels, particularly among users of DMPA. However, little concern exists about these effects with regard to POPs. The effects of DMPA might persist for some time after discontinuation.
Stroke (history of cerebrovascular accident) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation 2 Continuation 3	3	Initiation 2 Continuation 3	**Comment:** Concern exists about hypoestrogenic effects and reduced HDL levels, particularly among users of DMPA. However, little concern exists about these effects with regard to POPs. The effects of DMPA might persist for some time after discontinuation.
Valvular heart disease Complicated valvular heart disease is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Uncomplicated	1	1	1	—

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category				Clarifications/Evidence/Comments
	Implants	DMPA		POPs	
b. Complicated (pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis)	1	1		1	—
Peripartum cardiomyopathy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					**Evidence:** No direct evidence exists on the safety of POCs among women with peripartum cardiomyopathy. Limited indirect evidence from noncomparative studies of women with cardiac disease demonstrated few cases of hypertension, thromboembolism, and heart failure in women with cardiac disease using POPs and DMPA (*79*).
a. Normal or mildly impaired cardiac function (New York Heart Association Functional Class I or II: patients with no limitation of activities or patients with slight, mild limitation of activity) (*80*)					**Comment:** Progestin-only implants might induce cardiac arrhythmias in healthy women; women with peripartum cardiomyopathy have a high incidence of cardiac arrhythmias.
i. <6 months	1	1		1	
ii. ≥6 months	1	1		1	
b. Moderately or severely impaired cardiac function (New York Heart Association Functional Class III or IV: patients with marked limitation of activity or patients who should be at complete rest) (*80*)	2	2		2	
Rheumatic Diseases					
Systemic lupus erythematosus This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		Initiation	Continuation		
a. Positive (or unknown) antiphospholipid antibodies	3	3	3	3	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*81–99*). **Evidence:** Antiphospholipid antibodies are associated with a higher risk for both arterial and venous thrombosis (*100*,*101*).
b. Severe thrombocytopenia	2	3	2	2	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*81–99*). **Comment:** Severe thrombocytopenia increases the risk for bleeding. POCs might be useful in treating menorrhagia in women with severe thrombocytopenia. However, given the increased or erratic bleeding that might be seen on initiation of DMPA and its irreversibility for 11–13 weeks after administration, initiation of this method in women with severe thrombocytopenia should be done with caution.
c. Immunosuppressive therapy	2	2	2	2	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*81–99*).

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category				Clarifications/Evidence/Comments
	Implants	DMPA		POPs	
		Initiation	Continuation		
d. None of the above	2	2	2	2	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*81–99*).
Rheumatoid arthritis					
a. Receiving immunosuppressive therapy	1	2/3		1	**Clarification (DMPA):** DMPA use among women receiving long-term corticosteroid therapy with a history of, or with risk factors for, nontraumatic fractures is classified as category 3. Otherwise, DMPA use for women with rheumatoid arthritis is classified as category 2. **Evidence:** Limited evidence shows no consistent pattern of improvement or worsening of rheumatoid arthritis with use of oral contraceptives, progesterone, or estrogen (*102*).
b. Not receiving immunosuppressive therapy	1	2		1	**Evidence:** Limited evidence shows no consistent pattern of improvement or worsening of rheumatoid arthritis with use of oral contraceptives, progesterone, or estrogen (*102*).
Neurologic Conditions					
Headaches					
a. Nonmigraine (mild or severe)	1	1		1	—
b. Migraine					**Evidence:** No studies directly examined the risk for stroke among women with migraine using POCs (*103*). Limited evidence demonstrated that women using POPs, DMPA, or implants do not have an increased risk for ischemic stroke compared with nonusers (*104*).
i. Without aura (This category of migraine includes menstrual migraine.)	1	1		1	
ii. With aura	1	1		1	**Comment:** Menstrual migraine is a subtype of migraine without aura. For more information, see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf).
Epilepsy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1		1	**Clarification:** If a woman is taking anticonvulsants, see Drug Interactions section. Certain anticonvulsants lower POC effectiveness.
Multiple sclerosis					**Evidence:** Limited evidence suggests that use of COCs or oral contraceptives (type not specified) among women with multiple sclerosis does not worsen the clinical course of disease (*105*). **Comment:** Women with multiple sclerosis might have compromised bone health from disease-related disability, immobility, and use of corticosteroids. Use of DMPA, which has been associated with small changes in BMD, might be of concern.
a. With prolonged immobility	1	2		1	
b. Without prolonged immobility	1	2		1	
Depressive Disorders					
Depressive disorders	1	1		1	**Clarification:** If a woman is taking psychotropic medications or St. John's wort, see Drug Interactions section. **Evidence:** The frequency of psychiatric hospitalizations for women with bipolar disorder or depression did not significantly differ among women using DMPA, LNG-IUD, Cu-IUD, or sterilization (*106*).
Reproductive Tract Infections and Disorders					
Vaginal bleeding patterns					
a. Irregular pattern without heavy bleeding	2	2		2	**Comment:** Irregular menstrual bleeding patterns are common among healthy women. POC use frequently induces an irregular bleeding pattern. Implant use might induce irregular bleeding patterns, especially during the first 3–6 months, although these patterns might persist longer.
b. Heavy or prolonged bleeding (includes regular and irregular patterns)	2	2		2	**Clarification:** Unusually heavy bleeding should raise the suspicion of a serious underlying condition.

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Unexplained vaginal bleeding (suspicious for serious condition) before evaluation	3	3	2	**Clarification:** If pregnancy or an underlying pathological condition (e.g., pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation. **Comment:** POCs might cause irregular bleeding patterns, which might mask symptoms of underlying pathologic conditions. The effects of DMPA might persist for some time after discontinuation.
Endometriosis	1	1	1	—
Benign ovarian tumors (including cysts)	1	1	1	—
Severe dysmenorrhea	1	1	1	—
Gestational trophoblastic disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.
a. Suspected gestational trophoblastic disease (immediate postevacuation)				
i. Uterine size first trimester	1	1	1	
ii. Uterine size second trimester	1	1	1	
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)				
i. Undetectable/nonpregnant β–hCG levels	1	1	1	
ii. Decreasing β–hCG levels	1	1	1	
iii. Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	1	1	1	
iv. Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	1	1	1	
Cervical ectropion	1	1	1	—
Cervical intraepithelial neoplasia	2	2	1	**Evidence:** Among women with persistent human papillomavirus infection, long-term DMPA use (≥5 years) might increase the risk for carcinoma in situ and invasive carcinoma (*107*).
Cervical cancer (awaiting treatment)	2	2	1	**Comment:** Theoretical concern exists that POC use might affect prognosis of the existing disease. While awaiting treatment, women may use POCs. In general, treatment of this condition can render a woman sterile.
Breast disease Breast cancer is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Undiagnosed mass	2	2	2	**Clarification:** Evaluation should be pursued as early as possible.
b. Benign breast disease	1	1	1	—
c. Family history of cancer	1	1	1	—
d. Breast cancer				**Comment:** Breast cancer is a hormonally sensitive tumor, and the prognosis for women with current or recent breast cancer might worsen with POC use.
i. Current	4	4	4	
ii. Past and no evidence of current disease for 5 years	3	3	3	
Endometrial hyperplasia	1	1	1	—
Endometrial cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	**Comment:** While awaiting treatment, women may use POCs. In general, treatment of this condition renders a woman sterile.
Ovarian cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	**Comment:** While awaiting treatment, women may use POCs. In general, treatment of this condition can render a woman sterile.
Uterine fibroids	1	1	1	**Comment:** POCs do not appear to cause growth of uterine fibroids.

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Pelvic inflammatory disease				**Comment:** Whether POCs, like COCs, reduce the risk for PID among women with STDs is unknown; however, they do not protect against HIV or lower genital tract STDs.
a. Past PID				
i. With subsequent pregnancy	1	1	1	
ii. Without subsequent pregnancy	1	1	1	
b. Current PID	1	1	1	
Sexually transmitted diseases				
a. Current purulent cervicitis or chlamydial infection or gonococcal infection	1	1	1	—
b. Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	—
c. Other factors related to STDs	1	1	1	—
HIV				
High risk for HIV	1	1	1	**Clarification (DMPA):** Some studies suggest that women using progestin-only injectable contraception might be at increased risk for HIV acquisition; other studies do not show this association. CDC reviewed all available evidence and agreed that the data were not sufficiently conclusive to change current guidance. However, because of the inconclusive nature of the body of evidence on possible increased risk for HIV acquisition, women using progestin-only injectable contraception should be strongly advised to also always use condoms (male or female) and take other HIV preventive measures. Expansion of contraceptive method mix and further research on the relationship between hormonal contraception and HIV infection are essential. These recommendations will be continually reviewed in light of new evidence. **Evidence:** Overall, evidence does not support an association between oral contraceptives and risk for HIV acquisition, evidence is inconsistent regarding an association between DMPA and increased risk for HIV acquisition, and no studies have suggested an increased risk for HIV acquisition with etonogestrel implants although data are limited (*108*).
HIV infection For women with HIV infection who are not clinically well or not using ARV therapy, this condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	**Clarification:** Drug interactions might exist between hormonal contraceptives and ARV drugs; see Drug Interactions section. **Evidence:** Overall, evidence does not support an association between POC use and progression of HIV. Limited direct evidence on an association between POC use and transmission of HIV to noninfected partners, as well as studies measuring genital viral shedding as a proxy for infectivity, have had mixed results. Studies measuring whether hormonal contraceptive methods affect plasma HIV viral load generally have found no effect (*109–111*).
Other Infections				
Schistosomiasis Schistosomiasis with fibrosis of the liver is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Uncomplicated	1	1	1	**Evidence:** Among women with uncomplicated schistosomiasis, limited evidence showed that DMPA use had no adverse effects on liver function (*112*).
b. Fibrosis of the liver (if severe, see Cirrhosis section)	1	1	1	—
Tuberculosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				**Clarification:** If a woman is taking rifampin, see Drug Interactions section. Rifampin is likely to decrease the effectiveness of some POCs.
a. Nonpelvic	1	1	1	
b. Pelvic	1	1	1	
Malaria	1	1	1	—

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Endocrine Conditions				
Diabetes Insulin-dependent diabetes; diabetes with nephropathy, retinopathy, or neuropathy; diabetes with other vascular disease; or diabetes of >20 years' duration are associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. History of gestational disease	1	1	1	**Evidence:** POCs had no adverse effects on serum lipid levels in women with a history of gestational diabetes in two small studies (*113*,*114*). Limited evidence is inconsistent about the development of noninsulin-dependent diabetes among users of POCs with a history of gestational diabetes (*115*–*118*).
b. Nonvascular disease				**Evidence:** Among women with insulin-dependent or non–insulin-dependent diabetes, limited evidence on use of POCs (POPs, DMPA, and LNG implant) suggests that these methods have little effect on short-term or long-term diabetes control (e.g., glycosylated hemoglobin levels), hemostatic markers, or lipid profile (*119*–*122*).
i. Non-insulin dependent	2	2	2	
ii. Insulin dependent	2	2	2	
c. Nephropathy, retinopathy, or neuropathy	2	3	2	**Comment:** Concern exists about hypoestrogenic effects and reduced HDL levels, particularly among users of DMPA. The effects of DMPA might persist for some time after discontinuation. Some POCs might increase the risk for thrombosis, although this increase is substantially less than with COCs.
d. Other vascular disease or diabetes of >20 years' duration	2	3	2	**Comment:** Concern exists about hypoestrogenic effects and reduced HDL levels, particularly among users of DMPA. The effects of DMPA might persist for some time after discontinuation. Some POCs might increase the risk for thrombosis, although this increase is substantially less than with COCs.
Thyroid disorders				
a. Simple goiter	1	1	1	—
b. Hyperthyroid	1	1	1	—
c. Hypothyroid	1	1	1	—
Gastrointestinal Conditions				
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	1	2	2	**Evidence:** Risk for disease relapse among women with IBD using oral contraceptives (most studies did not specify formulation) did not increase significantly from that for nonusers (*123*). **Comment:** Absorption of POPs among women with IBD might be reduced if the woman has substantial malabsorption caused by severe disease or small bowel surgery. Women with IBD have a higher prevalence of osteoporosis and osteopenia than the general population. Use of DMPA, which has been associated with small changes in BMD, might be of concern.
Gallbladder disease				
a. Symptomatic				
i. Treated by cholecystectomy	2	2	2	—
ii. Medically treated	2	2	2	—
iii. Current	2	2	2	—
b. Asymptomatic	2	2	2	—
History of cholestasis				
a. Pregnancy related	1	1	1	—
b. Past COC related	2	2	2	**Comment:** Theoretical concern exists that a history of COC-related cholestasis might predict subsequent cholestasis with POC use. However, this has not been documented.
Viral hepatitis				
a. Acute or flare	1	1	1	—
b. Carrier	1	1	1	—
c. Chronic	1	1	1	—
Cirrhosis Severe cirrhosis is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Mild (compensated)	1	1	1	—
b. Severe (decompensated)	3	3	3	—

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Liver tumors Hepatocellular adenoma and malignant liver tumors are associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Benign				
i. Focal nodular hyperplasia	2	2	2	**Evidence:** Limited direct evidence suggests that hormonal contraceptive use does not influence either progression or regression of liver lesions among women with focal nodular hyperplasia (*124*).
ii. Hepatocellular adenoma	3	3	3	**Comment:** No evidence is available about hormonal contraceptive use among women with hepatocellular adenoma. COC use in healthy women is associated with development and growth of hepatocellular adenoma; whether other hormonal contraceptives have similar effects is not known.
b. Malignant (hepatoma)	3	3	3	—
Respiratory Conditions				
Cystic fibrosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	2	1	**Clarification:** Persons with cystic fibrosis are at increased risk for diabetes, liver disease, gallbladder disease, and VTE (particularly related to use of central venous catheters) and are frequently prescribed antibiotics. Categories assigned to such conditions in U.S. MEC should be the same for women with cystic fibrosis who have these conditions. For cystic fibrosis, classifications are based on the assumption that no other conditions are present; these classifications must be modified in the presence of such conditions. **Clarification:** Certain drugs to treat cystic fibrosis (e.g., lumacaftor) might reduce effectiveness of hormonal contraceptives, including oral, injectable, transdermal, and implantable contraceptives. **Evidence:** Limited evidence suggests that use of COCs or oral contraceptives (type not specified) among women with cystic fibrosis is not associated with worsening of disease severity. Very limited evidence suggests that cystic fibrosis does not impair the effectiveness of hormonal contraception (*125*). **Comment:** Women with cystic fibrosis have a higher prevalence of osteopenia, osteoporosis, and fragility fractures than the general population. Use of DMPA, which has been associated with small changes in BMD, might be of concern.
Anemias				
Thalassemia	1	1	1	—
Sickle cell disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	**Evidence:** Among women with sickle cell disease, POC use did not have adverse effects on hematologic parameters and, in some studies, was beneficial with respect to clinical symptoms (*126–133*).
Iron deficiency anemia	1	1	1	**Comment:** Changes in the menstrual pattern associated with POC use have little effect on hemoglobin levels.
Solid Organ Transplantation				
Solid organ transplantation This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Complicated: graft failure (acute or chronic), rejection, or cardiac allograft vasculopathy	2	2	2	—
b. Uncomplicated	2	2	2	—

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Drug Interactions				
Antiretroviral therapy				**Comment:** These recommendations generally are for ARV agents used alone. However, most women receiving ARV therapy are using multiple drugs in combination. In general, whether interactions between ARVs and hormonal contraceptives differ when ARVs are given alone or in combination is unknown.
a. Nucleoside reverse transcriptase inhibitors (NRTIs)				
i. Abacavir (ABC)	1	1	1	**Evidence:** NRTIs do not appear to have significant risk for interactions with hormonal contraceptive methods (*134–139*).
ii. Tenofovir (TDF)	1	1	1	
iii. Zidovudine (AZT)	1	1	1	
iv. Lamivudine (3TC)	1	1	1	
v. Didanosine (DDI)	1	1	1	
vi. Emtricitabine (FTC)	1	1	1	
vii. Stavudine (D4T)	1	1	1	
b. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)				
i. Efavirenz (EFV)	2	1	2	**Clarification:** Evidence suggests drug interactions between EFV and certain hormonal contraceptives. These interactions might reduce the effectiveness of the hormonal contraceptive. **Evidence:** One study found that women using etonogestrel implants with EFV had a higher pregnancy rate than women not using ARVs, although confidence intervals overlapped and absolute pregnancy rates were still lower than for other hormonal methods; another study found that etonogestrel levels were decreased and 5% of women had presumptive ovulation while using etonogestrel implants with EFV (*140*,*141*). Three studies of women using LNG implants showed increased pregnancy rates for women using EFV-containing ARV therapy compared with no ARV use, although absolute pregnancy rates were still lower than for other hormonal methods in one study (*141–143*); another study of LNG implant users found no difference in pregnancy rates with EFV compared with no EFV (*144*).No significant effects were found on pregnancy rates, DMPA levels, EFV levels, or HIV disease progression in women using DMPA and EFV compared with DMPA alone (*141*,*144–148*). No significant effects were found on HIV disease progression in women using LNG implants and EFV compared with no ARVs (*143*). No data have assessed effectiveness of contraceptive implants during later years of use when progestin concentrations are lower and risk for failure from drug interactions might be greater.
ii. Etravirine (ETR)	1	1	1	—
iii. Nevirapine (NVP)	1	1	1	**Evidence:** Five studies found no significant increase in pregnancy rates among women using implants and NVP compared with implants alone (*141–144*,*149*). Four studies found no significant increase in pregnancy rates among women using DMPA or other contraceptive injectables and NVP compared with DMPA or other contraceptive injectables alone (*141*,*144*,*147*,*150*). One study found no ovulations or changes in DMPA concentrations (*145*). No effect was found on HIV disease progression with use of NVP and DMPA or LNG implants (*143*,*145*,*147–149*,*151*). No data have assessed effectiveness of contraceptive implants during later years of use when progestin concentrations are lower and risk for failure from drug interactions might be greater.
iv. Rilpivirine (RPV)	1	1	1	—

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
c. Ritonavir-boosted protease inhibitors				
i. Ritonavir-boosted atazanavir (ATV/r)	2	1	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA. **Evidence:** One pharmacokinetic study demonstrated increased progestin concentrations with use of POPs and ATV/r compared with POPs alone (*152*).
ii. Ritonavir-boosted darunavir (DRV/r)	2	1	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.
iii. Ritonavir-boosted fosamprenavir (FPV/r)	2	1	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.
iv. Ritonavir-boosted lopinavir (LPV/r)	1	1	1	**Evidence:** One study demonstrated no pregnancies, no ovulations, no change in LPV/r level, and no change in HIV disease progression in women using DMPA (*153*); another study found a small increase in pregnancy rate in women using DMPA with LPV/r compared with no ARV therapy, however confidence intervals overlapped (*141*). Two studies found no increased risk for pregnancy in women using implants (*141*,*142*). Two studies found contraceptive hormones increased in women using LPV/r with DMPA or etonogestrel implants (*140*,*153*).
v. Ritonavir-boosted saquinavir (SQV/r)	2	1	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.
vi. Ritonavir-boosted tipranavir (TPV/r)	2	1	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.
d. Protease inhibitors without ritonavir				
i. Atazanavir (ATV)	1	1	1	**Comment:** When ATV is administered with Cobicistat, theoretical concern exists for a drug interaction with hormonal contraceptives. Cobicistat is an inhibitor of CYP3A and CYP2D6 and could theoretically increase contraceptive hormone levels. However, its effects on CYP enzymes and drug levels might vary when combined with other ARVs.
ii. Fosamprenavir (FPV)	2	2	2	**Clarification:** Theoretical concern exists that interactions between FPV and hormonal contraceptives leading to decreased levels of FPV might diminish effectiveness of the ARV drug. The drug interaction likely involves CYP3A4 pathways; POCs have less effect on CYP3A4 enzymes than CHCs.
iii. Indinavir (IDV)	1	1	1	—

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
iv. Nelfinavir (NFV)	2	1	2	**Clarification:** Theoretically, drug interactions might occur between certain protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA. Concern exists that interactions between NFV and POCs might decrease NFV levels. **Evidence:** One study found no pregnancies, no ovulations, no change in DMPA concentrations and no change in HIV disease progression with use of DMPA and NFV compared with DMPA alone; NFV concentrations were decreased with concomitant DMPA use (*145*,*147*).
e. CCR5 co-receptor antagonists				
i. Maraviroc (MVC)	1	1	1	
f. HIV integrase strand transfer inhibitors				
i. Raltegravir (RAL)	1	1	1	—
ii. Dolutegravir (DTG)	1	1	1	—
iii. Elvitegravir (EVG)	1	1	1	**Comment:** When EVG is administered with Cobicistat, theoretical concern exists for a drug interaction with hormonal contraceptives. Cobicistat is an inhibitor of CYP3A and CYP2D6 and could theoretically increase contraceptive hormone levels. However, its effects on CYP enzymes and drug levels may vary when combined with other ARVs.
g. Fusion inhibitors				
i. Enfuvirtide	1	1	1	—
Anticonvulsant therapy				—
a. Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, and oxcarbazepine)	2	1	3	**Clarification:** Although the interaction of certain anticonvulsants with POPs and etonogestrel implants is not harmful to women, it is likely to reduce the effectiveness of POPs and etonogestrel implants. Whether increasing the hormone dose of POPs alleviates this concern remains unclear. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. Use of DMPA is a category 1 because its effectiveness is not decreased by use of certain anticonvulsants. **Evidence:** Use of certain anticonvulsants might decrease the effectiveness of POCs (*154*–*156*).
b. Lamotrigine	1	1	1	**Evidence:** No drug interactions have been reported among women with epilepsy receiving lamotrigine and POCs (*157*).
Antimicrobial therapy				
a. Broad-spectrum antibiotics	1	1	1	—
b. Antifungals	1	1	1	—
c. Antiparasitics	1	1	1	—
d. Rifampin or rifabutin therapy	2	1	3	**Clarification:** Although the interaction of rifampin or rifabutin with POPs and etonogestrel implants is not harmful to women, it is likely to reduce the effectiveness of POPs and etonogestrel implants. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. Use of DMPA is a category 1 because its effectiveness is not decreased by use of rifampin or rifabutin. Whether increasing the hormone dose of POPs alleviates this concern remains unclear.

See table footnotes on page 49.

TABLE C1. (*Continued*) Classifications for progestin-only contraceptives, including implants, depot medroxyprogesterone acetate, and progestin-only pills

Condition	Category			Clarifications/Evidence/Comments
	Implants	DMPA	POPs	
Psychotropic medications				**Comment:** For many common psychotropic agents, limited or no theoretical concern exits for clinically significant drug interactions when co-administered with hormonal contraceptives. However, either no or very limited data exist examining potential interactions for these classes of medications.
a. SSRIs	1	1	1	**Evidence:** No evidence specifically examined the use of POCs with SSRIs. Limited clinical and pharmacokinetic data do not demonstrate concern for SSRIs decreasing the effectiveness of oral contraceptives. Limited evidence suggests that for women taking SSRIs, the use of hormonal contraceptives was not associated with differences in effectiveness of the SSRI for treatment or in adverse events when compared with women not taking hormonal contraceptives (*158*).
				Comment: Drugs that are inhibitors of CYP3A4 or CYP2C9 theoretically have the potential to increase levels of contraceptive steroid, which might increase adverse events. Fluvoxamine is an SSRI known to be a moderate inhibitor of both 3A4 and 2C9; however, no clinical or pharmacokinetic studies were identified to explore potential drug-drug interactions.
St. John's wort	2	1	2	**Evidence:** No evidence specifically examined the use of POCs with St John's wort. Although clinical data are limited, studies with pharmacokinetic and pharmacodynamics outcomes raise concern that St. John's wort might decrease effectiveness of hormonal contraceptives, including increased risk for breakthrough bleeding and ovulation and increased metabolism of estrogen and progestin. Any interactions might be dependent on the dose of St John's wort, and the concentration of active ingredients across types of St. John's wort preparations may vary (*159*).
				Comment: Any potential effect on contraceptive effectiveness is likely to be lower with DMPA than with other POCs because of the higher dose of DMPA.

Abbreviations: ARV = antiretroviral; BMD = bone mineral density; BMI = body mass index; COC = combined oral contraceptive; DMPA = depot medroxyprogesterone acetate; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; HDL = high-density lipoprotein; HIV = human immunodeficiency virus; IBD = inflammatory bowel disease; LDL = low-density lipoprotein; LNG = levonorgestrel; NA = not applicable; NET-EN = norethisterone enantate; PE = pulmonary embolism; PID = pelvic inflammatory disease; POC = progestin-only contraceptive; POP = progestin-only pill; SSRI = selective serotonin reuptake inhibitor; STD = sexually transmitted disease; VTE = venous thromboembolism.

References

1. Lanza LL, McQuay LJ, Rothman KJ, et al. Use of depot medroxyprogesterone acetate contraception and incidence of bone fracture. Obstet Gynecol 2013;121:593–600. http://dx.doi.org/10.1097/AOG.0b013e318283d1a1
2. Harel Z, Riggs S, Vaz R, Flanagan P, Harel D, Machan JT. Bone accretion in adolescents using the combined estrogen and progestin transdermal contraceptive method Ortho Evra: a pilot study. J Pediatr Adolesc Gynecol 2010;23:23–31. http://dx.doi.org/10.1016/j.jpag.2009.04.008
3. Kaunitz AM, Miller PD, Rice VM, Ross D, McClung MR. Bone mineral density in women aged 25–35 years receiving depot medroxyprogesterone acetate: recovery following discontinuation. Contraception 2006;74:90–9. http://dx.doi.org/10.1016/j.contraception.2006.03.010
4. Kaunitz AM, Arias R, McClung M. Bone density recovery after depot medroxyprogesterone acetate injectable contraception use. Contraception 2008;77:67–76. http://dx.doi.org/10.1016/j.contraception.2007.10.005
5. Kaunitz AM, Darney PD, Ross D, Wolter KD, Speroff L. Subcutaneous DMPA vs. intramuscular DMPA: a 2-year randomized study of contraceptive efficacy and bone mineral density. Contraception 2009;80:7–17. http://dx.doi.org/10.1016/j.contraception.2009.02.005
6. Lappe JM, Stegman MR, Recker RR. The impact of lifestyle factors on stress fractures in female Army recruits. Osteoporos Int 2001;12:35–42. http://dx.doi.org/10.1007/s001980170155
7. Lara-Torre E, Edwards CP, Perlman S, Hertweck SP. Bone mineral density in adolescent females using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol 2004;17:17–21. http://dx.doi.org/10.1016/j.jpag.2003.11.017
8. Lopez LM, Chen M, Mullins S, Curtis KM, Helmerhorst FM. Steroidal contraceptives and bone fractures in women: evidence from observational studies. Cochrane Database Syst Rev 2012;8:CD009849.
9. Lopez LM, Grimes DA, Schulz KF, Curtis KM. Steroidal contraceptives: effect on bone fractures in women. Cochrane Database Syst Rev 2011;(7):CD006033.
10. Meier C, Brauchli YB, Jick SS, Kraenzlin ME, Meier CR. Use of depot medroxyprogesterone acetate and fracture risk. J Clin Endocrinol Metab 2010;95:4909–16. http://dx.doi.org/10.1210/jc.2010-0032
11. Merki-Feld GS, Neff M, Keller PJ. A 2-year prospective study on the effects of depot medroxyprogesterone acetate on bone mass-response to estrogen and calcium therapy in individual users. Contraception 2003;67:79–86. http://dx.doi.org/10.1016/S0010-7824(02)00460-2
12. Monteiro-Dantas C, Espejo-Arce X, Lui-Filho JF, Fernandes AM, Monteiro I, Bahamondes L. A three-year longitudinal evaluation of the forearm bone density of users of etonogestrel- and levonorgestrel-releasing contraceptive implants. Reprod Health 2007;4:11. http://dx.doi.org/10.1186/1742-4755-4-11
13. Naessen T, Olsson SE, Gudmundson J. Differential effects on bone density of progestogen-only methods for contraception in premenopausal women. Contraception 1995;52:35–9. http://dx.doi.org/10.1016/0010-7824(95)00121-P
14. Sanches L, Marchi NM, Castro S, Juliato CT, Villarroel M, Bahamondes L. Forearm bone mineral density in postmenopausal former users of depot medroxyprogesterone acetate. Contraception 2008;78:365–9. http://dx.doi.org/10.1016/j.contraception.2008.07.013
15. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Injectable hormone contraception and bone density: results from a prospective study. Epidemiology 2002;13:581–7. http://dx.doi.org/10.1097/00001648-200209000-00015

16. Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Change in bone mineral density among adolescent women using and discontinuing depot medroxyprogesterone acetate contraception. Arch Pediatr Adolesc Med 2005;159:139–44. http://dx.doi.org/10.1001/archpedi.159.2.139
17. Segall-Gutierrez P, Agarwal R, Ge M, Lopez C, Hernandez G, Stanczyk FZ. A pilot study examining short-term changes in bone mineral density among class 3 obese users of depot-medroxyprogesterone acetate. Eur J Contracept Reprod Health Care 2013;18:199–205. http://dx.doi.org/10.3109/13625187.2013.774358
18. Tang OS, Tang G, Yip PS, Li B. Further evaluation on long-term depot-medroxyprogesterone acetate use and bone mineral density: a longitudinal cohort study. Contraception 2000;62:161–4. http://dx.doi.org/10.1016/S0010-7824(00)00168-2
19. Vestergaard P, Rejnmark L, Mosekilde L. The effects of depot medroxyprogesterone acetate and intrauterine device use on fracture risk in Danish women. Contraception 2008;78:459–64. http://dx.doi.org/10.1016/j.contraception.2008.07.014
20. Viola AS, Castro S, Marchi NM, Bahamondes MV, Viola CF, Bahamondes L. Long-term assessment of forearm bone mineral density in postmenopausal former users of depot medroxyprogesterone acetate. Contraception 2011;84:122–7. http://dx.doi.org/10.1016/j.contraception.2010.11.007
21. Walsh JS, Eastell R, Peel NF. Depot medroxyprogesterone acetate use after peak bone mass is associated with increased bone turnover but no decrease in bone mineral density. Fertil Steril 2010;93:697–701. http://dx.doi.org/10.1016/j.fertnstert.2008.10.004
22. Wetmore CM, Ichikawa L, LaCroix AZ, Ott SM, Scholes D. Association between caffeine intake and bone mass among young women: potential effect modification by depot medroxyprogesterone acetate use. Osteoporos Int 2008;19:519–27. http://dx.doi.org/10.1007/s00198-007-0473-2
23. Wong AY, Tang LC, Chin RK. Levonorgestrel-releasing intrauterine system (Mirena) and depot medroxyprogesterone acetate (Depoprovera) as long-term maintenance therapy for patients with moderate and severe endometriosis: a randomised controlled trial. Aust N Z J Obstet Gynaecol 2010;50:273–9. http://dx.doi.org/10.1111/j.1479-828X.2010.01152.x
24. Yang KY, Kim YS, Ji YI, Jung MH. Changes in bone mineral density of users of the levonorgestrel-releasing intrauterine system. J Nippon Med Sch 2012;79:190–4. http://dx.doi.org/10.1272/jnms.79.190
25. Zhang MH, Zhang W, Zhang AD, Yang Y, Gai L. Effect of depot medroxyprogesterone acetate on bone mineral density in adolescent women. Chin Med J (Engl) 2013;126:4043–7.
26. Bahamondes MV, Monteiro I, Castro S, Espejo-Arce X, Bahamondes L. Prospective study of the forearm bone mineral density of long-term users of the levonorgestrel-releasing intrauterine system. Hum Reprod 2010;25:1158–64. http://dx.doi.org/10.1093/humrep/deq043
27. Banks E, Berrington A, Casabonne D. Overview of the relationship between use of progestogen-only contraceptives and bone mineral density. BJOG 2001;108:1214–21. http://dx.doi.org/10.1111/j.1471-0528.2001.00296.x
28. Beerthuizen R, van Beek A, Massai R, Mäkäräinen L, Hout J, Bennink HC. Bone mineral density during long-term use of the progestagen contraceptive implant Implanon compared to a non-hormonal method of contraception. Hum Reprod 2000;15:118–22. http://dx.doi.org/10.1093/humrep/15.1.118
29. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM. Bone mineral density in adolescents using norethisterone enanthate, depot-medroxyprogesterone acetate or combined oral contraceptives for contraception. Contraception 2007;75:438–43. http://dx.doi.org/10.1016/j.contraception.2007.02.001
30. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM. Bone mineral density in a cohort of adolescents during use of norethisterone enanthate, depot-medroxyprogesterone acetate or combined oral contraceptives and after discontinuation of norethisterone enanthate. Contraception 2009;79:345–9. http://dx.doi.org/10.1016/j.contraception.2008.11.009
31. Berenson AB, Breitkopf CR, Grady JJ, Rickert VI, Thomas A. Effects of hormonal contraception on bone mineral density after 24 months of use. Obstet Gynecol 2004;103:899–906. http://dx.doi.org/10.1097/01.AOG.0000117082.49490.d5
32. Berenson AB, Rahman M, Breitkopf CR, Bi LX. Effects of depot medroxyprogesterone acetate and 20-microgram oral contraceptives on bone mineral density. Obstet Gynecol 2008;112:788–99. http://dx.doi.org/10.1097/AOG.0b013e3181875b78
33. Busen NH, Britt RB, Rianon N. Bone mineral density in a cohort of adolescent women using depot medroxyprogesterone acetate for one to two years. J Adolesc Health 2003;32:257–9. http://dx.doi.org/10.1016/S1054-139X(02)00567-0
34. Caird LE, Reid-Thomas V, Hannan WJ, Gow S, Glasier AF. Oral progestogen-only contraception may protect against loss of bone mass in breast-feeding women. Clin Endocrinol (Oxf) 1994;41:739–45. http://dx.doi.org/10.1111/j.1365-2265.1994.tb02788.x
35. Clark MK, Sowers M, Levy B, Nichols S. Bone mineral density loss and recovery during 48 months in first-time users of depot medroxyprogesterone acetate. Fertil Steril 2006;86:1466–74. http://dx.doi.org/10.1016/j.fertnstert.2006.05.024
36. Cromer BA, Lazebnik R, Rome E, et al. Double-blinded randomized controlled trial of estrogen supplementation in adolescent girls who receive depot medroxyprogesterone acetate for contraception. Am J Obstet Gynecol 2005;192:42–7. http://dx.doi.org/10.1016/j.ajog.2004.07.041
37. Cromer BA, Blair JM, Mahan JD, Zibners L, Naumovski Z. A prospective comparison of bone density in adolescent girls receiving depot medroxyprogesterone acetate (Depo-Provera), levonorgestrel (Norplant), or oral contraceptives. J Pediatr 1996;129:671–6. http://dx.doi.org/10.1016/S0022-3476(96)70148-8
38. Cromer BA, Bonny AE, Stager M, et al. Bone mineral density in adolescent females using injectable or oral contraceptives: a 24-month prospective study. Fertil Steril 2008;90:2060–7. http://dx.doi.org/10.1016/j.fertnstert.2007.10.070
39. Cromer BA, Stager M, Bonny A, et al. Depot medroxyprogesterone acetate, oral contraceptives and bone mineral density in a cohort of adolescent girls. J Adolesc Health 2004;35:434–41. http://dx.doi.org/10.1016/j.jadohealth.2004.07.005
40. Cundy T, Ames R, Horne A, et al. A randomized controlled trial of estrogen replacement therapy in long-term users of depot medroxyprogesterone acetate. J Clin Endocrinol Metab 2003;88:78–81. http://dx.doi.org/10.1210/jc.2002-020874
41. Cundy T, Cornish J, Evans MC, Roberts H, Reid IR. Recovery of bone density in women who stop using medroxyprogesterone acetate. BMJ 1994;308:247–8. http://dx.doi.org/10.1136/bmj.308.6923.247
42. Cundy T, Cornish J, Roberts H, Reid IR. Menopausal bone loss in long-term users of depot medroxyprogesterone acetate contraception. Am J Obstet Gynecol 2002;186:978–83. http://dx.doi.org/10.1067/mob.2002.122420
43. Di X, Li Y, Zhang C, Jiang J, Gu S. Effects of levonorgestrel-releasing subdermal contraceptive implants on bone density and bone metabolism. Contraception 1999;60:161–6. http://dx.doi.org/10.1016/S0010-7824(99)00080-3
44. Díaz S, Reyes MV, Zepeda A, et al. Norplant® implants and progesterone vaginal rings do not affect maternal bone turnover and density during lactation and after weaning. Hum Reprod 1999;14:2499–505. http://dx.doi.org/10.1093/humrep/14.10.2499
45. Gai L, Zhang J, Zhang H, Gai P, Zhou L, Liu Y. The effect of depot medroxyprogesterone acetate (DMPA) on bone mineral density (BMD) and evaluating changes in BMD after discontinuation of DMPA in Chinese women of reproductive age. Contraception 2011;83:218–22. http://dx.doi.org/10.1016/j.contraception.2010.07.027
46. Bahamondes L, Espejo-Arce X, Hidalgo MM, Hidalgo-Regina C, Teatin-Juliato C, Petta CA. A cross-sectional study of the forearm bone density of long-term users of levonorgestrel-releasing intrauterine system. Hum Reprod 2006;21:1316–9. http://dx.doi.org/10.1093/humrep/dei457
47. Bahamondes L, Monteiro-Dantas C, Espejo-Arce X, et al. A prospective study of the forearm bone density of users of etonorgestrel- and levonorgestrel-releasing contraceptive implants. Hum Reprod 2006;21:466–70. http://dx.doi.org/10.1093/humrep/dei358

48. Pitts SA, Feldman HA, Dorale A, Gordon CM. Bone mineral density, fracture, and vitamin D in adolescents and young women using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol 2012;25:23–6. http://dx.doi.org/10.1016/j.jpag.2011.07.014
49. US Department of Health and Human Services. Healthy people 2020: maternal, infant, and child health objectives. Washington, DC: US Department of Health and Human Services; 2015. http://www.healthypeople.gov/2020/topics-objectives/topic/maternal-infant-and-child-health/objectives
50. Braga GC, Ferriolli E, Quintana SM, Ferriani RA, Pfrimer K, Vieira CS. Immediate postpartum initiation of etonogestrel-releasing implant: a randomized controlled trial on breastfeeding impact. Contraception 2015;92:536–42. http://dx.doi.org/10.1016/j.contraception.2015.07.009
51. Phillips SJ, Tepper NK, Kapp N, Nanda K, Temmerman M, Curtis KM. Progestogen-only contraceptive use among breastfeeding women: a systematic review. Contraception 2015;S0010-7824(15)00585-5.
52. Kurunmäki H. Contraception with levonorgestrel-releasing subdermal capsules, Norplant, after pregnancy termination. Contraception 1983;27:473–82. http://dx.doi.org/10.1016/0010-7824(83)90044-6
53. Kurunmäki H, Toivonen J, Lähteenmäki PL, Luukkainen T. Immediate postabortal contraception with Norplant: levonorgestrel, gonadotropin, estradiol, and progesterone levels over two postabortal months and return of fertility after removal of Norplant capsules. Contraception 1984;30:431–42. http://dx.doi.org/10.1016/0010-7824(84)90035-0.
54. Lähteenmäki P, Toivonen J, Lähteenmäki PL. Postabortal contraception with norethisterone enanthate injections. Contraception 1983;27:553–62 http://dx.doi.org/10.1016/0010-7824(83)90020-3
55. Ortayli N, Bulut A, Sahin T, Sivin I. Immediate postabortal contraception with the levonorgestrel intrauterine device, Norplant, and traditional methods. Contraception 2001;63:309–14. http://dx.doi.org/10.1016/S0010-7824(01)00212-8
56. Beksinska ME, Smit JA, Kleinschmidt I, Milford C, Farley TM. Prospective study of weight change in new adolescent users of DMPA, NET-EN, COCs, nonusers and discontinuers of hormonal contraception. Contraception 2010;81:30–4. http://dx.doi.org/10.1016/j.contraception.2009.07.007
57. Bender NM, Segall-Gutierrez P, Najera SO, Stanczyk FZ, Montoro M, Mishell DR Jr. Effects of progestin-only long-acting contraception on metabolic markers in obese women. Contraception 2013;88:418–25. http://dx.doi.org/10.1016/j.contraception.2012.12.007
58. Berenson AB, Rahman M. Changes in weight, total fat, percent body fat, and central-to-peripheral fat ratio associated with injectable and oral contraceptive use. Am J Obstet Gynecol 2009;200:329.e1–8. http://dx.doi.org/10.1016/j.ajog.2008.12.052
59. Bonny AE, Secic M, Cromer B. Early weight gain related to later weight gain in adolescents on depot medroxyprogesterone acetate. Obstet Gynecol 2011;117:793–7. http://dx.doi.org/10.1097/AOG.0b013e31820f387c.
60. Bonny AE, Ziegler J, Harvey R, Debanne SM, Secic M, Cromer BA. Weight gain in obese and nonobese adolescent girls initiating depot medroxyprogesterone, oral contraceptive pills, or no hormonal contraceptive method. Arch Pediatr Adolesc Med 2006;160:40–5 http://dx.doi.org/10.1001/archpedi.160.1.40
61. Clark MK, Dillon JS, Sowers M, Nichols S. Weight, fat mass, and central distribution of fat increase when women use depot-medroxyprogesterone acetate for contraception. Int J Obes 2005;29:1252–8. http://dx.doi.org/10.1038/sj.ijo.0803023
62. Gerlach LS, Saldaña SN, Wang Y, Nick TG, Spigarelli MG. Retrospective review of the relationship between weight change and demographic factors following initial depot medroxyprogesterone acetate injection in adolescents. Clin Ther 2011;33:182–7. http://dx.doi.org/10.1016/j.clinthera.2011.02.008
63. Jain J, Jakimiuk AJ, Bode FR, Ross D, Kaunitz AM. Contraceptive efficacy and safety of DMPA-SC. Contraception 2004;70:269–75. http://dx.doi.org/10.1016/j.contraception.2004.06.011
64. Kozlowski KJ, Rickert VI, Hendon A, Davis P. Adolescents and Norplant: preliminary findings of side effects. J Adolesc Health 1995;16:373–8. http://dx.doi.org/10.1016/S1054-139X(94)00029-E
65. Le YC, Rahman M, Berenson AB. Early weight gain predicting later weight gain among depot medroxyprogesterone acetate users. Obstet Gynecol 2009;114:279–84. http://dx.doi.org/10.1097/AOG.0b013e3181af68b2
66. Leiman G. Depo-medroxyprogesterone acetate as a contraceptive agent: its effect on weight and blood pressure. Am J Obstet Gynecol 1972;114:97–102. http://dx.doi.org/10.1016/0002-9378(72)90296-7.
67. Lopez LM, Grimes DA, Chen M, et al. Hormonal contraceptives for contraception in overweight or obese women. Cochrane Database Syst Rev 2013;4:CD008452.
68. Mangan SA, Larsen PG, Hudson S. Overweight teens at increased risk for weight gain while using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol 2002;15:79–82. http://dx.doi.org/10.1016/S1083-3188(01)00147-4
69. Nyirati CM, Habash DL, Shaffer LE. Weight and body fat changes in postpartum depot-medroxyprogesterone acetate users. Contraception 2013;88:169–76. http://dx.doi.org/10.1016/j.contraception.2012.10.016
70. Pantoja M, Medeiros T, Baccarin MC, Morais SS, Bahamondes L, Fernandes AM. Variations in body mass index of users of depot-medroxyprogesterone acetate as a contraceptive. Contraception 2010;81:107–11. http://dx.doi.org/10.1016/j.contraception.2009.07.008
71. Risser WL, Gefter LR, Barratt MS, Risser JM. Weight change in adolescents who used hormonal contraception. J Adolesc Health 1999;24:433–6. http://dx.doi.org/10.1016/S1054-139X(98)00151-7
72. Segall-Gutierrez P, Xiang AH, Watanabe RM, et al. Deterioration in cardiometabolic risk markers in obese women during depot medroxyprogesterone acetate use. Contraception 2012;85:36–41. http://dx.doi.org/10.1016/j.contraception.2011.04.016
73. Westhoff C, Jain JK, Milsom I, Ray A. Changes in weight with depot medroxyprogesterone acetate subcutaneous injection 104 mg/0.65 mL. Contraception 2007;75:261–7. http://dx.doi.org/10.1016/j.contraception.2006.12.009
74. Paulen ME, Zapata LB, Cansino C, Curtis KM, Jamieson DJ. Contraceptive use among women with a history of bariatric surgery: a systematic review. Contraception 2010;82:86–94. http://dx.doi.org/10.1016/j.contraception.2010.02.008
75. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. Contraception 1998;57:315–24 http://dx.doi.org/10.1016/S0010-7824(98)00041-9
76. Heinemann LA, Assmann A, DoMinh T, Garbe E. Oral progestogen-only contraceptives and cardiovascular risk: results from the Transnational Study on Oral Contraceptives and the Health of Young Women. Eur J Contracept Reprod Health Care 1999;4:67–73. http://dx.doi.org/10.3109/13625189909064007
77. Vasilakis C, Jick H, del Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestagens alone. Lancet 1999;354:1610–1. http://dx.doi.org/10.1016/S0140-6736(99)04394-9
78. Sönmezer M, Atabekoğlu C, Cengiz B, Dökmeci F, Cengiz SD. Depot-medroxyprogesterone acetate in anticoagulated patients with previous hemorrhagic corpus luteum. Eur J Contracept Reprod Health Care 2005;10:9–14. http://dx.doi.org/10.1080/13625180400020952
79. Tepper NK, Paulen ME, Marchbanks PA, Curtis KM. Safety of contraceptive use among women with peripartum cardiomyopathy: a systematic review. Contraception 2010;82:95–101. http://dx.doi.org/10.1016/j.contraception.2010.02.004
80. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Little, Brown and Co; 1994.
81. Bernatsky S, Clarke A, Ramsey-Goldman R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford) 2004;43:1178–81. http://dx.doi.org/10.1093/rheumatology/keh282

82. Bernatsky S, Ramsey-Goldman R, Gordon C, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford) 2004;43:1386–9. http://dx.doi.org/10.1093/rheumatology/keh331
83. Chopra N, Koren S, Greer WL, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. J Rheumatol 2002;29:1683–8.
84. Esdaile JM, Abrahamowicz M, Grodzicky T, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum 2001;44:2331–7. http://dx.doi.org/10.1002/1529-0131(200110)44:10<2331::AID-ART395≥3.0.CO;2-I
85. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scand J Rheumatol 1991;20:427–33. http://dx.doi.org/10.3109/03009749109096822
86. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. Br J Rheumatol 1993;32:227–30. http://dx.doi.org/10.1093/rheumatology/32.3.227
87. Jungers P, Dougados M, Pélissier C, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis Rheum 1982;25:618–23. http://dx.doi.org/10.1002/art.1780250603
88. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol 1997;145:408–15. http://dx.doi.org/10.1093/oxfordjournals.aje.a009122
89. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephritis in systemic lupus erythematosus. Ann Rheum Dis 1993;52:720–4. http://dx.doi.org/10.1136/ard.52.10.720
90. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Ann Rheum Dis 1992;51:56–60. http://dx.doi.org/10.1136/ard.51.1.56
91. Mintz G, Gutiérrez G, Delezé M, Rodríguez E. Contraception with progestagens in systemic lupus erythematosus. Contraception 1984;30:29–38. http://dx.doi.org/10.1016/0010-7824(84)90076-3
92. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res 1995;8:137–45. http://dx.doi.org/10.1002/art.1790080305
93. Petri M. Lupus in Baltimore: evidence-based 'clinical pearls' from the Hopkins Lupus Cohort. Lupus 2005;14:970–3. http://dx.doi.org/10.1191/0961203305lu2230xx
94. Petri M, Kim MY, Kalunian KC, et al; OC-SELENA Trial. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med 2005;353:2550–8. http://dx.doi.org/10.1056/NEJMoa051135
95. Sánchez-Guerrero J, Uribe AG, Jiménez-Santana L, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. N Engl J Med 2005;353:2539–49. http://dx.doi.org/10.1056/NEJMoa050817
96. Sarabi ZS, Chang E, Bobba R, et al. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Rheum 2005;53:609–12. http://dx.doi.org/10.1002/art.21314
97. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. Am J Obstet Gynecol 2005;193:1361–3. http://dx.doi.org/10.1016/j.ajog.2005.05.002
98. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. J Rheumatol 2002;29:2531–6.
99. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, Ogryzlo MA. The bimodal mortality pattern of systemic lupus erythematosus. Am J Med 1976;60:221–5. http://dx.doi.org/10.1016/0002-9343(76)90431-9
100. Choojitarom K, Verasertniyom O, Totemchokchyakarn K, Nantiruj K, Sumethkul V, Janwityanujit S. Lupus nephritis and Raynaud's phenomenon are significant risk factors for vascular thrombosis in SLE patients with positive antiphospholipid antibodies. Clin Rheumatol 2008;27:345–51. http://dx.doi.org/10.1007/s10067-007-0721-z
101. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus—a meta-analysis. Lupus 1997;6:467–73. http://dx.doi.org/10.1177/096120339700600510
102. Farr SL, Folger SG, Paulen ME, Curtis KM. Safety of contraceptive methods for women with rheumatoid arthritis: a systematic review. Contraception 2010;82:64–71. http://dx.doi.org/10.1016/j.contraception.2010.02.003
103. Tepper NK, Whiteman MK, Zapata LB, Marchbanks PA, Curtis KM. Safety of hormonal contraceptives among women with migraine: a systematic review. Contraception 2016. Epub May 3, 2016. http://dx.doi.org/10.1016/j.contraception.2016.04.016
104. Tepper NK, Whiteman MK, Marchbanks PA, James AH, Curtis KM. Progestin-only contraception and thromboembolism: a systematic review. Contraception 2016. Epub May 3, 2016. http://dx.doi.org/10.1016/j.contraception.2016.04.014
105. Zapata LB, Oduyebo T, Whiteman MK, Marchbanks PA, Curtis KM. Contraceptive use among women with multiple sclerosis: a systematic review. Contraception. In press 2016.
106. Pagano HP, Zapata LB, Berry-Bibee EN, Nanda K, Curtis KM. Safety of hormonal contraception and intrauterine devices among women with depressive and bipolar disorders: a systematic review. Contraception 2016. Epub June 27, 2016. http://dx.doi.org/10.1016/j.contraception.2016.06.012
107. Smith JS, Green J, Berrington de Gonzalez A, et al. Cervical cancer and use of hormonal contraceptives: a systematic review. Lancet 2003;361:1159–67. http://dx.doi.org/10.1016/S0140-6736(03)12949-2.
108. Polis CB, Phillips SJ, Curtis KM, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. Contraception 2014;90:360–90 http://dx.doi.org/10.1016/j.contraception.2014.07.009
109. Phillips SJ, Curtis KM, Polis CB. Effect of hormonal contraceptive methods on HIV disease progression: a systematic review. AIDS 2013;27:787–94. http://dx.doi.org/10.1097/QAD.0b013e32835bb672
110. Polis CB, Phillips SJ, Curtis KM. Hormonal contraceptive use and female-to-male HIV transmission: a systematic review of the epidemiologic evidence. AIDS 2013;27:493–505. http://dx.doi.org/10.1097/QAD.0b013e32835ad539
111. Phillips SJ, Polis CB, Curtis KM. The safety of hormonal contraceptives for women living with HIV and their sexual partners. Contraception 2016;93:11–6 http://dx.doi.org/10.1016/j.contraception.2015.10.002.
112. Tagy AH, Saker ME, Moussa AA, Kolgah A. The effect of low-dose combined oral contraceptive pills versus injectable contraceptive (Depot Provera) on liver function tests of women with compensated bilharzial liver fibrosis. Contraception 2001;64:173–6. http://dx.doi.org/10.1016/S0010-7824(01)00248-7
113. Pyörälä T, Vähäpassi J, Huhtala M. The effect of lynestrenol and norethindrone on the carbohydrate and lipid metabolism in subjects with gestational diabetes. Ann Chir Gynaecol 1979;68:69–74.
114. Rådberg T, Gustafson A, Skryten A, Karlsson K. Metabolic studies in gestational diabetic women during contraceptive treatment: effects on glucose tolerance and fatty acid composition of serum lipids. Gynecol Obstet Invest 1982;13:17–29. http://dx.doi.org/10.1159/000299480

115. Kjos SL, Peters RK, Xiang A, Thomas D, Schaefer U, Buchanan TA. Contraception and the risk of type 2 diabetes mellitus in Latina women with prior gestational diabetes mellitus. JAMA 1998;280:533–8. http://dx.doi.org/10.1001/jama.280.6.533
116. Nelson AL, Le MH, Musherraf Z, Vanberckelaer A. Intermediate-term glucose tolerance in women with a history of gestational diabetes: natural history and potential associations with breastfeeding and contraception. Am J Obstet Gynecol 2008;198:699.e1–8.
117. Xiang AH, Kawakubo M, Buchanan TA, Kjos SL. A longitudinal study of lipids and blood pressure in relation to method of contraception in Latino women with prior gestational diabetes mellitus. Diabetes Care 2007;30:1952–8. http://dx.doi.org/10.2337/dc07-0180
118. Xiang AH, Kawakubo M, Kjos SL, Buchanan TA. Long-acting injectable progestin contraception and risk of type 2 diabetes in Latino women with prior gestational diabetes mellitus. Diabetes Care 2006;29:613–7. http://dx.doi.org/10.2337/diacare.29.03.06.dc05-1940
119. Diab KM, Zaki MM. Contraception in diabetic women: comparative metabolic study of Norplant, depot medroxyprogesterone acetate, low dose oral contraceptive pill and CuT380A. J Obstet Gynaecol Res 2000;26:17–26. http://dx.doi.org/10.1111/j.1447-0756.2000.tb01195.x
120. Lunt H, Brown LJ. Self-reported changes in capillary glucose and insulin requirements during the menstrual cycle. Diabet Med 1996;13:525–30. http://dx.doi.org/10.1002/(SICI)1096-9136(199606)13:6<525::AID-DIA123≥3.0.CO;2-D
121. Rådberg T, Gustafson A, Skryten A, Karlsson K. Oral contraception in diabetic women. A cross-over study on serum and high density lipoprotein (HDL) lipids and diabetes control during progestogen and combined estrogen/progestogen contraception. Horm Metab Res 1982;14:61–5.
122. Skouby SO, Mølsted-Pedersen L, Kühl C, Bennet P. Oral contraceptives in diabetic women: metabolic effects of four compounds with different estrogen/progestogen profiles. Fertil Steril 1986;46:858–64 http://dx.doi.org/10.1016/S0015-0282(16)49825-0.
123. Zapata LB, Paulen ME, Cansino C, Marchbanks PA, Curtis KM. Contraceptive use among women with inflammatory bowel disease: a systematic review. Contraception 2010;82:72–85. http://dx.doi.org/10.1016/j.contraception.2010.02.012
124. Kapp N, Curtis KM. Hormonal contraceptive use among women with liver tumors: a systematic review. Contraception 2009;80:387–90. http://dx.doi.org/10.1016/j.contraception.2009.01.021
125. Whiteman MK, Oduyebo T, Zapata LB, Walker S, Curtis KM. Contraceptive safety among women with cystic fibrosis: a systematic review. Contraception 2016. Epub June 7, 2016. http://dx.doi.org/10.1016/j.contraception.2016.05.016
126. Adadevoh BK, Isaacs WA. The effect of megestrol acetate on sickling. Am J Med Sci 1973;265:367–70. http://dx.doi.org/10.1097/00000441-197305000-00002
127. Barbosa IC, Ladipo OA, Nascimento ML, et al. Carbohydrate metabolism in sickle cell patients using a subdermal implant containing nomegestrol acetate (Uniplant). Contraception 2001;63:263–5. http://dx.doi.org/10.1016/S0010-7824(01)00202-5
128. de Abood M, de Castillo Z, Guerrero F, Espino M, Austin KL. Effect of Depo-Provera or Microgynon on the painful crises of sickle cell anemia patients. Contraception 1997;56:313–6. http://dx.doi.org/10.1016/S0010-7824(97)00156-X
129. De Ceulaer K, Hayes R, Gruber C, Serjeant GR. Medroxyprogesterone acetate and homozygous sickle-cell disease. Lancet 1982;320:229–31. http://dx.doi.org/10.1016/S0140-6736(82)90320-8
130. Howard RJ, Lillis C, Tuck SM. Contraceptives, counselling, and pregnancy in women with sickle cell disease. BMJ 1993;306:1735–7. http://dx.doi.org/10.1136/bmj.306.6894.1735
131. Ladipo OA, Falusi AG, Feldblum PJ, Osotimehin BO, Otolorin EO, Ojengbede OA. Norplant use by women with sickle cell disease. Int J Gynaecol Obstet 1993;41:85–7. http://dx.doi.org/10.1016/0020-7292(93)90159-T
132. Nascimento ML, Ladipo OA, Coutinho EM. Nomegestrol acetate contraceptive implant use by women with sickle cell disease. Clin Pharmacol Ther 1998;64:433–8. http://dx.doi.org/10.1016/S0009-9236(98)90074-1
133. Yoong WC, Tuck SM, Yardumian A. Red cell deformability in oral contraceptive pill users with sickle cell anaemia. Br J Haematol 1999;104:868–70. http://dx.doi.org/10.1046/j.1365-2141.1999.01255.x
134. Aweeka FT, Rosenkranz SL, Segal Y, et al; NIAID AIDS Clinical Trials Group. The impact of sex and contraceptive therapy on the plasma and intracellular pharmacokinetics of zidovudine. AIDS 2006;20:1833–41. http://dx.doi.org/10.1097/01.aids.0000244202.18629.36
135. Kearney BP, Mathias A. Lack of effect of tenofovir disoproxil fumarate on pharmacokinetics of hormonal contraceptives. Pharmacotherapy 2009;29:924–9. http://dx.doi.org/10.1592/phco.29.8.924
136. Todd CS, Deese J, Wang M, et al; FEM-PrEP Study Group. Sino-implant (II)® continuation and effect of concomitant tenofovir disoproxil fumarate-emtricitabine use on plasma levonorgestrel concentrations among women in Bondo, Kenya. Contraception 2015;91:248–52. http://dx.doi.org/10.1016/j.contraception.2014.10.008
137. Murnane PM, Heffron R, Ronald A, et al; Partners PrEP Study Team. Pre-exposure prophylaxis for HIV-1 prevention does not diminish the pregnancy prevention effectiveness of hormonal contraception. AIDS 2014;28:1825–30. http://dx.doi.org/10.1097/QAD.0000000000000290
138. Kasonde M, Niska RW, Rose C, et al. Bone mineral density changes among HIV-uninfected young adults in a randomised trial of pre-exposure prophylaxis with tenofovir-emtricitabine or placebo in Botswana. PLoS One 2014;9:e90111. http://dx.doi.org/10.1371/journal.pone.0090111
139. Callahan R, Nanda K, Kapiga S, et al; FEM-PrEP Study Group. Pregnancy and contraceptive use among women participating in the FEM-PrEP trial. J Acquir Immune Defic Syndr 2015;68:196–203. http://dx.doi.org/10.1097/QAI.0000000000000413
140. Vieira CS, Bahamondes MV, de Souza RM, et al. Effect of antiretroviral therapy including lopinavir/ritonavir or efavirenz on etonogestrel-releasing implant pharmacokinetics in HIV-positive women. J Acquir Immune Defic Syndr 2014;66:378–85. http://dx.doi.org/10.1097/QAI.0000000000000189
141. Patel RC, Onono M, Gandhi M, et al. Pregnancy rates in HIV-positive women using contraceptives and efavirenz-based or nevirapine-based antiretroviral therapy in Kenya: a retrospective cohort study. Lancet HIV 2015;2:e474–82. http://dx.doi.org/10.1016/S2352-3018(15)00184-8
142. Perry SH, Swamy P, Preidis GA, Mwanyumba A, Motsa N, Sarero HN. Implementing the Jadelle implant for women living with HIV in a resource-limited setting: concerns for drug interactions leading to unintended pregnancies. AIDS 2014;28:791–3. http://dx.doi.org/10.1097/QAD.0000000000000177
143. Scarsi KK, Darin KM, Nakalema S, et al. Unintended pregnancies observed with combined use of the levonorgestrel contraceptive implant and efavirenz-based antiretroviral therapy: a three-arm pharmacokinetic evaluation over 48 weeks. Clin Infect Dis 2015;62:675–82. http://dx.doi.org/10.1093/cid/civ1001

144. Pyra M, Heffron R, Mugo NR, et al; Partners in Prevention HSVHIV Transmission Study and Partners PrEP Study Teams. Effectiveness of hormonal contraception in HIV-infected women using antiretroviral therapy. AIDS 2015;29:2353–9. http://dx.doi.org/10.1097/QAD.0000000000000827
145. Cohn SE, Park JG, Watts DH, et al; ACTG A5093 Protocol Team. Depo-medroxyprogesterone in women on antiretroviral therapy: effective contraception and lack of clinically significant interactions. Clin Pharmacol Ther 2007;81:222–7. http://dx.doi.org/10.1038/sj.clpt.6100040
146. Nanda K, Amaral E, Hays M, Viscola MA, Mehta N, Bahamondes L. Pharmacokinetic interactions between depot medroxyprogesterone acetate and combination antiretroviral therapy. Fertil Steril 2008;90:965–71. http://dx.doi.org/10.1016/j.fertnstert.2007.07.1348
147. Watts DH, Park JG, Cohn SE, et al. Safety and tolerability of depot medroxyprogesterone acetate among HIV-infected women on antiretroviral therapy: ACTG A5093. Contraception 2008;77:84–90. http://dx.doi.org/10.1016/j.contraception.2007.10.002
148. Polis CB, Nakigozi G, Ssempijja V, et al. Effect of injectable contraceptive use on response to antiretroviral therapy among women in Rakai, Uganda. Contraception 2012;86:725–30. http://dx.doi.org/10.1016/j.contraception.2012.05.001
149. Hubacher D, Liku J, Kiarie J, et al. Effect of concurrent use of antiretroviral therapy and levonorgestrel sub-dermal implant for contraception on CD4 counts: a prospective cohort study in Kenya. J Int AIDS Soc 2013;16:18448. http://dx.doi.org/10.7448/IAS.16.1.18448
150. Myer L, Carter RJ, Katyal M, Toro P, El-Sadr WM, Abrams EJ. Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: a cohort study. PLoS Med 2010;7:e1000229. http://dx.doi.org/10.1371/journal.pmed.1000229
151. Day S, Graham SM, Masese LN, et al. A prospective cohort study of the effect of depot medroxyprogesterone acetate on detection of plasma and cervical HIV-1 in women initiating and continuing antiretroviral therapy. J Acquir Immune Defic Syndr 2014;66:452–6. http://dx.doi.org/10.1097/QAI.0000000000000187
152. DuBois BN, Atrio J, Stanczyk FZ, Cherala G. Increased exposure of norethindrone in HIV+ women treated with ritonavir-boosted atazanavir therapy. Contraception 2015;91:71–5. http://dx.doi.org/10.1016/j.contraception.2014.08.009
153. Luque AE, Cohn SE, Park JG, et al. Depot medroxyprogesterone acetate in combination with a twice-daily lopinavir-ritonavir-based regimen in HIV-infected women showed effective contraception and a lack of clinically significant interactions, with good safety and tolerability: results of the ACTG 5283 study. Antimicrob Agents Chemother 2015;59:2094–101. http://dx.doi.org/10.1128/AAC.04701-14
154. Odlind V, Olsson SE. Enhanced metabolism of levonorgestrel during phenytoin treatment in a woman with Norplant implants. Contraception 1986;33:257–61. http://dx.doi.org/10.1016/0010-7824(86)90018-1
155. Schindlbeck C, Janni W, Friese K. Failure of Implanon contraception in a patient taking carbamazepin for epilepsia. Arch Gynecol Obstet 2006;273:255–6. http://dx.doi.org/10.1007/s00404-005-0064-4
156. Shane-McWhorter L, Cerveny JD, MacFarlane LL, Osborn C. Enhanced metabolism of levonorgestrel during phenobarbital treatment and resultant pregnancy. Pharmacotherapy 1998;18:1360–4.
157. Reimers A, Helde G, Brodtkorb E. Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Epilepsia 2005;46:1414–7. http://dx.doi.org/10.1111/j.1528-1167.2005.10105.x
158. Berry-Bibee E, Kim MJ, Simmons K, Pagano P, Curtis K. Drug interactions between hormonal contraceptives and psychotropic drugs: a systematic review. Contraception. In press 2016.
159. Berry-Bibee E, Kim MJ, Tepper N, Riley H, Curtis K. The safety of St. John's wort and hormonal contraceptives: a systematic review. Contraception. In press 2016.

Appendix D

Classifications for Combined Hormonal Contraceptives

Combined hormonal contraceptives (CHCs) include low-dose (containing ≤35 μg ethinyl estradiol) combined oral contraceptives (COCs), the combined hormonal patch, and the combined vaginal ring (Box D1) (Table D1). Limited information is available about the safety of the combined hormonal patch and combined vaginal ring among women with specific medical conditions. Evidence indicates that the combined hormonal patch and the combined vaginal ring provide comparable safety and pharmacokinetic profiles to COCs with similar hormone formulations *(1–33)*. Pending further studies, the evidence available for recommendations about COCs applies to the recommendations for the combined hormonal patch and vaginal ring. Therefore, the patch and ring should have the same categories as COCs, except where noted. Therefore, the assigned categories should be considered a preliminary best judgement, which will be reevaluated as new data become available.

BOX D1. Categories for classifying combined hormonal contraceptives

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

COCs, the patch, and the ring do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited

TABLE D1. Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
Personal Characteristics and Reproductive History		
Pregnancy	NA	**Clarification:** Use of CHCs is not required. No known harm to the woman, the course of her pregnancy, or the fetus occurs if CHCs are inadvertently used during pregnancy.
Age		
a. Menarche to <40 years	1	**Evidence:** Evidence is inconsistent about whether CHC use affects fracture risk (*34*–*45*), although three recent studies show no effect (*34*,*35*,*45*). CHC use might decrease BMD in adolescents, especially in those choosing very low-dose formulations (COCs containing <30 μg ethinyl estradiol) (*46*–*59*). CHC use has little to no effect on BMD in premenopausal women (*60*–*74*) and might preserve bone mass in those who are perimenopausal (*75*–*83*). BMD is a surrogate marker for fracture risk that might not be valid for premenopausal women and therefore might not accurately predict current or future (postmenopausal) fracture risk (*84*–*86*).
b. ≥40 years	2	**Comment:** The risk for cardiovascular disease increases with age and might increase with CHC use. In the absence of other adverse clinical conditions, CHCs can be used until menopause.
Parity		
a. Nulliparous	1	—
b. Parous	1	—
Breastfeeding		
a. <21 days postpartum	4	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*87*). **Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs through breast milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk for either serious or subtle long-term effects exists (*88*). **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90*–*94*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications, and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
b. 21 to <30 days postpartum		
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	3	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*87*). **Clarification:** For women with other risk factors for VTE, these risk factors might increase the classification to a category 4. **Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs through breast milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk for either serious or subtle long-term effects exists (*88*). **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90*–*94*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications, and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
ii. Without other risk factors for VTE	3	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*87*). **Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs through breast milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk for either serious or subtle long-term effects exists (*88*). **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90–94*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications, and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
c. 30–42 days postpartum		
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	3	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*87*). **Clarification:** For women with other risk factors for VTE, these risk factors might increase the classification to a category 4. **Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs through breast milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk for either serious or subtle long-term effects exists (*88*). **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90–94*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications, and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
ii. Without other risk factors for VTE	2	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*87*). **Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs through breast milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk for either serious or subtle long-term effects exists (*88*). **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90–94*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications, and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
d. >42 days postpartum	2	**Clarification:** Breastfeeding provides important health benefits for mother and infant. The U.S. Department of Health and Human Services recommends increasing the proportion of infants initially breastfed, exclusively breastfed through 6 months of life, and continuing breastfeeding through at least 1 year of life as key public health goals (*87*). **Evidence:** Clinical studies demonstrate conflicting results regarding effects on breastfeeding continuation or exclusivity in women exposed to COCs during lactation. No consistent effects on infant growth or illness have been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to CHCs through breast milk have not been demonstrated; however, studies have been inadequately designed to determine whether a risk for either serious or subtle long-term effects exists (*88*). **Comment:** Certain women might be at risk for breastfeeding difficulties, such as women with previous breastfeeding difficulties, certain medical conditions, or certain perinatal complications, and those who deliver preterm. For these women, as for all women, discussions about contraception for breastfeeding women should include information about risks, benefits, and alternatives.
Postpartum (nonbreastfeeding women)		
a. <21 days postpartum	4	**Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90–94*). Risk for pregnancy during the first 21 days postpartum is very low but increases after that point; ovulation before first menses is common (*95*).
b. 21–42 days postpartum		
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2 postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	3	**Clarification:** For women with other risk factors for VTE, these risk factors might increase the classification to a category 4. **Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90–94*).
ii. Without other risk factors for VTE	2	**Evidence:** One study examined use of CHCs during the postpartum period and found that VTE rates were higher for CHC users compared with nonusers at all time points postpartum (*89*). Rates were significantly different only after 13 weeks postpartum; however, the numbers needed to harm were lowest in the first 6 weeks postpartum. VTE risk is increased during pregnancy and the postpartum period; this risk is most pronounced in the first 3 weeks after delivery, decreasing to near baseline levels by 42 days postpartum (*90–94*).
c. >42 days postpartum	1	—

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
Postabortion		**Clarification:** CHCs may be started immediately postabortion.
a. First trimester	1	**Evidence:** Women who started taking COCs immediately after first trimester medical or surgical abortion did not experience more side effects or adverse vaginal bleeding outcomes or clinically significant changes in coagulation parameters than did women who used a placebo, an IUD, a nonhormonal contraceptive method, or delayed COC initiation (*96–102*). Limited evidence on women using the ring immediately after first trimester medical or surgical abortion found no serious adverse events and no infection related to use of the combined vaginal ring during 3 cycles of follow-up postabortion (*103*).
b. Second trimester	1	
c. Immediate postseptic abortion	1	
Past ectopic pregnancy	1	**Comment:** The risk for future ectopic pregnancy is increased among women who have had an ectopic pregnancy in the past. CHCs protect against pregnancy in general, including ectopic gestation.
History of pelvic surgery	1	—
Smoking		**Evidence:** COC users who smoked were at increased risk for cardiovascular diseases, especially myocardial infarction, compared with those who did not smoke. Studies also showed an increased risk for myocardial infarction with increasing number of cigarettes smoked per day (*104–116*).
a. Age <35 years	2	
b. Age ≥35 years		
i. <15 cigarettes per day	3	
ii. ≥15 cigarettes per day	4	
Obesity		**Evidence:** Obese women who use COCs are more likely than obese women who do not use COCs to experience VTE. Research examining the interaction between COCs and BMI on VTE risk is limited, particularly for women in the highest BMI categories (BMI ≥35 kg/m^2). Although the absolute risk for VTE in otherwise healthy women of reproductive age is small, obese women are at 2–3 times higher risk for VTE than normal weight women regardless of COC use. Limited evidence suggests that obese women who use COCs do not have a higher risk for acute myocardial infarction or stroke than do obese nonusers (*117*). Limited evidence suggests that effectiveness of some COC formulations might decrease with increasing BMI, however the observed reductions in effectiveness are minimal and evidence is conflicting (*118–125*). Effectiveness of the patch might be reduced in women >90 kg (*126*). Limited evidence suggests obese women are no more likely to gain weight during COC or vaginal ring use than normal weight or overweight women (*117*,*127*).
a. BMI ≥30 kg/m^2	2	
b. Menarche to <18 years and BMI ≥30 kg/m^2	2	
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	1	**Evidence:** Limited evidence demonstrated no substantial decrease in effectiveness of oral contraceptives among women who underwent laparoscopic placement of an adjustable gastric band (*128*).
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	COCs: 3 Patch and ring: 1	**Evidence:** Limited evidence demonstrated no substantial decrease in effectiveness of oral contraceptives among women who underwent a biliopancreatic diversion; however, evidence from pharmacokinetic studies reported conflicting results of oral contraceptive effectiveness among women who underwent a jejunoileal bypass (*128*). **Comment:** Bariatric surgical procedures involving a malabsorptive component have the potential to decrease oral contraceptive effectiveness, perhaps further decreased by postoperative complications, such as long-term diarrhea or vomiting.
Cardiovascular Disease		
Multiple risk factors for atherosclerotic cardiovascular disease (e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	3/4	**Clarification:** When a woman has multiple major risk factors, any of which alone would substantially increase her risk for cardiovascular disease, use of CHCs might increase her risk to an unacceptable level. However, a simple addition of categories for multiple risk factors is not intended; for example, a combination of two category 2 risk factors might not necessarily warrant a higher category. **Clarification:** The recommendations apply to known preexisting medical conditions or characteristics. Few if any screening tests are needed before initiation of contraception. See the *U.S. Selected Practice Recommendations for Contraceptive Use* (http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usspr.htm).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
Hypertension Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg are associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. Adequately controlled hypertension	3	**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors exist for cardiovascular disease. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Clarification:** Women adequately treated for hypertension are at reduced risk for acute myocardial infarction and stroke compared with untreated women. Although no data exist, CHC users with adequately controlled and monitored hypertension should be at reduced risk for acute myocardial infarction and stroke compared with untreated hypertensive CHC users. **Evidence:** Among women with hypertension, COC users were at higher risk than nonusers for stroke, acute myocardial infarction, and peripheral arterial disease (*104*,*106*,*113–116*,*129–143*). Discontinuation of COCs in women with hypertension might improve blood pressure control (*144*).
b. Elevated blood pressure levels (properly taken measurements)		**Clarification:** For all categories of hypertension, classifications are based on the assumption that no other risk factors exist for cardiovascular disease. When multiple risk factors do exist, risk for cardiovascular disease might increase substantially. A single reading of blood pressure level is not sufficient to classify a woman as hypertensive. **Evidence:** Among women with hypertension, COC users were at higher risk than nonusers for stroke, acute myocardial infarction, and peripheral arterial disease (*104*,*106*,*113–116*,*129–143*). Discontinuation of COCs in women with hypertension might improve blood pressure control (*144*).
i. Systolic 140–159 mm Hg or diastolic 90–99 mm Hg	3	
ii. Systolic ≥160 mm Hg or diastolic ≥100 mm Hg	4	
c. Vascular disease	4	
History of high blood pressure during pregnancy (when current blood pressure is measurable and normal)	2	**Evidence:** Women with a history of high blood pressure in pregnancy who also used COCs had a higher risk for myocardial infarction and VTE than did COC users who did not have a history of high blood pressure during pregnancy. The absolute risks for acute myocardial infarction and VTE in this population remained small (*115*,*130*,*142*,*143*,*145–151*).
Deep venous thrombosis/Pulmonary embolism		
a. History of DVT/PE, not receiving anticoagulant therapy		
i. Higher risk for recurrent DVT/PE (one or more risk factors) • History of estrogen-associated DVT/PE • Pregnancy-associated DVT/PE • Idiopathic DVT/PE • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	4	—
ii. Lower risk for recurrent DVT/PE (no risk factors)	3	—
b. Acute DVT/PE	4	—
c. DVT/PE and established anticoagulant therapy for at least 3 months		**Clarification:** Women using anticoagulant therapy are at risk for gynecologic complications of therapy, such as hemorrhagic ovarian cysts and severe menorrhagia. Hormonal contraceptive methods can be of benefit in preventing or treating these complications. When a contraceptive method is used as a therapy, rather than solely to prevent pregnancy, the risk/benefit ratio might differ and should be considered on a case-by-case basis.
i. Higher risk for recurrent DVT/PE (one or more risk factors) • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DTV/PE	4	
ii. Lower risk for recurrent DVT/PE (no risk factors)	3	
d. Family history (first-degree relatives)	2	**Comment:** Some conditions that increase the risk for DTV/PE are heritable.
e. Major surgery		
i. With prolonged immobilization	4	—
ii. Without prolonged immobilization	2	—
f. Minor surgery without immobilization	1	—
Known thrombogenic mutations (e.g., factor V Leiden; prothrombin mutation; and protein S, protein C, and antithrombin deficiencies) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	4	**Clarification**: Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening. **Evidence:** Among women with thrombogenic mutations, COC users had a twofold to twentyfold higher risk for thrombosis than did nonusers (*152–175*).
Superficial venous disorders		
a. Varicose veins	1	**Evidence:** One study suggested that among women with varicose veins, the rate of VTE and superficial venous thrombosis was higher in oral contraceptive users compared with nonusers; however, statistical significance was not reported and the number of events was small (*176*).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
b. Superficial venous thrombosis (acute or history)	3	**Clarification:** Superficial venous thrombosis might be associated with an increased risk for VTE. If a woman has risk factors for concurrent DVT (e.g., known thrombophilia or cancer) or has current or history of DVT, see recommendations for DVT/PE. Superficial venous thrombosis associated with a peripheral intravenous catheter is less likely to be associated with additional thrombosis and use of CHCs may be considered. **Evidence:** One study demonstrated that among women with superficial venous thrombosis, the risk for VTE was higher in oral contraceptive users compared with nonusers (*176*).
Current and history of ischemic heart disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	4	—
Stroke (history of cerebrovascular accident) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	4	—
Valvular heart disease Complicated valvular heart disease is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. Uncomplicated	2	—
b. Complicated (pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis)	4	**Comment:** Among women with valvular heart disease, CHC use may further increase the risk for arterial thrombosis; women with complicated valvular heart disease are at greatest risk.
Peripartum cardiomyopathy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		**Evidence:** No direct evidence exists about the safety of CHCs among women with peripartum cardiomyopathy. Limited indirect evidence from noncomparative studies of women with cardiac disease demonstrated few cases of hypertension and transient ischemic attack in women with cardiac disease using COCs. No cases of heart failure were reported (*177*).
a. Normal or mildly impaired cardiac function (New York Heart Association Functional Class I or II: patients with no limitation of activities or patients with slight, mild limitation of activity) (*178*)		
i. <6 months	4	**Comment:** COCs might increase fluid retention in healthy women; fluid retention may worsen heart failure in women with peripartum cardiomyopathy. COCs might induce cardiac arrhythmias in healthy women; women with peripartum cardiomyopathy have a high incidence of cardiac arrhythmias.
ii. ≥6 months	3	
b. Moderately or severely impaired cardiac function (New York Heart Association Functional Class III or IV: patients with marked limitation of activity or patients who should be at complete rest) (*178*)	4	
Rheumatic Diseases		
Systemic lupus erythematosus This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. Positive (or unknown) antiphospholipid antibodies	4	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*179–197*). **Evidence:** Antiphospholipid antibodies are associated with a higher risk for both arterial and venous thrombosis (*198*,*199*).
b. Severe thrombocytopenia	2	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*179–197*).
c. Immunosuppressive therapy	2	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*179–197*).
d. None of the above	2	**Clarification:** Persons with SLE are at increased risk for ischemic heart disease, stroke, and VTE. Categories assigned to such conditions in U.S. MEC should be the same for women with SLE who have these conditions. For all subconditions of SLE, classifications are based on the assumption that no other risk factors for cardiovascular disease are present; these classifications must be modified in the presence of such risk factors. Many women with SLE can be considered good candidates for most contraceptive methods, including hormonal contraceptives (*179–197*).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
Rheumatoid arthritis		**Evidence:** Limited evidence shows no consistent pattern of improvement or worsening of rheumatoid arthritis with use of oral contraceptives, progesterone, or estrogen (*200*).
a. Receiving immunosuppressive therapy	2	
b. Not receiving immunosuppressive therapy	2	
Neurologic Conditions		
Headaches		
a. Nonmigraine (mild or severe)	1	**Clarification:** Classification depends on accurate diagnosis of those severe headaches that are migraines and those headaches that are not, as well as diagnosis of ever experiencing aura. Aura is a specific focal neurologic symptom. For more information about headache classification see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf). Any new headaches or marked changes in headaches should be evaluated.
b. Migraine		**Clarification:** Classification depends on accurate diagnosis of those severe headaches that are migraines and those headaches that are not, as well as diagnosis of ever experiencing aura. Aura is a specific focal neurologic symptom. For more information about headache classification see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf). Any new headaches or marked changes in headaches should be evaluated.
i. Without aura (This category of migraine includes menstrual migraine.)	2	
ii. With aura	4	
		Clarification: Classification is for women without any other risk factors for stroke (e.g., age, hypertension, and smoking).
		Evidence: Among women with migraine, oral contraceptive use is associated with about a threefold increased risk for ischemic stroke compared with nonuse, although most studies did not specify migraine type or oral contraceptive formulation. The only study to examine migraine type found that the risk for ischemic stroke among women with migraine with aura was increased to a similar level among both oral contraceptive users and nonusers, compared with women without migraine (*201*). The risk for ischemic stroke is increased among women using COCs, compared with women not using COCs (*104*,*202*). The risk for ischemic stroke is also increased among women with migraine with aura, compared with women without migraine (*203*–*205*). One older meta-analysis found that migraine without aura was associated with an increased risk for ischemic stroke, while two more recent meta-analyses did not find such an association (*203*–*205*).
		Comment: Menstrual migraine is a subtype of migraine without aura. For more information, see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf).
Epilepsy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	**Clarification:** If a woman is taking anticonvulsants, see Drug Interactions section. Certain anticonvulsants lower COC effectiveness. The extent to which patch or ring use is similar to COC use in this regard remains unclear.
Multiple sclerosis		**Evidence:** Limited evidence suggests that use of COCs or oral contraceptives (type not specified) among women with multiple sclerosis does not worsen the clinical course of disease (*206*).
a. With prolonged immobility	3	
b. Without prolonged immobility	1	
		Comment: No data exist that evaluate the increased risk for VTE among women with multiple sclerosis using CHCs. However, women with multiple sclerosis are at higher risk than unaffected women for VTE.
Depressive Disorders		
Depressive disorders	1	**Clarification**: If a woman is receiving psychotropic medications or St. John's wort, see Drug Interactions section.
		Evidence: COC use was not associated with increased depressive symptoms in women with depression or scoring above threshold levels on a validated depression screening instrument compared with baseline or with nonusers with depression. One small study of women with bipolar disorder found that oral contraceptives did not significantly change mood across the menstrual cycle (*207*).
Reproductive Tract Infections and Disorders		
Vaginal bleeding patterns		
a. Irregular pattern without heavy bleeding	1	**Comment:** Irregular menstrual bleeding patterns are common among healthy women.
b. Heavy or prolonged bleeding (includes regular and irregular patterns)	1	**Clarification:** Unusually heavy bleeding should raise the suspicion of a serious underlying condition.
		Evidence: A Cochrane Collaboration Review identified one randomized controlled trial evaluating the effectiveness of COC use compared with naproxen and danazol in treating menorrhagia. Women with menorrhagia did not report worsening of the condition or any adverse events related to COC use (*208*).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
Unexplained vaginal bleeding (suspicious for serious condition) before evaluation	2	**Clarification:** If pregnancy or an underlying pathological condition (e.g., pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation. **Comment:** No conditions that cause vaginal bleeding will be worsened in the short-term by use of CHCs.
Endometriosis	1	**Evidence:** A Cochrane Collaboration Review identified one randomized controlled trial evaluating the effectiveness of COC use compared with a gonadotropin-releasing hormone analog in treating the symptoms of endometriosis. Women with endometriosis did not report worsening of the condition or any adverse events related to COC use (*209*).
Benign ovarian tumors (including cysts)	1	
Severe dysmenorrhea	1	**Evidence:** Risk for side effects with COC use was not higher among women with dysmenorrhea than among women not using COCs. Some COC users had a reduction in pain and bleeding (*210*,*211*).
Gestational trophoblastic disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		**Clarification:** For all subconditions of gestational trophoblastic disease, classifications are based on the assumption that women are under close medical supervision because of the need for monitoring of β-hCG levels for appropriate disease surveillance.
a. Suspected gestational trophoblastic disease (immediate postevacuation)		**Evidence:** After molar pregnancy evacuation, the balance of evidence found COC use did not increase the risk for postmolar trophoblastic disease, and β–hCG levels regressed more rapidly in some COC users than in nonusers (*212*). Limited evidence suggests that use of COCs during chemotherapy does not significantly affect the regression or treatment of postmolar trophoblastic disease compared with women who used a nonhormonal contraceptive method or DMPA during chemotherapy (*212*).
i. Uterine size first trimester	1	
ii. Uterine size second trimester	1	
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)		
i. Undetectable/nonpregnant β-hCG levels	1	
ii. Decreasing β-hCG levels	1	
iii. Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	1	
iv. Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	1	
Cervical ectropion	1	**Comment:** Cervical ectropion is not a risk factor for cervical cancer, and restriction of CHC use is unnecessary.
Cervical intraepithelial neoplasia	2	**Evidence:** Among women with persistent human papillomavirus infection, long-term COC use (≥5 years) might increase the risk for carcinoma in situ and invasive carcinoma (*213*). Limited evidence on women with low-grade squamous intraepithelial lesions found use of the vaginal ring did not worsen the condition (*9*).
Cervical cancer (awaiting treatment)	2	**Comment:** Theoretical concern exists that CHC use might affect prognosis of the existing disease. While awaiting treatment, women may use CHCs. In general, treatment of this condition can render a woman sterile.
Breast disease Breast cancer is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. Undiagnosed mass	2	**Clarification:** The woman should be evaluated as early as possible.
b. Benign breast disease	1	—
c. Family history of cancer	1	**Evidence:** Women with breast cancer susceptibility genes (e.g., *BRCA1* and *BRCA2*) have a higher baseline risk for breast cancer than women without these genes. The baseline risk for breast cancer is also higher among women with a family history of breast cancer than among those who do not have such a history. However, evidence does not suggest that the increased risk for breast cancer among women with either a family history of breast cancer or breast cancer susceptibility genes is modified by the use of COCs (*214–231*).
d. Breast cancer		**Comment:** Breast cancer is a hormonally sensitive tumor, and the prognosis for women with current or recent breast cancer might worsen with CHC use.
i. Current	4	
ii. Past and no evidence of current disease for 5 years	3	
Endometrial hyperplasia	1	—
Endometrial cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	**Comment:** COC use reduces the risk for endometrial cancer; whether patch or ring use reduces the risk for endometrial cancer is not known. While awaiting treatment, women may use CHCs. In general, treatment of this condition renders a woman sterile.
Ovarian cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	**Comment:** COC use reduces the risk for ovarian cancer; whether patch or ring use reduces the risk for ovarian cancer is not known. While awaiting treatment, women may use CHCs. In general, treatment of this condition can render a woman sterile.
Uterine fibroids	1	**Comment:** COCs do not appear to cause growth of uterine fibroids, and patch and ring also are not expected to cause growth.

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
Pelvic inflammatory disease		**Comment:** COCs might reduce the risk for PID among women with STDs but do not protect against HIV or lower genital tract STDs. Whether use of patch or ring reduces the risk for PID among women with STDs is unknown; however, they do not protect against HIV or lower genital tract STDs.
a. Past PID		
i. With subsequent pregnancy	1	
ii. Without subsequent pregnancy	1	
b. Current PID	1	
Sexually transmitted diseases		
a. Current purulent cervicitis or chlamydial infection or gonococcal infection	1	—
b. Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	—
c. Other factors related to STDs	1	—
HIV		
High risk for HIV	1	**Evidence:** Overall, evidence does not support an association between oral contraceptives and risk for HIV acquisition (*232*).
HIV infection For women with HIV infection who are not clinically well or not receiving ARV therapy, this condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	**Clarification:** Drug interactions might exist between hormonal contraceptives and ARV drugs; see Drug Interactions section. **Evidence:** Overall, evidence does not support an association between COC use and progression of HIV. Limited direct evidence does not support an association between COC use and transmission of HIV to noninfected partners; studies measuring genital viral shedding as a proxy for infectivity have had mixed results. Studies measuring whether hormonal contraceptive methods affect plasma HIV viral load generally have found no effect (*233–235*).
Other Infections		
Schistosomiasis Schistosomiasis with fibrosis of the liver is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. Uncomplicated	1	**Evidence:** Among women with uncomplicated schistosomiasis, COC use had no adverse effects on liver function (*236–242*).
b. Fibrosis of the liver (if severe, see Cirrhosis section)	1	—
Tuberculosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		**Clarification:** If a woman is taking rifampin, see Drug Interactions section. Rifampin is likely to decrease COC effectiveness. The extent to which patch or ring use is similar to COC use in this regard remains unclear.
a. Nonpelvic	1	
b. Pelvic	1	
Malaria	1	—
Endocrine Conditions		
Diabetes Insulin-dependent diabetes; diabetes with nephropathy, retinopathy, or neuropathy; diabetes with other vascular disease; or diabetes of >20 years' duration are associated with increased risk for adverse health events as a result of pregnancy (Box 2).		
a. History of gestational disease	1	**Evidence:** The development of non–insulin-dependent diabetes in women with a history of gestational diabetes is not increased by use of COCs (*243–250*). Likewise, lipid levels appear to be unaffected by COC use (*251–253*).
b. Nonvascular disease		**Evidence:** Among women with insulin-dependent or non–insulin-dependent diabetes, COC use had limited effect on daily insulin requirements and no effect on long-term diabetes control (e.g., glycosylated hemoglobin levels) or progression to retinopathy. Changes in lipid profile and hemostatic markers were limited, and most changes remained within normal values (*254–263*).
i. Non-insulin dependent	2	
ii. Insulin dependent	2	
c. Nephropathy, retinopathy, or neuropathy	3/4	**Clarification:** The category should be assessed according to the severity of the condition.
d. Other vascular disease or diabetes of >20 years' duration	3/4	**Clarification:** The category should be assessed according to the severity of the condition.
Thyroid disorders		
a. Simple goiter	1	—
b. Hyperthyroid	1	—
c. Hypothyroid	1	—
Gastrointestinal Conditions		
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	2/3	**Clarification:** For women with mild IBD and with no other risk factor for VTE, the benefits of CHC use generally outweigh the risks (category 2). However, for women with IBD who are at increased risk for VTE (e.g., those with active or extensive disease, surgery, immobilization, corticosteroid use, vitamin deficiencies, or fluid depletion), the risks of CHC use generally outweigh the benefits (category 3). **Evidence:** Risk for disease relapse was not significantly higher among women with IBD using oral contraceptives (most studies did not specify type) than among nonusers (*264*). Absorption of COCs among women with mild ulcerative colitis and no or small ileal resections was similar to the absorption among healthy women (*264*). Findings might not apply to women with Crohn's disease or more extensive bowel resections. No data exist that evaluate the increased risk for VTE among women with IBD using CHCs. However, women with IBD are at higher risk than unaffected women for VTE (*264*).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs		Clarifications/Evidence/Comments
Gallbladder disease			**Comment:** CHCs might cause a small increased risk for gallbladder disease. CHCs might worsen existing gallbladder disease.
a. Symptomatic			
i. Treated by cholecystectomy		2	
ii. Medically treated		3	
iii. Current		3	
b. Asymptomatic		2	
History of cholestasis			
a. Pregnancy related		2	**Comment:** History of pregnancy-related cholestasis might predict an increased risk for COC-related cholestasis.
b. Past COC related		3	**Comment:** History of COC-related cholestasis predicts an increased risk with subsequent COC use.
Viral hepatitis	Initiation	Continuation	
a. Acute or flare	3/4	2	**Clarification (initiation):** The category should be assessed according to the severity of the condition. **Evidence:** Data suggest that in women with chronic hepatitis, COC use does not increase the rate or severity of cirrhotic fibrosis, nor does it increase the risk for hepatocellular carcinoma. For women who are carriers, COC use does not appear to trigger liver failure or severe dysfunction. Evidence is limited for COC use during active hepatitis (*265*).
b. Carrier	1	1	**Evidence:** Data suggest that in women with chronic hepatitis, COC use does not increase the rate or severity of cirrhotic fibrosis, nor does it increase the risk for hepatocellular carcinoma. For women who are carriers, COC use does not appear to trigger liver failure or severe dysfunction. Evidence is limited for COC use during active hepatitis (*265*).
c. Chronic	1	1	**Evidence:** Data suggest that in women with chronic hepatitis, COC use does not increase the rate or severity of cirrhotic fibrosis, nor does it increase the risk for hepatocellular carcinoma. For women who are carriers, COC use does not appear to trigger liver failure or severe dysfunction. Evidence is limited for COC use during active hepatitis (*265*).
Cirrhosis Severe cirrhosis is associated with increased risk for adverse health events as a result of pregnancy (Box 2).			
a. Mild (compensated)		1	—
b. Severe (decompensated)		4	—
Liver tumors Hepatocellular adenoma and malignant liver tumors are associated with increased risk for adverse health events as a result of pregnancy (Box 2).			
a. Benign			
i. Focal nodular hyperplasia		2	**Evidence:** Limited direct evidence suggests that hormonal contraceptive use does not influence either progression or regression of liver lesions among women with focal nodular hyperplasia (*266*).
ii. Hepatocellular adenoma		4	—
b. Malignant (hepatoma)		4	—
Respiratory Conditions			
Cystic fibrosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		1	**Clarification:** Persons with cystic fibrosis are at increased risk for diabetes, liver disease, gallbladder disease, and VTE (particularly related to use of central venous catheters) and are frequently prescribed antibiotics. Categories assigned to such conditions in U.S. MEC should be the same for women with cystic fibrosis who have these conditions. For cystic fibrosis, classifications are based on the assumption that no other conditions are present; these classifications must be modified in the presence of such conditions. **Clarification:** Certain drugs to treat cystic fibrosis (e.g., lumacaftor) might reduce effectiveness of hormonal contraceptives, including oral, injectable, transdermal, and implantable contraceptives. **Evidence:** Limited evidence suggests that use of COCs or oral contraceptives (type not specified) among women with cystic fibrosis is not associated with worsening of disease severity. Very limited evidence suggests that cystic fibrosis does not impair the effectiveness of hormonal contraception (*267*).
Anemias			
Thalassemia		1	**Comment:** Anecdotal evidence from countries where thalassemia is prevalent indicates that COC use does not worsen the condition.
Sickle cell disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).		2	—
Iron deficiency anemia		1	**Comment:** CHC use might decrease menstrual blood loss.
Solid Organ Transplantation			
Solid organ transplantation This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).			

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
a. Complicated: graft failure (acute or chronic), rejection, cardiac allograft vasculopathy	4	**Evidence:** Limited evidence of COC and patch users indicated no overall changes in biochemical measures. However, one study reported discontinuations of COC use in two (8%) of 26 women as a result of serious medical complications, and in one case report, a woman developed cholestasis associated with high-dose COC use (*268*).
b. Uncomplicated	2	**Clarification:** Women with Budd-Chiari syndrome should not use CHCs because of the increased risk for thrombosis. **Evidence:** Limited evidence of COC and patch users indicated no overall changes in biochemical measures. However, one study reported discontinuations of COC use in two (8%) of 26 women as a result of serious medical complications, and in one case report, a woman developed cholestasis associated with high-dose COC use (*268*).
Drug Interactions		
Antiretroviral therapy		**Comment:** These recommendations generally are for ARV agents used alone. However, most women receiving ARV therapy are using multiple drugs in combination. In general, whether interactions between ARVs and hormonal contraceptives differ when ARVs are given alone or in combination is unknown.
a. Nucleoside reverse transcriptase inhibitors (NRTIs)		
i. Abacavir (ABC)	1	**Evidence:** NRTIs do not appear to have significant risk for interactions with hormonal contraceptive methods (*269–274*).
ii. Tenofovir (TDF)	1	
iii. Zidovudine (AZT)	1	
iv. Lamivudine (3TC)	1	
v. Didanosine (DDI)	1	
vi. Emtricitabine (FTC)	1	
vii. Stavudine (D4T)	1	
b. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)		
i. Efavirenz (EFV)	2	**Clarification:** Evidence suggests drug interactions between EFV and certain hormonal contraceptives. These interactions might reduce the effectiveness of the hormonal contraceptive. **Evidence:** Two studies suggested that pregnancy rates might be higher among women using COCs and EFV compared with COCs alone, although one study found no difference in pregnancy rates (*275–277*) Two studies found conflicting results on ovulations in women receiving COCs and EFV compared with EFV alone (*278*,*279*). Two pharmacokinetic studies demonstrated decreases in ethinyl estradiol and progestin concentrations in women receiving COCs and EFV compared with COCs alone (*279*,*280*). Pharmacokinetic studies demonstrated generally no changes in EFV concentrations with concomitant COC use (*279*,*280*).
ii. Etravirine (ETR)	1	**Evidence:** One study demonstrated no clinically relevant pharmacokinetic or pharmacodynamic changes in women using COCs and ETR compared with COCs alone (*281*).
iii. Nevirapine (NVP)	1	**Evidence:** Five studies found no significant differences in pregnancy rates among women using COCs and NVP compared with women using COCs alone (*275–277*,*282*,*283*). Three studies reported no ovulations among women receiving COCs and NVP (*278*,*283*,*284*). Two pharmacokinetic studies demonstrated decreased concentrations of ethinyl estradiol and progestin among women using COCs and NVP compared with COCs alone, and one study found no change in contraceptive hormone concentrations (*278*,*284*,*285*). Pharmacokinetic studies demonstrated generally no changes in NVP concentrations with concomitant COC use (*278*,*285*,*286*).
iv. Rilpivirine (RPV)	1	**Evidence:** One study demonstrated no clinical significant pharmacokinetic changes or adverse events in women using COCs and RPV compared with COCs alone (*287*).
c. Ritonavir-boosted protease inhibitors		
i. Ritonavir-boosted atazanavir (ATV/r)	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. **Evidence:** One pharmacokinetic study demonstrated decreased estrogen but increased progestin concentrations in women using COCs and ATV/r compared with COCs alone (*288*).
ii. Ritonavir-boosted darunavir (DRV/r)	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. **Evidence:** One pharmacokinetic study demonstrated no change in follicle-stimulating hormone or luteinizing hormone but decreases in ethinyl estradiol and norethindrone in women using COCs with DRV/r compared with COCs alone (*289*).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
iii. Ritonavir-boosted fosamprenavir (FPV/r)	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. **Evidence:** Information from the package label states that both ethinyl estradiol and norethindrone concentrations decreased with concurrent administration of COCs and FPV/r (*290*).
iv. Ritonavir-boosted lopinavir (LPV/r)	1	**Evidence:** One study demonstrated a non-significant increase in pregnancy rates among women using COCs and LPV/r compared with COCs alone (*275*). One study demonstrated no ovulations in women using the combined hormonal patch and LPV/r compared with combined hormonal patch alone; ethinyl estradiol concentrations for COC and patch users decreased but norelgestromin concentrations increased with use of the patch (*291*).
v. Ritonavir-boosted saquinavir (SQV/r)	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. **Evidence:** One pharmacokinetic study demonstrated no change in SQV concentrations in women using COC and SQV compared with COCs alone (*292*).
iv. Ritonavir-boosted tipranavir (TPV/r)	2	**Clarification:** Theoretically, drug interactions might occur between certain ritonavir-boosted protease inhibitors and certain hormonal contraceptives that might reduce the effectiveness of the hormonal contraceptive. **Evidence:** Information from the package label states that ethinyl estradiol concentrations decrease but norethindrone concentrations increased with concurrent administration of COCs and TPV/r (*293*).
d. Protease inhibitors without ritonavir		
i. Atazanavir (ATV)	2	**Clarification:** Theoretical concern exists that increased levels of ethinyl estradiol because of interactions with ATV might increase the risk for adverse events. **Evidence:** Information from the package label states that there are inconsistent changes in ethinyl estradiol concentrations and increases in progestin concentrations with concurrent administration of two different COCs and ATV (*294*). **Comment:** When ATV is administered with Cobicistat, theoretical concern exists for a drug interaction with hormonal contraceptives. Cobicistat is an inhibitor of CYP3A and CYP2D6 and could theoretically increase contraceptive hormone levels. However, its effects on CYP enzymes and drug levels may vary when combined with other ARVs.
ii. Fosamprenavir (FPV)	3	**Clarification:** Concern exists that interactions between FPV and hormonal contraceptives leading to decreased levels of FPV might diminish effectiveness of the ARV drug. **Evidence:** Information from the package label states that amprenavir concentrations decreased with concurrent administration of COCs and amprenavir. Norethindrone concentrations increased and ethinyl estradiol concentrations did not change (*290*).
iii. Indinavir (IDV)	1	**Evidence:** One small study found no pregnancies in women using COCs and IDV (*277*).
iv. Nelfinavir (NFV)	2	**Clarification:** Evidence suggests drug interactions between certain protease inhibitors and certain hormonal contraceptives. These interactions might reduce the effectiveness of the hormonal contraceptive. **Evidence:** One small study suggested that women using COCs and NFV may have had higher pregnancy rates than those using COCs alone (*277*).
e. CCR5 co-receptor antagonists		
i. Maraviroc (MVC)	1	**Evidence:** COC concentrations were not altered by co-administration with MVC (*295*).
f. HIV integrase strand transfer inhibitors		
i. Raltegravir (RAL)	1	**Evidence:** One pharmacokinetic study demonstrated increased concentrations of norgestimate and no change in ethinyl estradiol among women using COCs and RAL compared with COCs alone (*296*).
ii. Dolutegravir (DTG)	1	**Evidence:** One study demonstrated no clinically relevant pharmacokinetic or pharmacodynamic changes in women using COCs and DTG compared with COCs alone (*297*).

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
iii. Elvitegravir (EVG)	1	**Evidence:** Information from the package label states that ethinyl estradiol concentrations decreased and norgestimate concentrations increased with concurrent administration of COCs and EVG (*298*).
		Comment: When ATV is administered with Cobicistat, theoretical concern exists for a drug interaction with hormonal contraceptives. Cobicistat is an inhibitor of CYP3A and CYP2D6 and could theoretically increase contraceptive hormone levels. However, its effects on CYP enzymes and drug levels may vary when combined with other ARVs.
g. Fusion inhibitors		
i. Enfuvirtide	1	—
Anticonvulsant therapy		
a. Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	3	**Clarification:** Although the interaction of certain anticonvulsants with CHCs is not harmful to women, it is likely to reduce the effectiveness of CHCs. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. When a COC is chosen, a preparation containing a minimum of 30 μg ethinyl estradiol should be used.
		Evidence: Use of certain anticonvulsants might decrease the effectiveness of COCs (*299–302*).
b. Lamotrigine	3	**Clarification:** The recommendation for lamotrigine applies only for situations where lamotrigine monotherapy is taken concurrently with COCs. Anticonvulsant treatment regimens that combine lamotrigine and non–enzyme-inducing antiepileptic drugs (e.g., sodium valproate) do not interact with COCs.
		Evidence: Pharmacokinetic studies show levels of lamotrigine decrease significantly during COC use (*303–307*). Some women who used both COCs and lamotrigine experienced increased seizure activity in one trial (*303*).
Antimicrobial therapy		
a. Broad-spectrum antibiotics	1	**Evidence:** Most broad-spectrum antibiotics do not affect the contraceptive effectiveness of COCs *(308–344)*, patch (*345*), or ring (*346*).
b. Antifungals	1	**Evidence:** Studies of antifungal agents have shown no clinically significant pharmacokinetic interactions with COCs (*347–356*), or ring (*357*).
c. Antiparasitics	1	**Evidence:** Studies of antiparasitic agents have shown no clinically significant pharmacokinetic interactions with COCs (*236*,*358–362*).
d. Rifampin or rifabutin therapy	3	**Clarification:** Although the interaction of rifampin or rifabutin therapy with CHCs is not harmful to women, it is likely to reduce the effectiveness of CHCs. Use of other contraceptives should be encouraged for women who are long-term users of either of these drugs. When a COC is chosen, a preparation containing a minimum of 30 μg ethinyl estradiol should be used.
		Evidence: The balance of the evidence suggests that rifampin reduces the effectiveness of COCs (*363–378*). Data on rifabutin are limited, but effects on metabolism of COCs are less than with rifampin, and small studies have not shown evidence of ovulation (*365*,*372*).
Psychotropic medications		**Comment:** For many common psychotropic agents, limited or no theoretical concern exists for clinically significant drug interactions when co-administered with hormonal contraceptives. However, either no or very limited data exist examining potential interactions for these classes of medications. For psychotropic agents that are CYP1A2 substrates, such as duloxetine, mirtazapine, ziprasidone, olanzapine, clomipramine, imipramine, and amitriptyline, co-administration with CHCs could theoretically yield increased concentrations of the psychotropic drug. For agents with narrow therapeutic windows, such as tricyclic antidepressants, increased drug concentrations might pose safety concerns that could necessitate closer monitoring.
a. SSRIs	1	**Evidence:** Limited clinical and pharmacokinetic data do not demonstrate concern for SSRIs decreasing the effectiveness of oral contraceptives. Limited evidence suggests that for women taking SSRIs, the use of hormonal contraceptives was not associated with differences in effectiveness of the SSRI for treatment or in adverse events when compared with women not taking hormonal contraceptives (*379*).
		Comment: Drugs that are inhibitors of CYP3A4 or CYP2C9 theoretically have the potential to increase levels of contraceptive steroids which might increase adverse events. Fluvoxamine is an SSRI known to be a moderate inhibitor of both CYP3A4 and CYP2C9; however, no clinical or pharmacokinetic studies were identified to explore potential drug-drug interactions.

See table footnotes on page 69.

TABLE D1. (*Continued*) Classifications for combined hormonal contraceptives, including pill, patch, and ring

Condition	Category CHCs	Clarifications/Evidence/Comments
St. John's wort	2	**Evidence:** Although clinical data are limited, studies with pharmacokinetic and pharmacodynamics outcomes raise concern that St. John's wort might decrease effectiveness of hormonal contraceptives, including increased risk for breakthrough bleeding and ovulation and increased metabolism of estrogen and progestins. Any interactions might be dependent on the dose of St John's wort, and the concentration of active ingredients across types of St. John's wort preparations may vary (*380*).

Abbreviations: ARV = antiretroviral; BMD = bone mineral density; BMI = body mass index; CHC = combined hormonal contraceptive; COC = combined oral contraceptive; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; HDL = high-density lipoprotein; HIV = human immunodeficiency virus; IBD = inflammatory bowel disease; LDL = low-density lipoprotein; PE = pulmonary embolism; PID = pelvic inflammatory disease; SLE = systemic lupus erythematosus; SSRI = selective serotonin reuptake inhibitor; STD = sexually transmitted infection; VTE = venous thromboembolism.

References

1. Abrams LS, Skee DM, Natarajan J, Wong FA, Lasseter KC. Multiple-dose pharmacokinetics of a contraceptive patch in healthy women participants. Contraception 2001;64:287–94. http://dx.doi.org/10.1016/S0010-7824(01)00273-6
2. Ahrendt HJ, Nisand I, Bastianelli C, et al. Efficacy, acceptability and tolerability of the combined contraceptive ring, NuvaRing, compared with an oral contraceptive containing 30 microg of ethinyl estradiol and 3 mg of drospirenone. Contraception 2006;74:451–7. http://dx.doi.org/10.1016/j.contraception.2006.07.004
3. Audet M-C, Moreau M, Koltun WD, et al; ORTHO EVRA/EVRA 004 Study Group. Evaluation of contraceptive efficacy and cycle control of a transdermal contraceptive patch vs an oral contraceptive: a randomized controlled trial. JAMA 2001;285:2347–54. http://dx.doi.org/10.1001/jama.285.18.2347
4. Bjarnadóttir RI, Tuppurainen M, Killick SR. Comparison of cycle control with a combined contraceptive vaginal ring and oral levonorgestrel/ethinyl estradiol. Am J Obstet Gynecol 2002;186:389–95. http://dx.doi.org/10.1067/mob.2002.121103
5. Boonyarangkul A, Taneepanichskul S. Comparison of cycle control and side effects between transdermal contraceptive patch and an oral contraceptive in women older than 35 years. J Med Assoc Thai 2007;90:1715–9.
6. Burkman RT. The transdermal contraceptive patch: a new approach to hormonal contraception. Int J Fertil Womens Med 2002;47:69–76.
7. Cole JA, Norman H, Doherty M, Walker AM. Venous thromboembolism, myocardial infarction, and stroke among transdermal contraceptive system users. Obstet Gynecol 2007;109:339–46. http://dx.doi.org/10.1097/01.AOG.0000250968.82370.04
8. Devineni D, Skee D, Vaccaro N, et al. Pharmacokinetics and pharmacodynamics of a transdermal contraceptive patch and an oral contraceptive. J Clin Pharmacol 2007;47:497–509. http://dx.doi.org/10.1177/0091270006297919.
9. Dieben TO, Roumen FJ, Apter D. Efficacy, cycle control, and user acceptability of a novel combined contraceptive vaginal ring. Obstet Gynecol 2002;100:585–93.
10. Dittrich R, Parker L, Rosen JB, Shangold G, Creasy GW, Fisher AC; Ortho Evra/Evra 001 Study Group. Transdermal contraception: evaluation of three transdermal norelgestromin/ethinyl estradiol doses in a randomized, multicenter, dose-response study. Am J Obstet Gynecol 2002;186:15–20. http://dx.doi.org/10.1067/mob.2002.118844
11. Duijkers I, Killick S, Bigrigg A, Dieben TO. A comparative study on the effects of a contraceptive vaginal ring NuvaRing and an oral contraceptive on carbohydrate metabolism and adrenal and thyroid function. Eur J Contracept Reprod Health Care 2004;9:131–40. http://dx.doi.org/10.1080/13625180400007199
12. Duijkers IJ, Klipping C, Verhoeven CH, Dieben TO. Ovarian function with the contraceptive vaginal ring or an oral contraceptive: a randomized study. Hum Reprod 2004;19:2668–73. http://dx.doi.org/10.1093/humrep/deh493
13. Elkind-Hirsch KE, Darensbourg C, Ogden B, Ogden LF, Hindelang P. Contraceptive vaginal ring use for women has less adverse metabolic effects than an oral contraceptive. Contraception 2007;76:348–56. http://dx.doi.org/10.1016/j.contraception.2007.08.001
14. Hedon B, Helmerhorst FM, Cronje HS, Shangold GA, Fisher AC, Creasy GW. Comparison of efficacy, cycle control, compliance, and safety in users of a contraceptive patch versus an oral contraceptive. Int J Gynaecol Obstet 2000;70(Suppl 2):B78. http://dx.doi.org/10.1016/S0020-7292(00)85161-9
15. Jick S, Kaye JA, Li L, Jick H. Further results on the risk of nonfatal venous thromboembolism in users of the contraceptive transdermal patch compared to users of oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. Contraception 2007;76:4–7. http://dx.doi.org/10.1016/j.contraception.2007.03.003
16. Jick SS, Jick H. Cerebral venous sinus thrombosis in users of four hormonal contraceptives: levonorgestrel-containing oral contraceptives, norgestimate-containing oral contraceptives, desogestrel-containing oral contraceptives and the contraceptive patch. Contraception 2006;74:290–2. http://dx.doi.org/10.1016/j.contraception.2006.05.071
17. Jick SS, Jick H. The contraceptive patch in relation to ischemic stroke and acute myocardial infarction. Pharmacotherapy 2007;27:218–20. http://dx.doi.org/10.1592/phco.27.2.218
18. Jick SS, Kaye JA, Russmann S, Jick H. Risk of nonfatal venous thromboembolism in women using a contraceptive transdermal patch and oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. Contraception 2006;73:223–8. http://dx.doi.org/10.1016/j.contraception.2006.01.001
19. Magnusdóttir EM, Bjarnadóttir RI, Onundarson PT, et al. The contraceptive vaginal ring (NuvaRing) and hemostasis: a comparative study. Contraception 2004;69:461–7. http://dx.doi.org/10.1016/j.contraception.2003.12.010
20. Massai R, Mäkäräinen L, Kuukankorpi A, Klipping C, Duijkers I, Dieben T. The combined contraceptive vaginal ring and bone mineral density in healthy pre-menopausal women. Hum Reprod 2005;20:2764–8. http://dx.doi.org/10.1093/humrep/dei117
21. Milsom I, Lete I, Bjertnaes A, et al. Effects on cycle control and bodyweight of the combined contraceptive ring, NuvaRing, versus an oral contraceptive containing 30 μg ethinyl estradiol and 3 mg drospirenone. Hum Reprod 2006;21:2304–11. http://dx.doi.org/10.1093/humrep/del162
22. Oddsson K, Leifels-Fischer B, de Melo NR, et al. Efficacy and safety of a contraceptive vaginal ring (NuvaRing) compared with a combined oral contraceptive: a 1-year randomized trial. Contraception 2005;71:176–82. http://dx.doi.org/10.1016/j.contraception.2004.09.001
23. Pierson RA, Archer DF, Moreau M, Shangold GA, Fisher AC, Creasy GW. Ortho Evra/Evra versus oral contraceptives: follicular development and ovulation in normal cycles and after an intentional dosing error. Fertil Steril 2003;80:34–42. http://dx.doi.org/10.1016/S0015-0282(03)00556-9
24. Radowicki S, Skórzewska K, Szlendak K. Safety evaluation of a transdermal contraceptive system with an oral contraceptive [Polish]. Ginekol Pol 2005;76:884–9.

25. Sabatini R, Cagiano R. Comparison profiles of cycle control, side effects and sexual satisfaction of three hormonal contraceptives. Contraception 2006;74:220–3. http://dx.doi.org/10.1016/j.contraception.2006.03.022
26. Smallwood GH, Meador ML, Lenihan JP, Shangold GA, Fisher AC, Creasy GW; ORTHO EVRA/EVRA 002 Study Group. Efficacy and safety of a transdermal contraceptive system. Obstet Gynecol 2001;98:799–805.
27. Timmer CJ, Mulders TM. Pharmacokinetics of etonogestrel and ethinylestradiol released from a combined contraceptive vaginal ring. Clin Pharmacokinet 2000;39:233–42. http://dx.doi.org/10.2165/00003088-200039030-00005
28. Tuppurainen M, Klimscheffskij R, Venhola M, Dieben TO. The combined contraceptive vaginal ring (NuvaRing) and lipid metabolism: a comparative study. Contraception 2004;69:389–94. http://dx.doi.org/10.1016/j.contraception.2004.01.004
29. Urdl W, Apter D, Alperstein A, et al; ORTHO EVRA/EVRA 003 Study Group. Contraceptive efficacy, compliance and beyond: factors related to satisfaction with once-weekly transdermal compared with oral contraception. Eur J Obstet Gynecol Reprod Biol 2005;121:202–10. http://dx.doi.org/10.1016/j.ejogrb.2005.01.021
30. van den Heuvel MW, van Bragt AJM, Alnabawy AKM, Kaptein MCJ. Comparison of ethinylestradiol pharmacokinetics in three hormonal contraceptive formulations: the vaginal ring, the transdermal patch and an oral contraceptive. Contraception 2005;72:168–74. http://dx.doi.org/10.1016/j.contraception.2005.03.005
31. Veres S, Miller L, Burington B. A comparison between the vaginal ring and oral contraceptives. Obstet Gynecol 2004;104:555–63. http://dx.doi.org/10.1097/01.AOG.0000136082.59644.13
32. White T, Ozel B, Jain JK, Stanczyk FZ. Effects of transdermal and oral contraceptives on estrogen-sensitive hepatic proteins. Contraception 2006;74:293–6. http://dx.doi.org/10.1016/j.contraception.2006.04.005
33. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril 2002;77(Suppl 2):S13–8. http://dx.doi.org/10.1016/S0015-0282(01)03275-7
34. Memon S, Iversen L, Hannaford PC. Is the oral contraceptive pill associated with fracture in later life? New evidence from the Royal College of General Practitioners Oral Contraception Study. Contraception 2011;84:40–7. http://dx.doi.org/10.1016/j.contraception.2010.11.019
35. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk in very young women using combined oral contraceptives. Contraception 2008;78:358–64. http://dx.doi.org/10.1016/j.contraception.2008.06.010
36. Vestergaard P, Rejnmark L, Mosekilde L. Oral contraceptive use and risk of fractures. Contraception 2006;73:571–6. http://dx.doi.org/10.1016/j.contraception.2006.01.006
37. Barad D, Kooperberg C, Wactawski-Wende J, Liu J, Hendrix SL, Watts NB. Prior oral contraception and postmenopausal fracture: a Women's Health Initiative observational cohort study. Fertil Steril 2005;84:374–83. http://dx.doi.org/10.1016/j.fertnstert.2005.01.132
38. Michaëlsson K, Baron JA, Farahmand BY, Ljunghall S. Influence of parity and lactation on hip fracture risk. Am J Epidemiol 2001;153:1166–72. http://dx.doi.org/10.1093/aje/153.12.1166
39. Michaëlsson K, Baron JA, Farahmand BY, Persson I, Ljunghall S. Oral-contraceptive use and risk of hip fracture: a case-control study. Lancet 1999;353:1481–4. http://dx.doi.org/10.1016/S0140-6736(98)09044-8
40. La Vecchia C, Tavani A, Gallus S. Oral contraceptives and risk of hip fractures. Lancet 1999;354:335–6. http://dx.doi.org/10.1016/S0140-6736(05)75239-9
41. Vessey M, Mant J, Painter R. Oral contraception and other factors in relation to hospital referral for fracture. Findings in a large cohort study. Contraception 1998;57:231–5. http://dx.doi.org/10.1016/S0010-7824(98)00026-2
42. O'Neill TW, Marsden D, Adams JE, Silman AJ. Risk factors, falls, and fracture of the distal forearm in Manchester, UK. J Epidemiol Community Health 1996;50:288–92. http://dx.doi.org/10.1136/jech.50.3.288
43. Mallmin H, Ljunghall S, Persson I, Bergström R. Risk factors for fractures of the distal forearm: a population-based case-control study. Osteoporos Int 1994;4:298–304. http://dx.doi.org/10.1007/BF01622186
44. Cooper C, Hannaford P, Croft P, Kay CR. Oral contraceptive pill use and fractures in women: a prospective study. Bone 1993;14:41–5. http://dx.doi.org/10.1016/8756-3282(93)90254-8
45. Meier C, Brauchli YB, Jick SS, Kraenzlin ME, Meier CR. Use of depot medroxyprogesterone acetate and fracture risk. J Clin Endocrinol Metab 2010;95:4909–16. http://dx.doi.org/10.1210/jc.2010-0032
46. Cibula D, Skrenkova J, Hill M, Stepan JJ. Low-dose estrogen combined oral contraceptives may negatively influence physiological bone mineral density acquisition during adolescence. Eur J Endocrinol 2012;166:1003–11. http://dx.doi.org/10.1530/EJE-11-1047
47. Gai L, Jia Y, Zhang M, et al. Effect of two kinds of different combined oral contraceptives use on bone mineral density in adolescent women. Contraception 2012;86:332–6. http://dx.doi.org/10.1016/j.contraception.2012.01.009
48. Scholes D, Hubbard RA, Ichikawa LE, et al. Oral contraceptive use and bone density change in adolescent and young adult women: a prospective study of age, hormone dose, and discontinuation. J Clin Endocrinol Metab 2011;96:E1380–7. http://dx.doi.org/10.1210/jc.2010-3027
49. Lattakova M, Borovsky M, Payer J, Killinger Z. Oral contraception usage in relation to bone mineral density and bone turnover in adolescent girls. Eur J Contracept Reprod Health Care 2009;14:207–14. http://dx.doi.org/10.1080/13625180902838828
50. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM. Bone mineral density in a cohort of adolescents during use of norethisterone enanthate, depot-medroxyprogesterone acetate or combined oral contraceptives and after discontinuation of norethisterone enanthate. Contraception 2009;79:345–9. http://dx.doi.org/10.1016/j.contraception.2008.11.009
51. Pikkarainen E, Lehtonen-Veromaa M, Möttönen T, Kautiainen H, Viikari J. Estrogen-progestin contraceptive use during adolescence prevents bone mass acquisition: a 4-year follow-up study. Contraception 2008;78:226–31. http://dx.doi.org/10.1016/j.contraception.2008.05.002
52. Cromer BA, Bonny AE, Stager M, et al. Bone mineral density in adolescent females using injectable or oral contraceptives: a 24-month prospective study. Fertil Steril 2008;90:2060–7. http://dx.doi.org/10.1016/j.fertnstert.2007.10.070
53. Berenson AB, Rahman M, Breitkopf CR, Bi LX. Effects of depot medroxyprogesterone acetate and 20-μg oral contraceptives on bone mineral density. Obstet Gynecol 2008;112:788–99. http://dx.doi.org/10.1097/AOG.0b013e3181875b78
54. Harel Z, Riggs S, Vaz R, Flanagan P, Harel D, Machan JT. Bone accretion in adolescents using the combined estrogen and progestin transdermal contraceptive method Ortho Evra: a pilot study. J Pediatr Adolesc Gynecol 2010;23:23–31. http://dx.doi.org/10.1016/j.jpag.2009.04.008
55. Cobb KL, Bachrach LK, Sowers M, et al. The effect of oral contraceptives on bone mass and stress fractures in female runners. Med Sci Sports Exerc 2007;39:1464–73. http://dx.doi.org/10.1249/mss.0b013e318074e532
56. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM. Bone mineral density in adolescents using norethisterone enanthate, depot-medroxyprogesterone acetate or combined oral contraceptives for contraception. Contraception 2007;75:438–43. http://dx.doi.org/10.1016/j.contraception.2007.02.001
57. Lara-Torre E, Edwards CP, Perlman S, Hertweck SP. Bone mineral density in adolescent females using depot medroxyprogesterone acetate. J Pediatr Adolesc Gynecol 2004;17:17–21. http://dx.doi.org/10.1016/j.jpag.2003.11.017
58. Cromer BA, Blair JM, Mahan JD, Zibners L, Naumovski Z. A prospective comparison of bone density in adolescent girls receiving depot medroxyprogesterone acetate (Depo-Provera), levonorgestrel (Norplant), or oral contraceptives. J Pediatr 1996;129:671–6. http://dx.doi.org/10.1016/S0022-3476(96)70148-8
59. Polatti F, Perotti F, Filippa N, Gallina D, Nappi RE. Bone mass and long-term monophasic oral contraceptive treatment in young women. Contraception 1995;51:221–4. http://dx.doi.org/10.1016/0010-7824(95)00036-A
60. Sørdal T, Grob P, Verhoeven C. Effects on bone mineral density of a monophasic combined oral contraceptive containing nomegestrol acetate/17ß-estradiol in comparison to levonorgestrel/ethinylestradiol. Acta Obstet Gynecol Scand 2012;91:1279–85. http://dx.doi.org/10.1111/j.1600-0412.2012.01498.x

61. Gargano V, Massaro M, Morra I, Formisano C, Di Carlo C, Nappi C. Effects of two low-dose combined oral contraceptives containing drospirenone on bone turnover and bone mineral density in young fertile women: a prospective controlled randomized study. Contraception 2008;78:10–5. http://dx.doi.org/10.1016/j.contraception.2008.01.016
62. Nappi C, Di Spiezio Sardo A, Greco E, Tommaselli GA, Giordano E, Guida M. Effects of an oral contraceptive containing drospirenone on bone turnover and bone mineral density. Obstet Gynecol 2005;105:53–60. http://dx.doi.org/10.1097/01.AOG.0000148344.26475.fc
63. Berenson AB, Radecki CM, Grady JJ, Rickert VI, Thomas A. A prospective, controlled study of the effects of hormonal contraception on bone mineral density. Obstet Gynecol 2001;98:576–82.
64. Berenson AB, Breitkopf CR, Grady JJ, Rickert VI, Thomas A. Effects of hormonal contraception on bone mineral density after 24 months of use. Obstet Gynecol 2004;103:899–906. http://dx.doi.org/10.1097/01.AOG.0000117082.49490.d5
65. Elgán C, Samsioe G, Dykes AK. Influence of smoking and oral contraceptives on bone mineral density and bone remodeling in young women: a 2-year study. Contraception 2003;67:439–47. http://dx.doi.org/10.1016/S0010-7824(03)00048-9
66. Elgán C, Dykes AK, Samsioe G. Bone mineral density changes in young women: a two year study. Gynecol Endocrinol 2004;19:169–77. http://dx.doi.org/10.1080/09513590400012119
67. Endrikat J, Mih E, Düsterberg B, et al. A 3-year double-blind, randomized, controlled study on the influence of two oral contraceptives containing either 20 μg or 30 μg ethinylestradiol in combination with levonorgestrel on bone mineral density. Contraception 2004;69:179–87. http://dx.doi.org/10.1016/j.contraception.2003.10.002
68. Paoletti AM, Orrù M, Lello S, et al. Short-term variations in bone remodeling markers of an oral contraception formulation containing 3 mg of drospirenone plus 30 microg of ethinyl estradiol: observational study in young postadolescent women. Contraception 2004;70:293–8. http://dx.doi.org/10.1016/j.contraception.2004.04.004
69. Nappi C, Di Spiezio Sardo A, Acunzo G, et al. Effects of a low-dose and ultra-low-dose combined oral contraceptive use on bone turnover and bone mineral density in young fertile women: a prospective controlled randomized study. Contraception 2003;67:355–9. http://dx.doi.org/10.1016/S0010-7824(03)00025-8
70. Reed SD, Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. Longitudinal changes in bone density in relation to oral contraceptive use. Contraception 2003;68:177–82. http://dx.doi.org/10.1016/S0010-7824(03)00147-1
71. Cobb KL, Kelsey JL, Sidney S, Ettinger B, Lewis CE. Oral contraceptives and bone mineral density in white and black women in CARDIA. Coronary Risk Development in Young Adults. Osteoporos Int 2002;13:893–900. http://dx.doi.org/10.1007/s001980200123
72. Burr DB, Yoshikawa T, Teegarden D, et al. Exercise and oral contraceptive use suppress the normal age-related increase in bone mass and strength of the femoral neck in women 18–31 years of age. Bone 2000;27:855–63. http://dx.doi.org/10.1016/S8756-3282(00)00403-8
73. Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. Bone gain in young adult women. JAMA 1992;268:2403–8. http://dx.doi.org/10.1001/jama.1992.03490170075028
74. Mazess RB, Barden HS. Bone density in premenopausal women: effects of age, dietary intake, physical activity, smoking, and birth-control pills. Am J Clin Nutr 1991;53:132–42.
75. Gambacciani M, Cappagli B, Lazzarini V, Ciaponi M, Fruzzetti F, Genazzani AR. Longitudinal evaluation of perimenopausal bone loss: effects of different low dose oral contraceptive preparations on bone mineral density. Maturitas 2006;54:176–80. http://dx.doi.org/10.1016/j.maturitas.2005.10.007
76. Gambacciani M, Spinetti A, Taponeco F, Cappagli B, Piaggesi L, Fioretti P. Longitudinal evaluation of perimenopausal vertebral bone loss: effects of a low-dose oral contraceptive preparation on bone mineral density and metabolism. Obstet Gynecol 1994;83:392–6.
77. Gambacciani M, Spinetti A, Cappagli B, et al. Hormone replacement therapy in perimenopausal women with a low dose oral contraceptive preparation: effects on bone mineral density and metabolism. Maturitas 1994;19:125–31. http://dx.doi.org/10.1016/0378-5122(94)90062-0
78. Gambacciani M, Cappagli B, Ciaponi M, Benussi C, Genazzani AR. Hormone replacement therapy in perimenopause: effect of a low dose oral contraceptive preparation on bone quantitative ultrasound characteristics. Menopause 1999;6:43–8. http://dx.doi.org/10.1097/00042192-199906010-00009
79. Volpe A, Malmusi S, Zanni AL, Landi S, Cagnacci A. Oral contraceptives and bone metabolism. Eur J Contracept Reprod Health Care 1997;2:225–8. http://dx.doi.org/10.3109/13625189709165298
80. Hansen MA, Overgaard K, Riis BJ, Christiansen C. Potential risk factors for development of postmenopausal osteoporosis—examined over a 12-year period. Osteoporos Int 1991;1:95–102. http://dx.doi.org/10.1007/BF01880450
81. Shargil AA. Hormone replacement therapy in perimenopausal women with a triphasic contraceptive compound: a three-year prospective study. Int J Fertil 1985;30:15, 18–28.
82. Taechakraichana N, Limpaphayom K, Ninlagarn T, Panyakhamlerd K, Chaikittisilpa S, Dusitsin N. A randomized trial of oral contraceptive and hormone replacement therapy on bone mineral density and coronary heart disease risk factors in postmenopausal women. Obstet Gynecol 2000;95:87–94.
83. Taechakraichana N, Jaisamrarn U, Panyakhamlerd K, Chaikittisilpa S, Limpaphayom K. Difference in bone acquisition among hormonally treated postmenopausal women with normal and low bone mass. J Med Assoc Thai 2001;84(Suppl 2):S586–92.
84. Grimes DA, Schulz KF. Surrogate end points in clinical research: hazardous to your health. Obstet Gynecol 2005;105:1114–8. http://dx.doi.org/10.1097/01.AOG.0000157445.67309.19
85. Schönau E. The peak bone mass concept: is it still relevant? Pediatr Nephrol 2004;19:825–31. http://dx.doi.org/10.1007/s00467-004-1465-5
86. Cohen A, Shane E. Treatment of premenopausal women with low bone mineral density. Curr Osteoporos Rep 2008;6:39–46. http://dx.doi.org/10.1007/s11914-008-0007-7
87. US Department of Health and Human Services. Healthy people 2020: maternal, infant, and child health objectives. Washington, DC: US Department of Health and Human Services; 2015. http://www.healthypeople.gov/2020/topics-objectives/topic/maternal-infant-and-child-health/objectives.
88. Tepper NK, Phillips SJ, Kapp N, Gaffield ME, Curtis KM. Combined hormonal contraceptive use among breastfeeding women: an updated systematic review. Contraception 2015;S0010-7824(15)00218-8.
89. Petersen JF, Bergholt T, Nielsen AK, Paidas MJ, Løkkegaard EC. Combined hormonal contraception and risk of venous thromboembolism within the first year following pregnancy. Danish nationwide historical cohort 1995–2009. Thromb Haemost 2014;112:73–8. http://dx.doi.org/10.1160/TH13-09-0797
90. Jackson E, Curtis KM, Gaffield ME. Risk of venous thromboembolism during the postpartum period: a systematic review. Obstet Gynecol 2011;117:691–703. http://dx.doi.org/10.1097/AOG.0b013e31820ce2db
91. Kamel H, Navi BB, Sriram N, Hovsepian DA, Devereux RB, Elkind MS. Risk of a thrombotic event after the 6-week postpartum period. N Engl J Med 2014;370:1307–15. http://dx.doi.org/10.1056/NEJMoa1311485
92. Sultan AA, Tata LJ, West J, et al. Risk factors for first venous thromboembolism around pregnancy: a population-based cohort study from the United Kingdom. Blood 2013;121:3953–61. http://dx.doi.org/10.1182/blood-2012-11-469551
93. Sultan AA, West J, Tata LJ, Fleming KM, Nelson-Piercy C, Grainge MJ. Risk of first venous thromboembolism in and around pregnancy: a population-based cohort study. Br J Haematol 2012;156:366–73. http://dx.doi.org/10.1111/j.1365-2141.2011.08956.x

94. Tepper NK, Boulet SL, Whiteman MK, et al. Postpartum venous thromboembolism: incidence and risk factors. Obstet Gynecol 2014;123:987–96. http://dx.doi.org/10.1097/AOG.0000000000000230
95. Jackson E, Glasier A. Return of ovulation and menses in postpartum nonlactating women: a systematic review. Obstet Gynecol 2011;117:657–62. http://dx.doi.org/10.1097/AOG.0b013e31820ce18c
96. Lähteenmäki P. Influence of oral contraceptives on immediate postabortal pituitary-ovarian function. Acta Obstet Gynecol Scand Suppl 1978;76:1–43.
97. Lähteenmäki P, Rasi V, Luukkainen T, Myllyä G. Coagulation factors in women using oral contraceptives or intrauterine contraceptive devices immediately after abortion. Am J Obstet Gynecol 1981;141:175–9.
98. Martin CW, Brown AH, Baird DT. A pilot study of the effect of methotrexate or combined oral contraceptive on bleeding patterns after induction of abortion with mifepristone and a prostaglandin pessary. Contraception 1998;58:99–103. http://dx.doi.org/10.1016/S0010-7824(98)00072-9
99. Niswonger JW, London GD, Anderson GV, Wolfe L. Oral contraceptives during immediate postabortal period. Obstet Gynecol 1968;32:325–7.
100. Peterson WF. Contraceptive therapy following therapeutic abortion: an analysis. Obstet Gynecol 1974;44:853–7.
101. Tang OS, Gao PP, Cheng L, Lee SW, Ho PC. A randomized double-blind placebo-controlled study to assess the effect of oral contraceptive pills on the outcome of medical abortion with mifepristone and misoprostol. Hum Reprod 1999;14:722–5. http://dx.doi.org/10.1093/humrep/14.3.722
102. Tang OS, Xu J, Cheng L, Lee SW, Ho PC. The effect of contraceptive pills on the measured blood loss in medical termination of pregnancy by mifepristone and misoprostol: a randomized placebo controlled trial. Hum Reprod 2002;17:99–102. http://dx.doi.org/10.1093/humrep/17.1.99
103. Fine PM, Tryggestad J, Meyers NJ, Sangi-Haghpeykar H. Safety and acceptability with the use of a contraceptive vaginal ring after surgical or medical abortion. Contraception 2007;75:367–71. http://dx.doi.org/10.1016/j.contraception.2007.01.009
104. Gillum LA, Mamidipudi SK, Johnston SC. Ischemic stroke risk with oral contraceptives: a meta-analysis. JAMA 2000;284:72–8. http://dx.doi.org/10.1001/jama.284.1.72
105. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. Br J Cancer 1989;59:618–21. http://dx.doi.org/10.1038/bjc.1989.125
106. Khader YS, Rice J, John L, Abueita O. Oral contraceptives use and the risk of myocardial infarction: a meta-analysis. Contraception 2003;68:11–7. http://dx.doi.org/10.1016/S0010-7824(03)00073-8
107. Lawson DH, Davidson JF, Jick H. Oral contraceptive use and venous thromboembolism: absence of an effect of smoking. BMJ 1977;2:729–30. http://dx.doi.org/10.1136/bmj.2.6089.729
108. Lidegaard O, Edström B, Kreiner S. Oral contraceptives and venous thromboembolism. A case-control study. Contraception 1998;57:291–301. http://dx.doi.org/10.1016/S0010-7824(98)00033-X
109. Nightingale AL, Lawrenson RA, Simpson EL, Williams TJ, MacRae KD, Farmer RD. The effects of age, body mass index, smoking and general health on the risk of venous thromboembolism in users of combined oral contraceptives. Eur J Contracept Reprod Health Care 2000;5:265–74. http://dx.doi.org/10.1080/13625180008500402
110. Petitti DB, Wingerd J, Pellegrin F, Ramcharan S. Risk of vascular disease in women. Smoking, oral contraceptives, noncontraceptive estrogens, and other factors. JAMA 1979;242:1150–4. http://dx.doi.org/10.1001/jama.1979.03300110022020
111. Rosenberg L, Palmer JR, Rao RS, Shapiro S. Low-dose oral contraceptive use and the risk of myocardial infarction. Arch Intern Med 2001;161:1065–70. http://dx.doi.org/10.1001/archinte.161.8.1065
112. Straneva P, Hinderliter A, Wells E, Lenahan H, Girdler S. Smoking, oral contraceptives, and cardiovascular reactivity to stress. Obstet Gynecol 2000;95:78–83.
113. Tanis BC, van den Bosch MA, Kemmeren JM, et al. Oral contraceptives and the risk of myocardial infarction. N Engl J Med 2001;345:1787–93. http://dx.doi.org/10.1056/NEJMoa003216
114. Van den Bosch MA, Kemmeren JM, Tanis BC, et al. The RATIO study: oral contraceptives and the risk of peripheral arterial disease in young women. J Thromb Hemost 2003;1:439–44.
115. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Venous thromboembolic disease and combined oral contraceptives: results of international multicentre case-control study. Lancet 1995;346:1575–82. http://dx.doi.org/10.1016/S0140-6736(95)91926-0
116. Collaborative Group for the Study of Stroke in Young Women. Oral contraceptives and stroke in young women. Associated risk factors. JAMA 1975;231:718–22. http://dx.doi.org/10.1001/jama.1975.03240190022010
117. Horton LG, Simmons KB, Curtis KM. Combined hormonal contraceptive use among obese women and risk for cardiovascular events: a systematic review. Contraception 2016. Epub June 1, 2016. http://dx.doi.org/10.1016/j.contraception.2016.05.014
118. Brunner Huber LR, Hogue CJ, Stein AD, Drews C, Zieman M. Body mass index and risk for oral contraceptive failure: a case-cohort study in South Carolina. Ann Epidemiol 2006;16:637–43. http://dx.doi.org/10.1016/j.annepidem.2006.01.001
119. Brunner Huber LR, Toth JL. Obesity and oral contraceptive failure: findings from the 2002 National Survey of Family Growth. Am J Epidemiol 2007;166:1306–11. http://dx.doi.org/10.1093/aje/kwm221
120. Brunner LR, Hogue CJ. The role of body weight in oral contraceptive failure: results from the 1995 national survey of family growth. Ann Epidemiol 2005;15:492–9. http://dx.doi.org/10.1016/j.annepidem.2004.10.009
121. Holt VL, Cushing-Haugen KL, Daling JR. Body weight and risk of oral contraceptive failure. Obstet Gynecol 2002;99:820–7.
122. Holt VL, Scholes D, Wicklund KG, Cushing-Haugen KL, Daling JR. Body mass index, weight, and oral contraceptive failure risk. Obstet Gynecol 2005;105:46–52. http://dx.doi.org/10.1097/01.AOG.0000149155.11912.52
123. Trussell J, Schwarz EB, Guthrie K. Obesity and oral contraceptive pill failure. Contraception 2009;79:334–8. http://dx.doi.org/10.1016/j.contraception.2008.11.017
124. Vessey M. Oral contraceptive failures and body weight: findings in a large cohort study. J Fam Plann Reprod Health Care 2001;27:90–1. http://dx.doi.org/10.1783/147118901101195092
125. Yamazaki M, Dwyer K, Sobhan M, et al. Effect of obesity on the effectiveness of hormonal contraceptives: an individual participant data meta-analysis. Contraception 2015;92:445–52. http://dx.doi.org/10.1016/j.contraception.2015.07.016
126. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril 2002;77(Suppl 2):S13–8. http://dx.doi.org/10.1016/S0015-0282(01)03275-7
127. O'Connell KJ, Osborne LM, Westhoff C. Measured and reported weight change for women using a vaginal contraceptive ring vs. a low-dose oral contraceptive. Contraception 2005;72:323–7. http://dx.doi.org/10.1016/j.contraception.2005.05.008

128. Paulen ME, Zapata LB, Cansino C, Curtis KM, Jamieson DJ. Contraceptive use among women with a history of bariatric surgery: a systematic review. Contraception 2010;82:86–94. http://dx.doi.org/10.1016/j.contraception.2010.02.008
129. Lidegaard Ø, Edström B, Kreiner S. Oral contraceptives and venous thromboembolism: a five-year national case-control study. Contraception 2002;65:187–96. http://dx.doi.org/10.1016/S0010-7824(01)00307-9
130. Croft P, Hannaford PC. Risk factors for acute myocardial infarction in women: evidence from the Royal College of General Practitioners' oral contraception study. BMJ 1989;298:165–8. http://dx.doi.org/10.1136/bmj.298.6667.165
131. D'Avanzo B, La Vecchia C, Negri E, Parazzini F, Franceschi S. Oral contraceptive use and risk of myocardial infarction: an Italian case-control study. J Epidemiol Community Health 1994;48:324–5. http://dx.doi.org/10.1136/jech.48.3.324
132. Dunn NR, Faragher B, Thorogood M, et al. Risk of myocardial infarction in young female smokers. Heart 1999;82:581–3. http://dx.doi.org/10.1136/hrt.82.5.581
133. Hannaford PC, Croft PR, Kay CR. Oral contraception and stroke. Evidence from the Royal College of General Practitioners' Oral Contraception Study. Stroke 1994;25:935–42. http://dx.doi.org/10.1161/01.STR.25.5.935
134. Heinemann LA, Lewis MA, Spitzer WO, Thorogood M, Guggenmoos-Holzmann I, Bruppacher R; Transnational Research Group on Oral Contraceptives and the Health of Young Women. Thromboembolic stroke in young women. A European case-control study on oral contraceptives. Contraception 1998;57:29–37. http://dx.doi.org/10.1016/S0010-7824(97)00204-7
135. Kemmeren JM, Tanis BC, van den Bosch MA, et al. Risk of Arterial Thrombosis in Relation to Oral Contraceptives (RATIO) study: oral contraceptives and the risk of ischemic stroke. Stroke 2002;33:1202–8. http://dx.doi.org/10.1161/01.STR.0000015345.61324.3F
136. Lewis MA, Heinemann LA, Spitzer WO, MacRae KD, Bruppacher R. The use of oral contraceptives and the occurrence of acute myocardial infarction in young women. Results from the Transnational Study on Oral Contraceptives and the Health of Young Women. Contraception 1997;56:129–40. http://dx.doi.org/10.1016/S0010-7824(97)00118-2
137. Lidegaard O. Oral contraception and risk of a cerebral thromboembolic attack: results of a case-control study. BMJ 1993;306:956–63. http://dx.doi.org/10.1136/bmj.306.6883.956
138. Lidegaard O. Oral contraceptives, pregnancy and the risk of cerebral thromboembolism: the influence of diabetes, hypertension, migraine and previous thrombotic disease. Br J Obstet Gynaecol 1995;102:153–9. http://dx.doi.org/10.1111/j.1471-0528.1995.tb09070.x
139. Lubianca JN, Faccin CS, Fuchs FD. Oral contraceptives: a risk factor for uncontrolled blood pressure among hypertensive women. Contraception 2003;67:19–24. http://dx.doi.org/10.1016/S0010-7824(02)00429-8
140. Narkiewicz K, Graniero GR, D'Este D, Mattarei M, Zonzin P, Palatini P. Ambulatory blood pressure in mild hypertensive women taking oral contraceptives. A case-control study. Am J Hypertens 1995;8:249–53. http://dx.doi.org/10.1016/0895-7061(95)96212-3
141. Siritho S, Thrift AG, McNeil JJ, You RX, Davis SM, Donnan GA; Melbourne Risk Factor Study (MERFS) Group. Risk of ischemic stroke among users of the oral contraceptive pill: The Melbourne Risk Factor Study (MERFS) Group. Stroke 2003;34:1575–80. http://dx.doi.org/10.1161/01.STR.0000077925.16041.6B
142. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Ischaemic stroke and combined oral contraceptives: results of an international, multicentre, case-control study. Lancet 1996;348:498–505. http://dx.doi.org/10.1016/S0140-6736(95)12393-8
143. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Acute myocardial infarction and combined oral contraceptives: results of an international multicentre case-control study. Lancet 1997;349:1202–9. http://dx.doi.org/10.1016/S0140-6736(97)02358-1
144. Lubianca JN, Moreira LB, Gus M, Fuchs FD. Stopping oral contraceptives: an effective blood pressure-lowering intervention in women with hypertension. J Hum Hypertens 2005;19:451–5. http://dx.doi.org/10.1038/sj.jhh.1001841
145. Aberg H, Karlsson L, Melander S. Studies on toxaemia of pregnancy with special reference to blood pressure. II. Results after 6–11 years' follow-up. Ups J Med Sci 1978;83:97–102. http://dx.doi.org/10.3109/03009737809179119
146. Carmichael SM, Taylor MM, Ayers CR. Oral contraceptives, hypertension, and toxemia. Obstet Gynecol 1970;35:371–6.
147. Meinel H, Ihle R, Laschinski M. [Effect of hormonal contraceptives on blood pressure following pregnancy-induced hypertension]. Zentralbl Gynakol 1987;109:527–31.
148. Pritchard JA, Pritchard SA. Blood pressure response to estrogen-progestin oral contraceptive after pregnancy-induced hypertension. Am J Obstet Gynecol 1977;129:733–9 http://dx.doi.org/10.1016/0002-9378(77)90390-8.
149. Sibai BM, Taslimi MM, el-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. Am J Obstet Gynecol 1986;155:501–7. http://dx.doi.org/10.1016/0002-9378(86)90266-8
150. Sibai BM, Ramadan MK, Chari RS, Friedman SA. Pregnancies complicated by HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): subsequent pregnancy outcome and long-term prognosis. Am J Obstet Gynecol 1995;172:125–9. http://dx.doi.org/10.1016/0002-9378(95)90099-3
151. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Haemorrhagic stroke, overall stroke risk, and combined oral contraceptives: results of an international, multicentre, case-control study. Lancet 1996;348:505–10. http://dx.doi.org/10.1016/S0140-6736(95)12394-6
152. Sidney S, Petitti DB, Soff GA, Cundiff DL, Tolan KK, Quesenberry CP Jr. Venous thromboembolic disease in users of low-estrogen combined estrogen-progestin oral contraceptives. Contraception 2004;70:3–10. http://dx.doi.org/10.1016/j.contraception.2004.02.010
153. Andersen BS, Olsen J, Nielsen GL, et al. Third generation oral contraceptives and heritable thrombophilia as risk factors of non-fatal venous thromboembolism. Thromb Haemost 1998;79:28–31.
154. Aznar J, Mira Y, Vayá A, et al. Factor V Leiden and prothrombin G20210A mutations in young adults with cryptogenic ischemic stroke. Thromb Haemost 2004;91:1031–4.
155. Bennet L, Odeberg H. Resistance to activated protein C, highly prevalent amongst users of oral contraceptives with venous thromboembolism. J Intern Med 1998;243:27–32. http://dx.doi.org/10.1046/j.1365-2796.1998.00310.x
156. Bloemenkamp KW, Rosendaal FR, Helmerhorst FM, Vandenbroucke JP. Higher risk of venous thrombosis during early use of oral contraceptives in women with inherited clotting defects.[comment]. Arch Intern Med 2000;160:49–52. http://dx.doi.org/10.1001/archinte.160.1.49

157. Bloemenkamp KW, Helmerhorst FM, Rosendaal FR, Vandenbroucke JP, Büller HR. Enhancement by factor V Leiden mutation of risk of deep-vein thrombosis associated with oral contraceptives containing a third-generation progestagen. Lancet 1995;346:1593–6. http://dx.doi.org/10.1016/S0140-6736(95)91929-5
158. de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP; The Cerebral Venous Sinus Thrombosis Study Group. Case-control study of risk of cerebral sinus thrombosis in oral contraceptive users and in [correction of who are] carriers of hereditary prothrombotic conditions. BMJ 1998;316:589–92. http://dx.doi.org/10.1136/bmj.316.7131.589
159. Emmerich J, Rosendaal FR, Cattaneo M, et al; Study Group for Pooled-Analysis in Venous Thromboembolism. Combined effect of factor V Leiden and prothrombin 20210A on the risk of venous thromboembolism—pooled analysis of 8 case-control studies including 2310 cases and 3204 controls. Thromb Haemost 2001;86:809–16.
160. Gadelha T, André C, Jucá AA, Nucci M. Prothrombin 20210A and oral contraceptive use as risk factors for cerebral venous thrombosis. Cerebrovasc Dis 2005;19:49–52. http://dx.doi.org/10.1159/000081911
161. Legnani C, Palareti G, Guazzaloca G, et al. Venous thromboembolism in young women; role of thrombophilic mutations and oral contraceptive use. Eur Heart J 2002;23:984–90. http://dx.doi.org/10.1053/euhj.2001.3082
162. Martinelli I, Battaglioli T, Bucciarelli P, Passamonti SM, Mannucci PM. Risk factors and recurrence rate of primary deep vein thrombosis of the upper extremities. Circulation 2004;110:566–70. http://dx.doi.org/10.1161/01.CIR.0000137123.55051.9B
163. Martinelli I, Sacchi E, Landi G, Taioli E, Duca F, Mannucci PM. High risk of cerebral-vein thrombosis in carriers of a prothrombin-gene mutation and in users of oral contraceptives.[comment]. N Engl J Med 1998;338:1793–7. http://dx.doi.org/10.1056/NEJM199806183382502
164. Martinelli I, Taioli E, Bucciarelli P, Akhavan S, Mannucci PM. Interaction between the G20210A mutation of the prothrombin gene and oral contraceptive use in deep vein thrombosis. Arterioscler Thromb Vasc Biol 1999;19:700–3. http://dx.doi.org/10.1161/01.ATV.19.3.700
165. Middeldorp S, Meinardi JR, Koopman MM, et al. A prospective study of asymptomatic carriers of the factor V Leiden mutation to determine the incidence of venous thromboembolism. [comment]. Ann Intern Med 2001;135:322–7. http://dx.doi.org/10.7326/0003-4819-135-5-200109040-00008
166. Pabinger I, Schneider B; The GTH Study Group on Natural Inhibitors. Thrombotic risk of women with hereditary antithrombin III-, protein C- and protein S-deficiency taking oral contraceptive medication. Thromb Haemost 1994;71:548–52.
167. Pezzini A, Grassi M, Iacoviello L, et al. Inherited thrombophilia and stratification of ischaemic stroke risk among users of oral contraceptives. J Neurol Neurosurg Psychiatry 2007;78:271–6. http://dx.doi.org/10.1136/jnnp.2006.101675
168. Santamaría A, Mateo J, Oliver A, et al. Risk of thrombosis associated with oral contraceptives of women from 97 families with inherited thrombophilia: high risk of thrombosis in carriers of the G20210A mutation of the prothrombin gene. Haematologica 2001;86:965–71.
169. Slooter AJ, Rosendaal FR, Tanis BC, Kemmeren JM, van der Graaf Y, Algra A. Prothrombotic conditions, oral contraceptives, and the risk of ischemic stroke. J Thromb Haemost 2005;3:1213–7. http://dx.doi.org/10.1111/j.1538-7836.2005.01442.x
170. Spannagl M, Heinemann LA, Schramm W. Are factor V Leiden carriers who use oral contraceptives at extreme risk for venous thromboembolism? Eur J Contracept Reprod Health Care 2000;5:105–12. http://dx.doi.org/10.1080/13625180008500383
171. van Boven HH, Vandenbroucke JP, Briët E, Rosendaal FR. Gene-gene and gene-environment interactions determine risk of thrombosis in families with inherited antithrombin deficiency. Blood 1999;94:2590–4.
172. van Vlijmen EF, Brouwer JL, Veeger NJ, Eskes TK, de Graeff PA, van der Meer J. Oral contraceptives and the absolute risk of venous thromboembolism in women with single or multiple thrombophilic defects: results from a retrospective family cohort study. Arch Intern Med 2007;167:282–9. http://dx.doi.org/10.1001/archinte.167.3.282
173. Vandenbroucke JP, Koster T, Rosendaal FR, Briët E, Reitsma PH, Bertina RM. Increased risk of venous thrombosis in oral-contraceptive users who are carriers of factor V Leiden mutation.[comment]. Lancet 1994;344:1453–7. http://dx.doi.org/10.1016/S0140-6736(94)90286-0
174. Vayá A, Mira Y, Mateo J, et al. Prothrombin G20210A mutation and oral contraceptive use increase upper-extremity deep vein thrombotic risk. Thromb Haemost 2003;89:452–7.
175. Martinelli I, Battaglioli T, Burgo I, Di Domenico S, Mannucci PM. Oral contraceptive use, thrombophilia and their interaction in young women with ischemic stroke. Haematologica 2006;91:844–7.
176. Tepper NK, Marchbanks PA, Curtis KM. Superficial venous disease and combined hormonal contraceptives: a systematic review. Contraception 2015;S0010-7824(15)00128-6.
177. Tepper NK, Paulen ME, Marchbanks PA, Curtis KM. Safety of contraceptive use among women with peripartum cardiomyopathy: a systematic review. Contraception 2010;82:95–101. http://dx.doi.org/10.1016/j.contraception.2010.02.004
178. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Little, Brown and Co; 1994.
179. Bernatsky S, Clarke A, Ramsey-Goldman R, et al. Hormonal exposures and breast cancer in a sample of women with systemic lupus erythematosus. Rheumatology (Oxford) 2004;43:1178–81. http://dx.doi.org/10.1093/rheumatology/keh282
180. Bernatsky S, Ramsey-Goldman R, Gordon C, et al. Factors associated with abnormal Pap results in systemic lupus erythematosus. Rheumatology (Oxford) 2004;43:1386–9. http://dx.doi.org/10.1093/rheumatology/keh331
181. Chopra N, Koren S, Greer WL, et al. Factor V Leiden, prothrombin gene mutation, and thrombosis risk in patients with antiphospholipid antibodies. J Rheumatol 2002;29:1683–8.
182. Esdaile JM, Abrahamowicz M, Grodzicky T, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum 2001;44:2331–7. http://dx.doi.org/10.1002/1529-0131(200110)44:10<2331::AID-ART395≥3.0.CO;2-I
183. Julkunen HA. Oral contraceptives in systemic lupus erythematosus: side-effects and influence on the activity of SLE. Scand J Rheumatol 1991;20:427–33. http://dx.doi.org/10.3109/03009749109096822
184. Julkunen HA, Kaaja R, Friman C. Contraceptive practice in women with systemic lupus erythematosus. Br J Rheumatol 1993;32:227–30. http://dx.doi.org/10.1093/rheumatology/32.3.227
185. Jungers P, Dougados M, Pélissier C, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. Arthritis Rheum 1982;25:618–23. http://dx.doi.org/10.1002/art.1780250603
186. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol 1997;145:408–15. http://dx.doi.org/10.1093/oxfordjournals.aje.a009122

187. McAlindon T, Giannotta L, Taub N, D'Cruz D, Hughes G. Environmental factors predicting nephritis in systemic lupus erythematosus. Ann Rheum Dis 1993;52:720–4. http://dx.doi.org/10.1136/ard.52.10.720
188. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. Ann Rheum Dis 1992;51:56–60. http://dx.doi.org/10.1136/ard.51.1.56
189. Mintz G, Gutiérrez G, Delezé M, Rodríguez E. Contraception with progestagens in systemic lupus erythematosus. Contraception 1984;30:29–38. http://dx.doi.org/10.1016/0010-7824(84)90076-3
190. Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res 1995;8:137–45. http://dx.doi.org/10.1002/art.1790080305
191. Petri M. Lupus in Baltimore: evidence-based 'clinical pearls' from the Hopkins Lupus Cohort. Lupus 2005;14:970–3. http://dx.doi.org/10.1191/0961203305lu2230xx
192. Petri M, Kim MY, Kalunian KC, et al; OC-SELENA Trial. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med 2005;353:2550–8. http://dx.doi.org/10.1056/NEJMoa051135
193. Sánchez-Guerrero J, Uribe AG, Jiménez-Santana L, et al. A trial of contraceptive methods in women with systemic lupus erythematosus. N Engl J Med 2005;353:2539–49. http://dx.doi.org/10.1056/NEJMoa050817
194. Sarabi ZS, Chang E, Bobba R, et al. Incidence rates of arterial and venous thrombosis after diagnosis of systemic lupus erythematosus. Arthritis Rheum 2005;53:609–12. http://dx.doi.org/10.1002/art.21314
195. Schaedel ZE, Dolan G, Powell MC. The use of the levonorgestrel-releasing intrauterine system in the management of menorrhagia in women with hemostatic disorders. Am J Obstet Gynecol 2005;193:1361–3. http://dx.doi.org/10.1016/j.ajog.2005.05.002
196. Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. J Rheumatol 2002;29:2531–6.
197. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, Ogryzlo MA. The bimodal mortality pattern of systemic lupus erythematosus. Am J Med 1976;60:221–5. http://dx.doi.org/10.1016/0002-9343(76)90431-9
198. Choojitarom K, Verasertniyom O, Totemchokchyakarn K, Nantiruj K, Sumethkul V, Janwityanujit S. Lupus nephritis and Raynaud's phenomenon are significant risk factors for vascular thrombosis in SLE patients with positive antiphospholipid antibodies. Clin Rheumatol 2008;27:345–51. http://dx.doi.org/10.1007/s10067-007-0721-z
199. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus—a meta-analysis. Lupus 1997;6:467–73. http://dx.doi.org/10.1177/096120339700600510
200. Farr SL, Folger SG, Paulen ME, Curtis KM. Safety of contraceptive methods for women with rheumatoid arthritis: a systematic review. Contraception 2010;82:64–71. http://dx.doi.org/10.1016/j.contraception.2010.02.003
201. Tepper NK, Whiteman MK, Zapata LB, Marchbanks PA, Curtis KM. Safety of hormonal contraceptives among women with migraine: a systematic review. Contraception 2016. Epub May 3, 2016. http:// dx.doi.org/10.1016/j.contraception.2016.04.016
202. Xu Z, Li Y, Tang S, Huang X, Chen T. Current use of oral contraceptives and the risk of first-ever ischemic stroke: A meta-analysis of observational studies. Thromb Res 2015;136:52–60. http://dx.doi.org/10.1016/j.thromres.2015.04.021
203. Etminan M, Takkouche B, Isorna FC, Samii A. Risk of ischaemic stroke in people with migraine: systematic review and meta-analysis of observational studies. BMJ 2005;330:63. http://dx.doi.org/10.1136/bmj.38302.504063.8F
204. Schürks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and cardiovascular disease: systematic review and meta-analysis. BMJ 2009;339:b3914. http://dx.doi.org/10.1136/bmj.b3914
205. Spector JT, Kahn SR, Jones MR, Jayakumar M, Dalal D, Nazarian S. Migraine headache and ischemic stroke risk: an updated meta-analysis. Am J Med 2010;123:612–24. http://dx.doi.org/10.1016/j.amjmed.2009.12.021
206. Zapata LB, Oduyebo T, Whiteman MK, Marchbanks PA, Curtis KM. Contraceptive use among women with multiple sclerosis: a systematic review. Contraception. In press 2016.
207. Pagano HP, Zapata LB, Berry-Bibee EN, Nanda K, Curtis KM. Safety of hormonal contraception and intrauterine devices among women with depressive and bipolar disorders: a systematic review. Contraception 2016. Epub June 27, 2016. http://dx.doi.org/10.1016/j.contraception.2016.06.012
208. Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding. Cochrane Database Syst Rev 2000;(2):CD000154.
209. Davis L, Kennedy SS, Moore J, Prentice A. Oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev 2007;(3):CD001019.
210. Hendrix SL, Alexander NJ. Primary dysmenorrhea treatment with a desogestrel-containing low-dose oral contraceptive. Contraception 2002;66:393–9. http://dx.doi.org/10.1016/S0010-7824(02)00414-6
211. Proctor ML, Roberts H, Farquhar CM. Combined oral contraceptive pill (OCP) as treatment for primary dysmenorrhoea. Cochrane Database Syst Rev 2001;(4):CD002120.
212. Gaffield ME, Kapp N, Curtis KM. Combined oral contraceptive and intrauterine device use among women with gestational trophoblastic disease. Contraception 2009;80:363–71. http://dx.doi.org/10.1016/j.contraception.2009.03.022
213. Smith JS, Green J, Berrington de Gonzalez A, et al. Cervical cancer and use of hormonal contraceptives: a systematic review. Lancet 2003;361:1159–67. http://dx.doi.org/10.1016/S0140-6736(03)12949-2
214. Black MM, Barclay THC, Polednak A, Kwon CS, Leis HP Jr, Pilnik S. Family history, oral contraceptive usage, and breast cancer. Cancer 1983;51:2147–51. http://dx.doi.org/10.1002/1097-0142(19830601)51:11<2147::AID-CNCR2820511133≥3.0.CO;2-X
215. Brinton LA, Hoover R, Szklo M, Fraumeni JF Jr. Oral contraceptives and breast cancer. Int J Epidemiol 1982;11:316–22. http://dx.doi.org/10.1093/ije/11.4.316
216. Brohet RM, Goldgar DE, Easton DF, et al. Oral contraceptives and breast cancer risk in the international BRCA1/2 carrier cohort study: a report from EMBRACE, GENEPSO, GEO-HEBON, and the IBCCS Collaborating Group. J Clin Oncol 2007;25:3831–6. http://dx.doi.org/10.1200/JCO.2007.11.1179
217. Claus EB, Stowe M, Carter D. Oral contraceptives and the risk of ductal breast carcinoma in situ. Breast Cancer Res Treat 2003;81:129–36. http://dx.doi.org/10.1023/A:1025728524310
218. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet 2001;358:1389–99. http://dx.doi.org/10.1016/S0140-6736(01)06524-2
219. Grabrick DM, Hartmann LC, Cerhan JR, et al. Risk of breast cancer with oral contraceptive use in women with a family history of breast cancer.[comment]. JAMA 2000;284:1791–8. http://dx.doi.org/10.1001/jama.284.14.1791
220. Gronwald J, Byrski T, Huzarski T, et al. Influence of selected lifestyle factors on breast and ovarian cancer risk in BRCA1 mutation carriers from Poland. Breast Cancer Res Treat 2006;95:105–9. http://dx.doi.org/10.1007/s10549-005-9051-5

221. Haile RW, Thomas DC, McGuire V, et al; kConFab Investigators; Ontario Cancer Genetics Network Investigators. BRCA1 and BRCA2 mutation carriers, oral contraceptive use, and breast cancer before age 50. Cancer Epidemiol Biomarkers Prev 2006;15:1863–70. http://dx.doi.org/10.1158/1055-9965.EPI-06-0258
222. Harris NV, Weiss NS, Francis AM, Polissar L. Breast cancer in relation to patterns of oral contraceptive use. Am J Epidemiol 1982;116:643–51.
223. Hennekens CH, Speizer FE, Lipnick RJ, et al. A case-control study of oral contraceptive use and breast cancer. J Natl Cancer Inst 1984;72:39–42.
224. Jernström H, Loman N, Johannsson OT, Borg A, Olsson H. Impact of teenage oral contraceptive use in a population-based series of early-onset breast cancer cases who have undergone BRCA mutation testing. Eur J Cancer 2005;41:2312–20. http://dx.doi.org/10.1016/j.ejca.2005.03.035
225. Marchbanks PA, McDonald JA, Wilson HG, et al. Oral contraceptives and the risk of breast cancer. N Engl J Med 2002;346:2025–32. http://dx.doi.org/10.1056/NEJMoa013202
226. Milne RL, Knight JA, John EM, et al. Oral contraceptive use and risk of early-onset breast cancer in carriers and noncarriers of BRCA1 and BRCA2 mutations. Cancer Epidemiol Biomarkers Prev 2005;14:350–6. http://dx.doi.org/10.1158/1055-9965.EPI-04-0376
227. Narod SA, Dubé MP, Klijn J, et al. Oral contraceptives and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. J Natl Cancer Inst 2002;94:1773–9. http://dx.doi.org/10.1093/jnci/94.23.1773
228. Rosenberg L, Palmer JR, Rao RS, et al. Case-control study of oral contraceptive use and risk of breast cancer. Am J Epidemiol 1996;143:25–37. http://dx.doi.org/10.1093/oxfordjournals.aje.a008654
229. Silvera SA, Miller AB, Rohan TE. Oral contraceptive use and risk of breast cancer among women with a family history of breast cancer: a prospective cohort study. Cancer Causes Control 2005;16:1059–63. http://dx.doi.org/10.1007/s10552-005-0343-1
230. Ursin G, Henderson BE, Haile RW, et al. Does oral contraceptive use increase the risk of breast cancer in women with BRCA1/BRCA2 mutations more than in other women? Cancer Res 1997;57:3678–81.
231. Ursin G, Ross RK, Sullivan-Halley J, Hanisch R, Henderson B, Bernstein L. Use of oral contraceptives and risk of breast cancer in young women. Breast Cancer Res Treat 1998;50:175–84. http://dx.doi.org/10.1023/A:1006037823178
232. Polis CB, Phillips SJ, Curtis KM, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. Contraception 2014;90:360–90. http://dx.doi.org/10.1016/j.contraception.2014.07.009
233. Polis CB, Phillips SJ, Curtis KM. Hormonal contraceptive use and female-to-male HIV transmission: a systematic review of the epidemiologic evidence. AIDS 2013;27:493–505. http://dx.doi.org/10.1097/QAD.0b013e32835ad539
234. Phillips SJ, Polis CB, Curtis KM. The safety of hormonal contraceptives for women living with HIV and their sexual partners. Contraception 2016;93:11–6 http://dx.doi.org/10.1016/j.contraception.2015.10.002.
235. Phillips SJ, Curtis KM, Polis CB. Effect of hormonal contraceptive methods on HIV disease progression: a systematic review. AIDS 2013;27:787–94. http://dx.doi.org/10.1097/QAD.0b013e32835bb672
236. el-Raghy I, Back DJ, Osman F, Orme ML, Fathalla M. Contraceptive steroid concentrations in women with early active schistosomiasis: lack of effect of antischistosomal drugs. Contraception 1986;33:373–7. http://dx.doi.org/10.1016/0010-7824(86)90099-5
237. Gad-el-Mawla N, Abdallah A. Liver function in bilharzial females receiving contraceptive pills. Acta Hepatosplenol 1969;16:308–10.
238. Gad-el-Mawla N, el-Roubi O, Sabet S, Abdallah A. Plasma lipids and lipoproteins in bilharzial females during oral contraceptive therapy. J Egypt Med Assoc 1972;55:137–47.
239. Shaaban MM, Hammad WA, Falthalla MF, et al. Effects of oral contraception on liver function tests and serum proteins in women with active schistosomiasis. Contraception 1982;26:75–82. http://dx.doi.org/10.1016/0010-7824(82)90174-3
240. Shaaban MM, Ghaneimah SA, Mohamed MA, Abdel-Chani S, Mostafa SA. Effect of oral contraception on serum bile acid. Int J Gynaecol Obstet 1984;22:111–5. http://dx.doi.org/10.1016/0020-7292(84)90023-7
241. Sy FS, Osteria TS, Opiniano V, Gler S. Effect of oral contraceptive on liver function tests of women with schistosomiasis in the Philippines. Contraception 1986;34:283–94. http://dx.doi.org/10.1016/0010-7824(86)90009-0
242. Tagy AH, Saker ME, Moussa AA, Kolgah A. The effect of low-dose combined oral contraceptive pills versus injectable contraceptive (Depot Provera) on liver function tests of women with compensated bilharzial liver fibrosis. Contraception 2001;64:173–6. http://dx.doi.org/10.1016/S0010-7824(01)00248-7
243. Beck P, Wells SA. Comparison of the mechanisms underlying carbohydrate intolerance in subclinical diabetic women during pregnancy and during post-partum oral contraceptive steroid treatment. J Clin Endocrinol Metab 1969;29:807–18. http://dx.doi.org/10.1210/jcem-29-6-807
244. Kjos SL, Peters RK, Xiang A, Thomas D, Schaefer U, Buchanan TA. Contraception and the risk of type 2 diabetes mellitus in Latina women with prior gestational diabetes mellitus. JAMA 1998;280:533–8. http://dx.doi.org/10.1001/jama.280.6.533
245. Kung AW, Ma JT, Wong VC, et al. Glucose and lipid metabolism with triphasic oral contraceptives in women with history of gestational diabetes. Contraception 1987;35:257–69. http://dx.doi.org/10.1016/0010-7824(87)90027-8
246. Rådberg T, Gustafson A, Skryten A, Karlsson K. Metabolic studies in gestational diabetic women during contraceptive treatment: effects on glucose tolerance and fatty acid composition of serum lipids. Gynecol Obstet Invest 1982;13:17–29. http://dx.doi.org/10.1159/000299480
247. Skouby SO, Andersen O, Kühl C. Oral contraceptives and insulin receptor binding in normal women and those with previous gestational diabetes. Am J Obstet Gynecol 1986;155:802–7. http://dx.doi.org/10.1016/S0002-9378(86)80024-2
248. Skouby SO, Andersen O, Saurbrey N, Kühl C. Oral contraception and insulin sensitivity: in vivo assessment in normal women and women with previous gestational diabetes. J Clin Endocrinol Metab 1987;64:519–23. http://dx.doi.org/10.1210/jcem-64-3-519
249. Skouby SO, Mølsted-Pedersen L, Kühl C. Low dosage oral contraception in women with previous gestational diabetes. Obstet Gynecol 1982;59:325–8.
250. Xiang AH, Kawakubo M, Kjos SL, Buchanan TA. Long-acting injectable progestin contraception and risk of type 2 diabetes in Latino women with prior gestational diabetes mellitus. Diabetes Care 2006;29:613–7. http://dx.doi.org/10.2337/diacare.29.03.06.dc05-1940
251. Kjos SL, Shoupe D, Douyan S, et al. Effect of low-dose oral contraceptives on carbohydrate and lipid metabolism in women with recent gestational diabetes: results of a controlled, randomized, prospective study. Am J Obstet Gynecol 1990;163:1822–7. http://dx.doi.org/10.1016/0002-9378(90)90757-X
252. Rådberg T, Gustafson A, Skryten A, Karlsson K. Metabolic studies in women with previous gestational diabetes during contraceptive treatment: effects on serum lipids and high density lipoproteins. Acta Endocrinol (Copenh) 1982;101:134–9.

253. Skouby SO, Kühl C, Mølsted-Pedersen L, Petersen K, Christensen MS. Triphasic oral contraception: metabolic effects in normal women and those with previous gestational diabetes. Am J Obstet Gynecol 1985;153:495–500. http://dx.doi.org/10.1016/0002-9378(85)90460-0
254. Beck P, Arnett DM, Alsever RN, Eaton RP. Effect of contraceptive steroids on arginine- stimulated glucagon and insulin secretion in women. II. Carbohydrate and lipid physiology in insulin-dependent diabetics. Metabolism 1976;25:23–31 http://dx.doi.org/10.1016/0026-0495(76)90156-6.
255. Diab KM, Zaki MM. Contraception in diabetic women: comparative metabolic study of Norplant, depot medroxyprogesterone acetate, low dose oral contraceptive pill and CuT380A. J Obstet Gynaecol Res 2000;26:17–26. http://dx.doi.org/10.1111/j.1447-0756.2000.tb01195.x
256. Garg SK, Chase HP, Marshall G, Hoops SL, Holmes DL, Jackson WE. Oral contraceptives and renal and retinal complications in young women with insulin-dependent diabetes mellitus. JAMA 1994;271:1099–102. http://dx.doi.org/10.1001/jama.1994.03510380055037
257. Grigoryan OR, Grodnitskaya EE, Andreeva EN, Shestakova MV, Melnichenko GA, Dedov II. Contraception in perimenopausal women with diabetes mellitus. Gynecol Endocrinol 2006;22:198–206. http://dx.doi.org/10.1080/09513590600624317
258. Margolis KL, Adami H-O, Luo J, Ye W, Weiderpass E. A prospective study of oral contraceptive use and risk of myocardial infarction among Swedish women. Fertil Steril 2007;88:310–6. http://dx.doi.org/10.1016/j.fertnstert.2006.11.206
259. Petersen KR, Skouby SO, Jespersen J. Balance of coagulation activity with fibrinolysis during use of oral contraceptives in women with insulin-dependent diabetes mellitus. Int J Fertil Menopausal Stud 1995;40(Suppl 2):105–11.
260. Petersen KR, Skouby SO, Sidelmann J, Jespersen J. Assessment of endothelial function during oral contraception in women with insulin-dependent diabetes mellitus. Metabolism 1994;43:1379–83. http://dx.doi.org/10.1016/0026-0495(94)90031-0
261. Rådberg T, Gustafson A, Skryten A, Karlsson K. Oral contraception in diabetic women. A cross-over study on serum and high density lipoprotein (HDL) lipids and diabetes control during progestogen and combined estrogen/progestogen contraception. Horm Metab Res 1982;14:61–5.
262. Skouby SO, Jensen BM, Kühl C, Mølsted-Pedersen L, Svenstrup B, Nielsen J. Hormonal contraception in diabetic women: acceptability and influence on diabetes control and ovarian function of a nonalkylated estrogen/progestogen compound. Contraception 1985;32:23–31. http://dx.doi.org/10.1016/0010-7824(85)90113-1
263. Skouby SO, Mølsted-Pedersen L, Kühl C, Bennet P. Oral contraceptives in diabetic women: metabolic effects of four compounds with different estrogen/progestogen profiles. Fertil Steril 1986;46:858–64 http://dx.doi.org/10.1016/S0015-0282(16)49825-0.
264. Zapata LB, Paulen ME, Cansino C, Marchbanks PA, Curtis KM. Contraceptive use among women with inflammatory bowel disease: A systematic review. Contraception 2010;82:72–85. http://dx.doi.org/10.1016/j.contraception.2010.02.012
265. Kapp N, Tilley IB, Curtis KM. The effects of hormonal contraceptive use among women with viral hepatitis or cirrhosis of the liver: a systematic review. Contraception 2009;80:381–6. http://dx.doi.org/10.1016/j.contraception.2009.04.007
266. Kapp N, Curtis KM. Hormonal contraceptive use among women with liver tumors: a systematic review. Contraception 2009;80:387–90. http://dx.doi.org/10.1016/j.contraception.2009.01.021
267. Whiteman MK, Oduyebo T, Zapata LB, Walker S, Curtis KM. Contraceptive safety among women with cystic fibrosis: a systematic review. Contraception 2016. Epub June 7, 2016. http://dx.doi.org/10.1016/j.contraception.2016.05.016
268. Paulen ME, Folger SG, Curtis KM, Jamieson DJ. Contraceptive use among solid organ transplant patients: a systematic review. Contraception 2010;82:102–12. http://dx.doi.org/10.1016/j.contraception.2010.02.007
269. Aweeka FT, Rosenkranz SL, Segal Y, et al; NIAID AIDS Clinical Trials Group. The impact of sex and contraceptive therapy on the plasma and intracellular pharmacokinetics of zidovudine. AIDS 2006;20:1833–41. http://dx.doi.org/10.1097/01.aids.0000244202.18629.36
270. Kearney BP, Mathias A. Lack of effect of tenofovir disoproxil fumarate on pharmacokinetics of hormonal contraceptives. Pharmacotherapy 2009;29:924–9. http://dx.doi.org/10.1592/phco.29.8.924
271. Todd CS, Deese J, Wang M, et al; FEM-PrEP Study Group. Sino-implant (II)® continuation and effect of concomitant tenofovir disoproxil fumarate-emtricitabine use on plasma levonorgestrel concentrations among women in Bondo, Kenya. Contraception 2015;91:248–52. http://dx.doi.org/10.1016/j.contraception.2014.10.008
272. Murnane PM, Heffron R, Ronald A, et al; Partners PrEP Study Team. Pre-exposure prophylaxis for HIV-1 prevention does not diminish the pregnancy prevention effectiveness of hormonal contraception. AIDS 2014;28:1825–30. http://dx.doi.org/10.1097/QAD.0000000000000290
273. Kasonde M, Niska RW, Rose C, et al. Bone mineral density changes among HIV-uninfected young adults in a randomised trial of pre-exposure prophylaxis with tenofovir-emtricitabine or placebo in Botswana. PLoS One 2014;9:e90111. http://dx.doi.org/10.1371/journal.pone.0090111
274. Callahan R, Nanda K, Kapiga S, et al; FEM-PrEP Study Group. Pregnancy and contraceptive use among women participating in the FEM-PrEP trial. J Acquir Immune Defic Syndr 2015;68:196–203. http://dx.doi.org/10.1097/QAI.0000000000000413
275. Patel RC, Onono M, Gandhi M, et al. Pregnancy rates in HIV-positive women using contraceptives and efavirenz-based or nevirapine-based antiretroviral therapy in Kenya: a retrospective cohort study. Lancet HIV 2015;2:e474–82. http://dx.doi.org/10.1016/S2352-3018(15)00184-8
276. Pyra M, Heffron R, Mugo NR, et al; Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study Teams. Effectiveness of hormonal contraception in HIV-infected women using antiretroviral therapy. AIDS 2015;29:2353–9. http://dx.doi.org/10.1097/QAD.0000000000000827
277. Clark RA, Theall K. Population-based study evaluating association between selected antiretroviral therapies and potential oral contraceptive failure. J Acquir Immune Defic Syndr 2004;37:1219–20. http://dx.doi.org/10.1097/01.qai.0000136724.15758.ae
278. Landolt NK, Phanuphak N, Ubolyam S, et al. Efavirenz, in contrast to nevirapine, is associated with unfavorable progesterone and antiretroviral levels when coadministered with combined oral contraceptives. J Acquir Immune Defic Syndr 2013;62:534–9. http://dx.doi.org/10.1097/QAI.0b013e31827e8f98
279. Sevinsky H, Eley T, Persson A, et al. The effect of efavirenz on the pharmacokinetics of an oral contraceptive containing ethinyl estradiol and norgestimate in healthy HIV-negative women. Antivir Ther 2011;16:149–56. http://dx.doi.org/10.3851/IMP1725
280. Landolt NK, Phanuphak N, Ubolyam S, et al. Significant decrease of ethinylestradiol with nevirapine, and of etonogestrel with efavirenz in HIV-positive women. J Acquir Immune Defic Syndr 2014;66:e50–2.
281. Schöller-Gyüre M, Kakuda TN, Woodfall B, et al. Effect of steady-state etravirine on the pharmacokinetics and pharmacodynamics of ethinylestradiol and norethindrone. Contraception 2009;80:44–52. http://dx.doi.org/10.1016/j.contraception.2009.01.009

282. Myer L, Carter RJ, Katyal M, Toro P, El-Sadr WM, Abrams EJ. Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: a cohort study. PLoS Med 2010;7:e1000229. http://dx.doi.org/10.1371/journal.pmed.1000229
283. Nanda K, Delany-Moretlwe S, Dubé K, et al. Nevirapine-based antiretroviral therapy does not reduce oral contraceptive effectiveness. AIDS 2013;27(Suppl 1):S17–25. http://dx.doi.org/10.1097/QAD.0000000000000050
284. Stuart GS, Moses A, Corbett A, et al. Combined oral contraceptives and antiretroviral PK/PD in Malawian women: pharmacokinetics and pharmacodynamics of a combined oral contraceptive and a generic combined formulation antiretroviral in Malawi. J Acquir Immune Defic Syndr 2011;58:e40–3. http://dx.doi.org/10.1097/QAI.0b013e31822b8bf8
285. Mildvan D, Yarrish R, Marshak A, et al. Pharmacokinetic interaction between nevirapine and ethinyl estradiol/norethindrone when administered concurrently to HIV-infected women. J Acquir Immune Defic Syndr 2002;29:471–7. http://dx.doi.org/10.1097/00042560-200204150-00007
286. Muro E, Droste JA, Hofstede HT, Bosch M, Dolmans W, Burger DM. Nevirapine plasma concentrations are still detectable after more than 2 weeks in the majority of women receiving single-dose nevirapine: implications for intervention studies. J Acquir Immune Defic Syndr 2005;39:419–2. http://dx.doi.org/10.1097/01.qai.0000167154.37357.f9
287. Crauwels HM, van Heeswijk RP, Buelens A, Stevens M, Hoetelmans RM. Lack of an effect of rilpivirine on the pharmacokinetics of ethinylestradiol and norethindrone in healthy volunteers. Int J Clin Pharmacol Ther 2014;52:118–28. http://dx.doi.org/10.5414/CP201943
288. Zhang J, Chung E, Yones C, et al. The effect of atazanavir/ritonavir on the pharmacokinetics of an oral contraceptive containing ethinyl estradiol and norgestimate in healthy women. Antivir Ther 2011;16:157–64. http://dx.doi.org/10.3851/IMP1724
289. Sekar VJ, Lefebvre E, Guzman SS, et al. Pharmacokinetic interaction between ethinyl estradiol, norethindrone and darunavir with low-dose ritonavir in healthy women. Antivir Ther 2008;13:563–9.
290. Glaxo Smith Kline. Lexiva (fosamprenavir calcium) [Package insert]. Research Triangle Park, NC: Glaxo Smith Kline; 2015.
291. Vogler MA, Patterson K, Kamemoto L, et al. Contraceptive efficacy of oral and transdermal hormones when co-administered with protease inhibitors in HIV-1-infected women: pharmacokinetic results of ACTG trial A5188. J Acquir Immune Defic Syndr 2010;55:473–82. http://dx.doi.org/10.1097/QAI.0b013e3181eb5ff5
292. Fröhlich M, Burhenne J, Martin-Facklam M, et al. Oral contraception does not alter single dose saquinavir pharmacokinetics in women. Br J Clin Pharmacol 2004;57:244–52 http://dx.doi.org/10.1111/j.1365-2125.2003.01983.x.
293. Boehringer Ingelheim Pharmaceuticals. Aptivus (tipranavir) [Package insert]. Ridgefield, CT; 2005.
294. Bristol-Myers Squibb. Reyataz (atazanavir sulfate) [Package insert]. Princeton, NJ; 2003.
295. Abel S, Russell D, Whitlock LA, Ridgway CE, Muirhead GJ. Effect of maraviroc on the pharmacokinetics of midazolam, lamivudine/zidovudine, and ethinyloestradiol/levonorgestrel in healthy volunteers. Br J Clin Pharmacol 2008;65(Suppl 1):19–26. http://dx.doi.org/10.1111/j.1365-2125.2008.03132.x
296. Anderson MS, Hanley WD, Moreau AR, et al. Effect of raltegravir on estradiol and norgestimate plasma pharmacokinetics following oral contraceptive administration in healthy women. Br J Clin Pharmacol 2011;71:616–20. http://dx.doi.org/10.1111/j.1365-2125.2010.03885.x
297. Song IH, Borland J, Chen S, Wajima T, Peppercorn AF, Piscitelli SC. Dolutegravir has no effect on the pharmacokinetics of oral contraceptives with norgestimate and ethinyl estradiol. Ann Pharmacother 2015;49:784–9. http://dx.doi.org/10.1177/1060028015580637
298. Gilead Sciences. Vitekta (elvitegravir) [Package insert]. Foster City, CA; 2012.
299. Back DJ, Bates M, Bowden A, et al. The interaction of phenobarbital and other anticonvulsants with oral contraceptive steroid therapy. Contraception 1980;22:495–503. http://dx.doi.org/10.1016/0010-7824(80)90102-X
300. Doose DR, Wang SS, Padmanabhan M, Schwabe S, Jacobs D, Bialer M. Effect of topiramate or carbamazepine on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in healthy obese and nonobese female subjects. Epilepsia 2003;44:540–9. http://dx.doi.org/10.1046/j.1528-1157.2003.55602.x
301. Fattore C, Cipolla G, Gatti G, et al. Induction of ethinylestradiol and levonorgestrel metabolism by oxcarbazepine in healthy women. Epilepsia 1999;40:783–7. http://dx.doi.org/10.1111/j.1528-1157.1999.tb00779.x
302. Rosenfeld WE, Doose DR, Walker SA, Nayak RK. Effect of topiramate on the pharmacokinetics of an oral contraceptive containing norethindrone and ethinyl estradiol in patients with epilepsy. Epilepsia 1997;38:317–23. http://dx.doi.org/10.1111/j.1528-1157.1997.tb01123.x
303. Christensen J, Petrenaite V, Atterman J, et al. Oral contraceptives induce lamotrigine metabolism: evidence from a double-blind, placebo-controlled trial. Epilepsia 2007;48:484–9. http://dx.doi.org/10.1111/j.1528-1167.2007.00997.x
304. Contin M, Albani F, Ambrosetto G, et al. Variation in lamotrigine plasma concentrations with hormonal contraceptive monthly cycles in patients with epilepsy. Epilepsia 2006;47:1573–5. http://dx.doi.org/10.1111/j.1528-1167.2006.00558.x
305. Reimers A, Helde G, Brodtkorb E. Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Epilepsia 2005;46:1414–7. http://dx.doi.org/10.1111/j.1528-1167.2005.10105.x
306. Sabers A, Buchholt JM, Uldall P, Hansen EL. Lamotrigine plasma levels reduced by oral contraceptives. Epilepsy Res 2001;47:151–4. http://dx.doi.org/10.1016/S0920-1211(01)00305-9
307. Sabers A, Ohman I, Christensen J, Tomson T. Oral contraceptives reduce lamotrigine plasma levels. Neurology 2003;61:570–1. http://dx.doi.org/10.1212/01.WNL.0000076485.09353.7A
308. Back DJ, Breckenridge AM, MacIver M, et al. The effects of ampicillin on oral contraceptive steroids in women. Br J Clin Pharmacol 1982;14:43–8. http://dx.doi.org/10.1111/j.1365-2125.1982.tb04932.x
309. Back DJ, Grimmer SF, Orme ML, Proudlove C, Mann RD, Breckenridge AM. Evaluation of Committee on Safety of Medicines yellow card reports on oral contraceptive-drug interactions with anticonvulsants and antibiotics. Br J Clin Pharmacol 1988;25:527–32. http://dx.doi.org/10.1111/j.1365-2125.1988.tb03341.x
310. Back DJ, Tjia J, Martin C, et al. The lack of interaction between temafloxacin and combined oral contraceptive steroids. Contraception 1991;43:317–23. http://dx.doi.org/10.1016/0010-7824(91)90070-V
311. Bacon JF, Shenfield GM. Pregnancy attributable to interaction between tetracycline and oral contraceptives. BMJ 1980;280:293. http://dx.doi.org/10.1136/bmj.280.6210.293
312. Bainton R. Interaction between antibiotic therapy and contraceptive medication. Oral Surg Oral Med Oral Pathol 1986;61:453–5. http://dx.doi.org/10.1016/0030-4220(86)90385-3
313. Bollen M. Use of antibiotics when taking the oral contraceptive pill. [comment]. Aust Fam Physician 1995;24:928–9.
314. Bromham DR, Cartmill RS. Knowledge and use of secondary contraception among patients requesting termination of pregnancy. BMJ 1993;306:556–7. http://dx.doi.org/10.1136/bmj.306.6877.556

315. Côté J. Interaction of griseofulvin and oral contraceptives.[comment]. J Am Acad Dermatol 1990;22:124–5. http://dx.doi.org/10.1016/S0190-9622(08)80010-2
316. Csemiczky G, Alvendal C, Landgren BM. Risk for ovulation in women taking a low-dose oral contraceptive (Microgynon) when receiving antibacterial treatment with a fluoroquinolone (ofloxacin). Adv Contracept 1996;12:101–9. http://dx.doi.org/10.1007/BF01849631
317. de Groot AC, Eshuis H, Stricker BH. Inefficacy of oral contraception during use of minocycline [Dutch]. Ned Tijdschr Geneeskd 1990;134:1227–9.
318. DeSano EA Jr, Hurley SC. Possible interactions of antihistamines and antibiotics with oral contraceptive effectiveness. Fertil Steril 1982;37:853–4 http://dx.doi.org/10.1016/S0015-0282(16)46350-8.
319. Donley TG, Smith RF, Roy B. Reduced oral contraceptive effectiveness with concurrent antibiotic use: a protocol for prescribing antibiotics to women of childbearing age. Compendium 1990;11:392–6.
320. Friedman CI, Huneke AL, Kim MH, Powell J. The effect of ampicillin on oral contraceptive effectiveness. Obstet Gynecol 1980;55:33–7.
321. Grimmer SF, Allen WL, Back DJ, Breckenridge AM, Orme M, Tjia J. The effect of cotrimoxazole on oral contraceptive steroids in women. Contraception 1983;28:53–9. http://dx.doi.org/10.1016/S0010-7824(83)80005-5
322. Helms SE, Bredle DL, Zajic J, Jatjoura D, Brodell RT, Krishnarao I. Oral contraceptive failure rates and oral antibiotics. J Am Acad Dermatol 1997;36:705–10. http://dx.doi.org/10.1016/S0190-9622(97)80322-2
323. Hempel E, Böhm W, Carol W, Klinger G. [Enzyme induction by drugs and hormonal contraception]. Zentralbl Gynakol 1973;95:1451–7.
324. Hempel E, Zorn C, Graf K. [Effect of chemotherapy agents and antibiotics on hormonal contraception]. Z Arztl Fortbild (Jena) 1978;72:924–6.
325. Hetényi G. Possible interactions between antibiotics and oral contraceptives. Ther Hung 1989;37:86–9.
326. Hughes BR, Cunliffe WJ. Interactions between the oral contraceptive pill and antibiotics.[comment]. Br J Dermatol 1990;122:717–8. http://dx.doi.org/10.1111/j.1365-2133.1990.tb07299.x
327. Joshi JV, Joshi UM, Sankholi GM, et al. A study of interaction of low-dose combination oral contraceptive with Ampicillin and Metronidazole. Contraception 1980;22:643–52. http://dx.doi.org/10.1016/0010-7824(80)90089-X
328. Kakouris H, Kovacs GT. Pill failure and nonuse of secondary precautions. Br J Fam Plann 1992;18:41–4.
329. Kakouris H, Kovacs GT. How common are predisposing factors to pill failure among pill users? Br J Fam Plann 1994;20:33–5.
330. Kovacs GT, Riddoch G, Duncombe P, et al. Inadvertent pregnancies in oral contraceptive users. Med J Aust 1989;150:549–51.
331. Lequeux A. [Pregnancy under oral contraceptives after treatment with tetracycline]. Louv Med 1980;99:413–4.
332. London BM, Lookingbill DP. Frequency of pregnancy in acne patients taking oral antibiotics and oral contraceptives. Arch Dermatol 1994;130:392–3. http://dx.doi.org/10.1001/archderm.1994.01690030128027
333. Maggiolo F, Puricelli G, Dottorini M, Caprioli S, Bianchi W, Suter F. The effect of ciprofloxacin on oral contraceptive steroid treatments. Drugs Exp Clin Res 1991;17:451–4.
334. Murphy AA, Zacur HA, Charache P, Burkman RT. The effect of tetracycline on levels of oral contraceptives. Am J Obstet Gynecol 1991;164:28–33. http://dx.doi.org/10.1016/0002-9378(91)90617-Z
335. Neely JL, Abate M, Swinker M, D'Angio R. The effect of doxycycline on serum levels of ethinyl estradiol, norethindrone, and endogenous progesterone. Obstet Gynecol 1991;77:416–20.
336. Pillans PI, Sparrow MJ. Pregnancy associated with a combined oral contraceptive and itraconazole.[comment]. N Z Med J 1993;106:436.
337. Scholten PC, Droppert RM, Zwinkels MG, Moesker HL, Nauta JJ, Hoepelman IM. No interaction between ciprofloxacin and an oral contraceptive. Antimicrob Agents Chemother 1998;42:3266–8.
338. Silber TJ. Apparent oral contraceptive failure associated with antibiotic administration. J Adolesc Health Care 1983;4:287–9. http://dx.doi.org/10.1016/S0197-0070(83)80014-X
339. Sparrow MJ. Pill method failures. N Z Med J 1987;100:102–5.
340. Sparrow MJ. Pregnancies in reliable pill takers. N Z Med J 1989;102:575–7.
341. Sparrow MJ. Pill method failures in women seeking abortion: fourteen years experience. N Z Med J 1998;111:386–8.
342. van Dijke CP, Weber JC. Interaction between oral contraceptives and griseofulvin. Br Med J (Clin Res Ed) 1984;288:1125–6. http://dx.doi.org/10.1136/bmj.288.6424.1125-a
343. Wermeling DP, Chandler MH, Sides GD, Collins D, Muse KN. Dirithromycin increases ethinyl estradiol clearance without allowing ovulation. Obstet Gynecol 1995;86:78–84. http://dx.doi.org/10.1016/0029-7844(95)00075-3
344. Young LK, Farquhar CM, McCowan LM, Roberts HE, Taylor J. The contraceptive practices of women seeking termination of pregnancy in an Auckland clinic. N Z Med J 1994;107:189–92.
345. Abrams LS, Skee D, Natarajan J, Wong FA. Pharmacokinetic overview of Ortho Evra/Evra. Fertil Steril 2002;77(Suppl 2):S3–12. http://dx.doi.org/10.1016/S0015-0282(01)03261-7
346. Dogterom P, van den Heuvel MW, Thomsen T. Absence of pharmacokinetic interactions of the combined contraceptive vaginal ring NuvaRing with oral amoxicillin or doxycycline in two randomised trials. Clin Pharmacokinet 2005;44:429–38. http://dx.doi.org/10.2165/00003088-200544040-00007
347. Devenport MH, Crook D, Wynn V, Lees LJ. Metabolic effects of low-dose fluconazole in healthy female users and non-users of oral contraceptives. Br J Clin Pharmacol 1989;27:851–9. http://dx.doi.org/10.1111/j.1365-2125.1989.tb03449.x
348. Hilbert J, Messig M, Kuye O, Friedman H. Evaluation of interaction between fluconazole and an oral contraceptive in healthy women. Obstet Gynecol 2001;98:218–23.
349. Kovács I, Somos P, Hámori M. Examination of the potential interaction between ketoconazole (Nizoral) and oral contraceptives with special regard to products of low hormone content (Rigevidon, anteovin). Ther Hung 1986;34:167–70.
350. Lunell NO, Pschera H, Zador G, Carlström K. Evaluation of the possible interaction of the antifungal triazole SCH 39304 with oral contraceptives in normal healthy women. Gynecol Obstet Invest 1991;32:91–7. http://dx.doi.org/10.1159/000293003
351. McDaniel PA, Caldroney RD. Oral contraceptives and griseofulvin interactions. Drug Intell Clin Pharm 1986;20:384.
352. Meyboom RH, van Puijenbroek EP, Vinks MH, Lastdrager CJ. Disturbance of withdrawal bleeding during concomitant use of itraconazole and oral contraceptives. N Z Med J 1997;110:300.
353. Rieth H, Sauerbrey N. [Interaction studies with fluconazole, a new triazole antifungal drug]. Wien Med Wochenschr 1989;139:370–4.
354. Sinofsky FE, Pasquale SA. The effect of fluconazole on circulating ethinyl estradiol levels in women taking oral contraceptives. Am J Obstet Gynecol 1998;178:300–4. http://dx.doi.org/10.1016/S0002-9378(98)80016-1

355. van Puijenbroek EP, Feenstra J, Meyboom RH. [Pill cycle disturbance in simultaneous use of itraconazole and oral contraceptives]. Ned Tijdschr Geneeskd 1998;142:146–9.
356. Van Puijenbroek EP, Egberts AC, Meyboom RH, Leufkens HG. Signalling possible drug-drug interactions in a spontaneous reporting system: delay of withdrawal bleeding during concomitant use of oral contraceptives and itraconazole. Br J Clin Pharmacol 1999;47:689–93. http://dx.doi.org/10.1046/j.1365-2125.1999.00957.x
357. Verhoeven CH, van den Heuvel MW, Mulders TM, Dieben TO. The contraceptive vaginal ring, NuvaRing, and antimycotic co-medication. Contraception 2004;69:129–32. http://dx.doi.org/10.1016/j.contraception.2003.10.001
358. Back DJ, Breckenridge AM, Grimmer SF, Orme ML, Purba HS. Pharmacokinetics of oral contraceptive steroids following the administration of the antimalarial drugs primaquine and chloroquine. Contraception 1984;30:289–95. http://dx.doi.org/10.1016/0010-7824(84)90092-1
359. Croft AM, Herxheimer A. Adverse effects of the antimalaria drug, mefloquine: due to primary liver damage with secondary thyroid involvement? BMC Public Health 2002;2:6. http://dx.doi.org/10.1186/1471-2458-2-6
360. Karbwang J, Looareesuwan S, Back DJ, Migasana S, Bunnag D, Breckenridge AM. Effect of oral contraceptive steroids on the clinical course of malaria infection and on the pharmacokinetics of mefloquine in Thai women. Bull World Health Organ 1988;66:763–7.
361. McGready R, Stepniewska K, Seaton E, et al. Pregnancy and use of oral contraceptives reduces the biotransformation of proguanil to cycloguanil. Eur J Clin Pharmacol 2003;59:553–7. http://dx.doi.org/10.1007/s00228-003-0651-x
362. Wanwimolruk S, Kaewvichit S, Tanthayaphinant O, Suwannarach C, Oranratnachai A. Lack of effect of oral contraceptive use on the pharmacokinetics of quinine. Br J Clin Pharmacol 1991;31:179–81. http://dx.doi.org/10.1111/j.1365-2125.1991.tb05509.x
363. Back DJ, Breckenridge AM, Crawford F, et al. The effect of rifampicin on norethisterone pharmacokinetics. Eur J Clin Pharmacol 1979;15:193–7. http://dx.doi.org/10.1007/BF00563105
364. Back DJ, Breckenridge AM, Crawford FE, et al. The effect of rifampicin on the pharmacokinetics of ethynylestradiol in women. Contraception 1980;21:135–43. http://dx.doi.org/10.1016/0010-7824(80)90125-0
365. Barditch-Crovo P, Trapnell CB, Ette E, et al. The effects of rifampin and rifabutin on the pharmacokinetics and pharmacodynamics of a combination oral contraceptive. Clin Pharmacol Ther 1999;65:428–38. http://dx.doi.org/10.1016/S0009-9236(99)70138-4
366. Bolt HM, Bolt M, Kappus H. Interaction of rifampicin treatment with pharmacokinetics and metabolism of ethinyloestradiol in man. Acta Endocrinol (Copenh) 1977;85:189–97.
367. Gupta KC, Ali MY. Failure of oral contraceptive with rifampicin. Med J Zambia 1980;15:23.
368. Hirsch A. [Letter: Sleeping pills]. Nouv Presse Med 1973;2:2957.
369. Hirsch A, Tillement JP, Chretien J. Effets contrariants de la rifampicine sur les contraceptifs oraux: a propos de trois grossesses non desiree chez trois malades. Rev Fr Mal Respir 1975;2:174–82.
370. Joshi JV, Joshi UM, Sankolli GM, et al. A study of interaction of a low-dose combination oral contraceptive with anti-tubercular drugs. Contraception 1980;21:617–29. http://dx.doi.org/10.1016/0010-7824(80)90034-7
371. Kropp R. [Rifampicin and oral contraceptives (author's transl)]. Prax Pneumol 1974;28:270–2.
372. LeBel M, Masson E, Guilbert E, et al. Effects of rifabutin and rifampicin on the pharmacokinetics of ethinylestradiol and norethindrone. J Clin Pharmacol 1998;38:1042–50. http://dx.doi.org/10.1177/009127009803801109
373. Meyer B, Müller F, Wessels P, Maree J. A model to detect interactions between roxithromycin and oral contraceptives. Clin Pharmacol Ther 1990;47:671–4. http://dx.doi.org/10.1038/clpt.1990.92
374. Nocke-Finck L, Breuer H, Reimers D. Dtsch Med Wochenschr 1973;98:1521–3. http://dx.doi.org/10.1055/s-0028-1107071
375. Piguet B, Muglioni JF, Chaline G. [Letter: Oral contraception and rifampicin]. Nouv Presse Med 1975;04:115–6.
376. Reimers D, Jezek A. [The simultaneous use of rifampicin and other antitubercular agents with oral contraceptives]. Prax Pneumol 1971;25:255–62.
377. Skolnick JL, Stoler BS, Katz DB, Anderson WH. Rifampin, oral contraceptives, and pregnancy. JAMA 1976;236:1382. http://dx.doi.org/10.1001/jama.1976.03270130044027
378. Szoka PR, Edgren RA. Drug interactions with oral contraceptives: compilation and analysis of an adverse experience report database. Fertil Steril 1988;49(Suppl 2):31S–8S.
379. Berry-Bibee E, Kim MJ, Simmons K, Pagano P, Curtis K. Drug interactions between hormonal contraceptives and psychotropic drugs: a systematic review. Contraception. In press 2016.
380. Berry-Bibee E, Kim MJ, Tepper N, Riley H, Curtis K. The safety of St John's wort and hormonal contraceptives: a systematic review. Contraception. In press 2016.

Appendix E

Classifications for Barrier Methods

Classifications for barrier contraceptive methods include those for condoms, which include male latex condoms, male polyurethane condoms, and female condoms; spermicides; and diaphragm with spermicide or cervical cap (Box E1) (Table E1).

Women with conditions that make pregnancy an unacceptable risk should be advised that barrier methods for pregnancy prevention might not be appropriate for those who cannot use them consistently and correctly because of the relatively higher typical-use failure rates of these methods. Women should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of human immunodeficiency virus (HIV) and other sexually transmitted diseases (STDs). Use of female condoms can provide protection from transmission of STDs, although data are limited.

BOX E1. Categories for classifying barrier methods

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

TABLE E1. Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
Personal Characteristics and Reproductive History				
Pregnancy	NA	NA	NA	**Clarification:** None of these methods are relevant for contraception during known pregnancy. However, for women who remain at risk for STDs/HIV during pregnancy, the correct and consistent use of condoms is recommended.
Age				
a. Menarche to <40 years	1	1	1	—
b. ≥40 years	1	1	1	—
Parity				
a. Nulliparous	1	1	1	—
b. Parous	1	1	2	**Clarification:** Risk for cervical cap failure is higher in parous women than in nulliparous women.
Postpartum (breastfeeding and nonbreastfeeding)				
a. <6 weeks postpartum	1	1	NA	**Clarification:** Diaphragm and cap are unsuitable until uterine involution is complete.
b. ≥6 weeks postpartum	1	1	1	—
Postabortion				
a. First trimester	1	1	1	—
b. Second trimester	1	1	1	**Clarification:** Diaphragm and cap are unsuitable until 6 weeks after second trimester abortion.
c. Immediate postseptic abortion	1	1	1	—
Past ectopic pregnancy	1	1	1	—
History of pelvic surgery	1	1	1	—
Smoking				
a. Age <35 years	1	1	1	—
b. Age ≥35 years				
i. <15 cigarettes per day	1	1	1	—
ii. ≥15 cigarettes per day	1	1	1	—
Obesity				**Comment:** Severe obesity might make diaphragm and cap placement difficult.
a. BMI ≥30 kg/m^2	1	1	1	
b. Menarche to <18 years and BMI ≥30 kg/m^2	1	1	1	

See table footnotes on page 87.

TABLE E1. (*Continued*) Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	1	1	1	—
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	1	1	1	—
Cardiovascular Disease				
Multiple risk factors for atherosclerotic cardiovascular disease (e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	1	1	1	—
Hypertension Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg are associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Adequately controlled hypertension	1	1	1	—
b. Elevated blood pressure levels (properly taken measurements)				
i. Systolic 140–159 mm Hg or diastolic 90–99 mm Hg	1	1	1	—
ii. Systolic ≥160 mm Hg or diastolic ≥100 mm Hg	1	1	1	—
c. Vascular disease	1	1	1	—
History of high blood pressure during pregnancy (when current blood pressure is measurable and normal)	1	1	1	—
Deep venous thrombosis/Pulmonary embolism				
a. History of DVT/PE, not receiving anticoagulant therapy				
i. Higher risk for recurrent DVT/PE (one or more risk factors) • History of estrogen-associated DVT/PE • Pregnancy-associated DVT/PE • Idiopathic DVT/PE • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	1	1	1	—
ii. Lower risk for recurrent DVT/PE (no risk factors)	1	1	1	—
b. Acute DVT/PE	1	1	1	—
c. DVT/PE and established anticoagulant therapy for at least 3 months				
i. Higher risk for recurrent DVT/PE (one or more risk factors) • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	1	1	1	
ii. Lower risk for recurrent DVT/PE (no risk factors)	1	1	1	—
d. Family history (first-degree relatives)	1	1	1	—
e. Major surgery				
i. With prolonged immobilization	1	1	1	—
ii. Without prolonged immobilization	1	1	1	—
f. Minor surgery without immobilization	1	1	1	—

See table footnotes on page 87.

TABLE E1. (*Continued*) Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
Known thrombogenic mutations (e.g., factor V Leiden; prothrombin mutation; or protein S, protein C, and antithrombin deficiencies) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	**Clarification:** Routine screening is not appropriate because of the rarity of the conditions and the high cost of screening.
Superficial venous disorders				
a. Varicose veins	1	1	1	—
b. Superficial venous thrombosis (acute or history)	1	1	1	—
Current and history of ischemic heart disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	—
Stroke (history of cerebrovascular accident) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	—
Valvular heart disease Complicated valvular heart disease is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Uncomplicated	1	1	1	—
b. Complicated (pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis)	1	1	2	—
Peripartum cardiomyopathy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Normal or mildly impaired cardiac function (New York Heart Association Functional Class I or II: patients with no limitation of activities or patients with slight, mild limitation of activity) (*1*)				
i. <6 months	1	1	1	—
ii. ≥6 months	1	1	1	—
b. Moderately or severely impaired cardiac function (New York Heart Association Functional Class III or IV: patients with marked limitation of activity or patients who should be at complete rest) (*1*)	1	1	1	—
Rheumatic Diseases				
Systemic lupus erythematosus This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Positive (or unknown) antiphospholipid antibodies	1	1	1	—
b. Severe thrombocytopenia	1	1	1	—
c. Immunosuppressive therapy	1	1	1	—
d. None of the above	1	1	1	—
Rheumatoid arthritis				
a. Receiving immunosuppressive therapy	1	1	1	—
b. Not receiving immunosuppressive therapy	1	1	1	—
Neurologic Conditions				
Headaches				—
a. Nonmigraine (mild or severe)	1	1	1	—
b. Migraine				
i. Without aura (This category of migraine includes menstrual migraine.)	1	1	1	**Comment:** Menstrual migraine is a subtype of migraine without aura. For more information see *The International Headache Society Classification, 3rd edition* (http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf).
ii. With aura	1	1	1	—
Epilepsy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	—
Multiple sclerosis				
a. With prolonged immobility	1	1	1	—
b. Without prolonged immobility	1	1	1	—
Depressive Disorders				
Depressive disorders	1	1	1	—
Reproductive Tract Infections and Disorders				
Unexplained vaginal bleeding (suspicious for serious condition) before evaluation	1	1	1	**Clarification:** If pregnancy or an underlying pathological condition (e.g., pelvic malignancy) is suspected, it must be evaluated and the category adjusted after evaluation.

See table footnotes on page 87.

TABLE E1. (*Continued*) Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
Endometriosis	1	1	1	—
Benign ovarian tumors (including cysts)	1	1	1	—
Severe dysmenorrhea	1	1	1	—
Gestational trophoblastic disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Suspected gestational trophoblastic disease (immediate postevacuation)				
i. Uterine size first trimester	1	1	1	—
ii. Uterine size second trimester	1	1	1	—
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)				
i. Undetectable/nonpregnant β–hCG levels	1	1	1	—
ii. Decreasing β–hCG levels	1	1	1	—
iii. Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	1	1	1	—
iv. Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	1	1	1	—
Cervical ectropion	1	1	1	—
Cervical intraepithelial neoplasia	1	1	1	**Clarification:** The cap should not be used. Diaphragm use has no restrictions.
Cervical cancer (awaiting treatment)	1	2	1	**Clarification:** The cap should not be used. Diaphragm use has no restrictions. **Comment:** Repeated and high-dose use of the spermicide nonoxynol-9 can cause vaginal and cervical irritation or abrasions.
Breast disease Breast cancer is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Undiagnosed mass	1	1	1	—
b. Benign breast disease	1	1	1	—
c. Family history of cancer	1	1	1	—
d. Breast cancer				
i. Current	1	1	1	—
ii. Past and no evidence of current disease for 5 years	1	1	1	—
Endometrial hyperplasia	1	1	1	—
Endometrial cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	—
Ovarian cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1	—
Uterine fibroids	1	1	1	—
Anatomical abnormalities	1	1	NA	**Clarification:** The diaphragm cannot be used in certain cases of prolapse. Cap use is not appropriate for a woman with markedly distorted cervical anatomy.
Pelvic inflammatory disease				
a. Past PID				
i. With subsequent pregnancy	1	1	1	—
ii. Without subsequent pregnancy	1	1	1	—
b. Current PID	1	1	1	—
Sexually transmitted diseases				
a. Current purulent cervicitis or chlamydial infection or gonococcal infection	1	1	1	—
b. Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	1	1	1	—
c. Other factors related to STDs	1	1	1	—
HIV				
High risk for HIV	1	4	4	**Evidence:** Repeated and high-dose use of the spermicide nonoxynol-9 was associated with increased risk for genital lesions, which might increase the risk for HIV infection (*2*). **Comment:** Diaphragm use is assigned category 4 because of concerns about the spermicide, not the diaphragm.

See table footnotes on page 87.

TABLE E1. (*Continued*) Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
HIV infection For women with HIV infection who are not clinically well or not receiving ARV therapy, this condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	3	3	**Comment:** Use of spermicides or diaphragms (with spermicide) can disrupt the cervical mucosa, which might increase viral shedding and HIV transmission to noninfected sex partners.
Other Infections				
Schistosomiasis Schistosomiasis with fibrosis of the liver is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Uncomplicated	1	1	1	—
b. Fibrosis of the liver	1	1	1	—
Tuberculosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Nonpelvic	1	1	1	—
b. Pelvic	1	1	1	—
Malaria	1	1	1	—
History of toxic shock syndrome	1	1	3	**Comment:** Toxic shock syndrome has been reported in association with contraceptive sponge and diaphragm use.
Urinary tract infection	1	1	2	**Comment:** Use of diaphragms and spermicides might increase risk for urinary tract infection.
Endocrine Conditions				
Diabetes Insulin-dependent diabetes; diabetes with nephropathy, retinopathy, or neuropathy; diabetes with other vascular disease; or diabetes of >20 years' duration are associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. History of gestational disease	1	1	1	—
b. Nonvascular disease				
i. Non-insulin dependent	1	1	1	—
ii. Insulin dependent	1	1	1	—
c. Nephropathy, retinopathy, or neuropathy	1	1	1	—
d. Other vascular disease or diabetes of >20 years' duration	1	1	1	—
Thyroid disorders				
a. Simple goiter	1	1	1	—
b. Hyperthyroid	1	1	1	—
c. Hypothyroid	1	1	1	—
Gastrointestinal Conditions				
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	1	1	1	—
Gallbladder disease				
a. Symptomatic				
i. Treated by cholecystectomy	1	1	1	—
ii. Medically treated	1	1	1	—
iii. Current	1	1	1	—
b. Asymptomatic	1	1	1	—
History of cholestasis				
a. Pregnancy related	1	1	1	—
b. Past COC related	1	1	1	—
Viral hepatitis				
a. Acute or flare	1	1	1	—
b. Carrier	1	1	1	—
c. Chronic	1	1	1	—
Cirrhosis Severe cirrhosis is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Mild (compensated)	1	1	1	—
b. Severe (decompensated)	1	1	1	—

See table footnotes on page 87.

TABLE E1. (*Continued*) Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
Liver tumors				
Hepatocellular adenoma and malignant liver tumors are associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Benign				
i. Focal nodular hyperplasia	1	1	1	—
ii. Hepatocellular adenoma	1	1	1	—
b. Malignant (hepatoma)	1	1	1	—
Respiratory Conditions				
Cystic fibrosis	1	1	1	—
This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
Anemias				
Thalassemia	1	1	1	—
Sickle cell disease	1	1	1	—
This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
Iron deficiency anemia	1	1	1	—
Solid Organ Transplantation				
Solid organ transplantation				
This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).				
a. Complicated: graft failure (acute or chronic), rejection, or cardiac allograft vasculopathy	1	1	1	—
b. Uncomplicated	1	1	1	—
Drug Interactions				
Antiretroviral therapy				**Clarification:** No drug interaction between ARV therapy and barrier method use is known. However, HIV infection is classified as category 3 for spermicides and diaphragms (see HIV section).
a. Nucleoside reverse transcriptase inhibitors (NRTIs)				
i. Abacavir (ABC)	1	3	3	
ii. Tenofovir (TDF)	1	3	3	
iii. Zidovudine (AZT)	1	3	3	
iv. Lamivudine (3TC)	1	3	3	
v. Didanosine (DDI)	1	3	3	
vi. Emtricitabine (FTC)	1	3	3	
vii. Stavudine (D4T)	1	3	3	
b. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)				
i. Efavirenz (EFV)	1	3	3	
ii. Etravirine (ETR)	1	3	3	
iii. Nevirapine (NVP)	1	3	3	
iv. Rilpivirine (RPV)	1	3	3	
c. Ritonavir-boosted protease inhibitors				
i. Ritonavir-boosted atazanavir (ATV/r)	1	3	3	
ii. Ritonavir-boosted darunavir (DRV/r)	1	3	3	
iii. Ritonavir-boosted fosamprenavir (FPV/r)	1	3	3	
iv. Ritonavir-boosted lopinavir (LPV/r)	1	3	3	
v. Ritonavir-boosted saquinavir (SQV/r)	1	3	3	
vi. Ritonavir-boosted tipranavir (TPV/r)	1	3	3	
d. Protease inhibitors without ritonavir				
i. Atazanavir (ATV)	1	3	3	
ii. Fosamprenavir (FPV)	1	3	3	
iii. Indinavir (IDV)	1	3	3	
iv. Nelfinavir (NFV)	1	3	3	
e. CCR5 co-receptor antagonists				
i. Maraviroc (MVC)	1	3	3	
f. HIV integrase strand transfer inhibitors				
i. Raltegravir (RAL)	1	3	3	
ii. Dolutegravir (DTG)	1	3	3	
iii. Elvitegravir (EVG)	1	3	3	
g. Fusion inhibitors				
i. Enfuvirtide	1	3	3	
Anticonvulsant therapy				
a. Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, or oxcarbazepine)	1	1	1	—
b. Lamotrigine	1	1	1	—

See table footnotes on page 87.

TABLE E1. (*Continued*) Classifications for barrier methods, including condoms, spermicides, diaphragms (with spermicide), and cap

Condition	Category			Clarifications/Evidence/Comments
	Condom	Spermicide	Diaphragm (with spermicide)/Cap	
Antimicrobial therapy				
a. Broad-spectrum antibiotics	1	1	1	—
b. Antifungals	1	1	1	—
c. Antiparasitics	1	1	1	—
d. Rifampin or rifabutin therapy	1	1	1	—
Psychotropic medications				
a. SSRIs	1	1	1	—
St. John's wort	1	1	1	—
Allergy to latex	3	1	3	**Clarification:** The condition of allergy to latex does not apply to plastic condoms/diaphragms.

Abbreviations: ARV = antiretroviral; BMI = body mass index; COC = combined oral contraceptive; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; HDL = high-density lipoprotein; HIV = human immunodeficiency virus; LDL = low-density lipoprotein; NA = not applicable; PE = pulmonary embolism; PID = pelvic inflammatory disease; SSRI = selective serotonin reuptake inhibitor; STD = sexually transmitted disease.

References

1. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Little, Brown and Co; 1994.

2. Wilkinson D, Ramjee G, Tholandi M, Rutherford G. Nonoxynol-9 for preventing vaginal acquisition of HIV infection by women from men. Cochrane Database Syst Rev 2002;4(CD003936):CD003936.

Appendix F

Classifications for Fertility Awareness–Based Methods

Fertility awareness–based (FAB) methods of family planning involve identifying the fertile days of the menstrual cycle, whether by observing fertility signs such as cervical secretions and basal body temperature or by monitoring cycle days (Box F1) (Table F1). FAB methods can be used in combination with abstinence or barrier methods during the fertile time. If barrier methods are used, see the Classifications for Barrier Methods (Appendix E).

No medical conditions worsen because of FAB methods. In general, FAB methods can be used without concern for health effects in persons who choose them. However, several conditions make their use more complex. The existence of these conditions suggests that 1) use of these methods should be delayed until the condition is corrected or resolved, or 2) persons using FAB methods need special counseling, and a provider with particular training in use of these methods is generally necessary to ensure correct use.

Women with conditions that make pregnancy an unacceptable risk should be advised that FAB methods might not be appropriate for them because of the relatively higher typical-use failure rates of these methods. Symptoms-based and calendar-based methods do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

BOX F1. Definitions for terms associated with fertility awareness–based methods

- **Symptoms-based methods:** FAB methods based on observation of fertility signs (e.g., cervical secretions or basal body temperature) such as the cervical mucus method, the symptothermal method, and the TwoDay method.
- **Calendar-based methods:** FAB methods based on calendar calculations such as the calendar rhythm method and the standard days method.
- **Accept:** No medical reason exists to deny the particular FAB method to a woman in this circumstance.
- **Caution:** The method normally is provided in a routine setting but with extra preparation and precautions. For FAB methods, this usually means that special counseling might be needed to ensure correct use of the method by a woman in this circumstance.
- **Delay:** Use of this method should be delayed until the condition is evaluated or corrected. Alternative temporary methods of contraception should be offered.

Abbreviation: FAB = fertility awareness–based.

TABLE F1. Fertility awareness–based methods, including symptoms-based and calendar-based methods

Condition	Category: Symptoms-based method	Category: Calendar-based method	Clarifications/Evidence/Comments
Personal Characteristics and Reproductive History			
Pregnancy	NA	NA	**Clarification:** FAB methods are not relevant during pregnancy.
Life stage			**Comment:** Menstrual irregularities are common in postmenarche and perimenopause and might complicate the use of FAB methods.
a. Postmenarche	Caution	Caution	
b. Perimenopause	Caution	Caution	
Breastfeeding			**Comment:** Use of FAB methods when breastfeeding might be less effective than when not breastfeeding.
a. <6 weeks postpartum	Delay	Delay	**Comment:** Women who are primarily breastfeeding and are amenorrheic are unlikely to have sufficient ovarian function to produce detectable fertility signs and hormonal changes during the first 6 months postpartum. However, the likelihood of resumption of fertility increases with time postpartum and with substitution of breast milk by other foods.
b. ≥6 weeks	Caution	Delay	
c. After menses begin	Caution	Caution	**Clarification:** When the woman notices fertility signs, particularly cervical secretions, she can use a symptoms-based method. First postpartum menstrual cycles in breastfeeding women vary significantly in length. Return to regularity takes several cycles. When she has had at least three postpartum menses and her cycles are regular again, she can use a calendar-based method. When she has had at least four postpartum menses and her most recent cycle lasted 26–32 days, she can use the standard days method. Before that time, a barrier method should be offered if the woman plans to use a FAB method later.
Postpartum (nonbreastfeeding women)			
a. <4 weeks	Delay	Delay	**Clarification:** Nonbreastfeeding women are not likely to have detectable fertility signs or hormonal changes before 4 weeks postpartum. Although the risk for pregnancy is low, ovulation before first menses is common; therefore, a method appropriate for the postpartum period should be offered.
b. ≥4 weeks	Accept	Delay	**Clarification:** Nonbreastfeeding women are likely to have sufficient ovarian function to produce detectable fertility signs, hormonal changes, or both at this time; likelihood increases rapidly with time postpartum. Women can use calendar-based methods as soon as they have completed three postpartum menses. Methods appropriate for the postpartum period should be offered before that time.
Postabortion	Caution	Delay	**Clarification:** After abortion, women are likely to have sufficient ovarian function to produce detectable fertility signs, hormonal changes, or both; likelihood increases with time postabortion. Women can start using calendar-based methods after they have had at least one postabortion menses (e.g., women who before this pregnancy primarily had cycles of 26–32 days can then use the standard days method). Methods appropriate for the postabortion period should be offered before that time.
Reproductive Tract Infections and Disorders			
Irregular vaginal bleeding	Delay	Delay	**Clarification:** Presence of this condition makes FAB methods unreliable. Therefore, barrier methods should be recommended until the bleeding pattern is compatible with proper method use. The condition should be evaluated and treated as necessary.
Vaginal discharge	Delay	Accept	**Clarification:** Because vaginal discharge makes recognition of cervical secretions difficult, the condition should be evaluated and treated if needed before providing methods based on cervical secretions.
Other			
Use of drugs that affect cycle regularity, hormones, or fertility signs	Caution /Delay	Caution/Delay	**Clarification:** Use of certain mood-altering drugs such as lithium, tricyclic antidepressants, and antianxiety therapies, as well as certain antibiotics and anti-inflammatory drugs, might alter cycle regularity or affect fertility signs. The condition should be carefully evaluated and a barrier method offered until the degree of effect has been determined or the drug is no longer being used.
Diseases that elevate body temperature			
a. Chronic diseases	Caution	Accept	**Clarification:** Elevated temperatures might make basal body temperature difficult to interpret but have no effect on cervical secretions. Thus, use of a method that relies on temperature should be delayed until the acute febrile disease abates. Temperature-based methods are not appropriate for women with chronically elevated temperatures. In addition, some chronic diseases interfere with cycle regularity, making calendar-based methods difficult to interpret.
b. Acute diseases	Delay	Accept	

Abbreviations: FAB = fertility awareness–based; NA = not applicable.

Appendix G

Lactational Amenorrhea Method

The Bellagio Consensus provided the scientific basis for defining the conditions under which breastfeeding can be used safely and effectively for birth-spacing purposes; programmatic guidelines were developed at a meeting of family planning experts for its use as a method of family planning, and the method was then given the name the lactational amenorrhea method (*1*,*2*). These guidelines include the following three criteria, all of which must be met to ensure adequate protection from an unplanned pregnancy: 1) amenorrhea; 2) fully or nearly fully breastfeeding (no interval of >4–6 hours between breastfeeds); and 3) <6 months postpartum.

All major medical organizations recommend exclusive breastfeeding for the first 6 months of life, with continuing breastfeeding through the first year and beyond for as long as mutually desired (*3*). No medical conditions exist for which use of the lactational amenorrhea method for contraception is restricted. However, breastfeeding might not be recommended for women or infants with certain conditions.

Women with conditions that make pregnancy an unacceptable risk should be advised that the lactational amenorrhea method might not be appropriate for them because of its relatively higher typical-use failure rates. The lactational amenorrhea method does not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using this method should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

HIV Infection

HIV can be transmitted from mother to infant through breastfeeding. Therefore, in the United States, where replacement feeding is affordable, feasible, acceptable, sustainable, and safe, breastfeeding for women with HIV is not recommended (*3*,*4*).

Other Medical Conditions

The American Academy of Pediatrics (AAP) also recommends against breastfeeding for women with active untreated tuberculosis disease, untreated brucellosis, varicella, H1N1 influenza, or positivity for human T-cell lymphotropic virus types I or II or for those who have herpes simplex lesions on a breast. In addition, infants with classic galactosemia should not breastfeed (*3*).

Medication Used During Breastfeeding

AAP recommends that the benefits of breastfeeding outweigh the risk of exposure to most therapeutic agents via human milk. More information about specific drugs and radioactive compounds is provided by AAP (*5*) and LactMed (http://toxnet.nlm.nih.gov).

References

1. Kennedy KI, Rivera R, McNeilly AS. Consensus statement on the use of breastfeeding as a family planning method. Contraception 1989;39:477–96. http://dx.doi.org/10.1016/0010-7824(89)90103-0
2. Labbok M, Cooney K, Coly S. Guidelines: breastfeeding, family planning, and the Lactational Amenorrhea Method-LAM. Washington, DC: Institute for Reproductive Health; 1994.
3. American Academy of Pediatrics Section on Breastfeeding. Breastfeeding and the use of human milk [Policy statement]. Pediatrics 2012;129:e827–41. http://dx.doi.org/10.1542/peds.2011-3552
4. Perinatal HIV Guidelines Working Group. Public Service Task Force recommendations for use of antiretroviral drugs in pregnant HIV-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Rockville, MD: Public Health Service Task Force; 2009.
5. Sachs HC; Committee On Drugs. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. Pediatrics 2013;132:e796–809. http://dx.doi.org/10.1542/peds.2013-1985

Appendix H

Coitus Interruptus (Withdrawal)

Coitus interruptus, also known as withdrawal, is a traditional family planning method in which the man completely removes his penis from the vagina and away from the external genitalia of the female partner before he ejaculates. Coitus interruptus prevents sperm from entering the woman's vagina, thereby preventing contact between spermatozoa and the ovum.
This method might be appropriate for couples

- who are highly motivated and able to use this method effectively;
- with religious or philosophical reasons for not using other methods of contraception;
- who need contraception immediately and have entered into a sexual act without alternative methods available;
- who need a temporary method while awaiting the start of another method; or
- who have intercourse infrequently.

Some benefits of coitus interruptus are that the method, if used correctly, does not affect breastfeeding and is always available for primary use or use as a back-up method. In addition, coitus interruptus involves no economic cost or use of chemicals and has no directly associated health risks. Coitus interruptus does not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using this method should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

Coitus interruptus is unforgiving of incorrect use, and its effectiveness depends on the willingness and ability of the couple to use withdrawal with every act of intercourse. Women with conditions that make pregnancy an unacceptable risk should be advised that coitus interruptus might not be appropriate for them because of its relatively higher typical-use failure rates.

Appendix I

Female and Male Sterilization

Tubal sterilization for women and vasectomy for men are permanent, safe, and highly effective methods of contraception. In general, no medical conditions absolutely restrict a person's eligibility for sterilization (with the exception of known allergy or hypersensitivity to any materials used to complete the sterilization method). However, certain conditions place a woman at high surgical risk; in these cases, careful consideration should be given to the risks and benefits of other acceptable alternatives, including long-acting, highly effective, reversible methods and vasectomy. Female and male sterilization do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

Because these methods are intended to be irreversible, persons who choose sterilization should be certain that they want to prevent pregnancy permanently. Most persons who choose sterilization remain satisfied with their decision. However, a small proportion of women regret this decision (1%–26% from different studies, with higher rates of regret reported by women who were younger at sterilization) (*1*,*2*). Regret among men about vasectomy has been reported to be approximately 5% (*3*), similar to the proportion of women who report regretting their husbands' vasectomy (6%) (*4*). Therefore, all persons should be appropriately counseled about the permanency of sterilization and the availability of highly effective, reversible methods of contraception.

References

1. Hillis SD, Marchbanks PA, Tylor LR, Peterson HB. Poststerilization regret: findings from the United States Collaborative Review of Sterilization. Obstet Gynecol 1999;93:889–95.
2. Peterson HB. Sterilization. Obstet Gynecol 2008;111:189–203. http://dx.doi.org/10.1097/01.AOG.0000298621.98372.62
3. Ehn BE, Liljestrand J. A long-term follow-up of 108 vasectomized men. Good counselling routines are important. Scand J Urol Nephrol 1995;29:477–81. http://dx.doi.org/10.3109/00365599509180030
4. Jamieson DJ, Kaufman SC, Costello C, Hillis SD, Marchbanks PA, Peterson HB; US Collaborative Review of Sterilization Working Group. A comparison of women's regret after vasectomy versus tubal sterilization. Obstet Gynecol 2002;99:1073–9.

Appendix J

Classifications for Emergency Contraception

A copper-containing intrauterine device (Cu-IUD) can be used within 5 days of unprotected intercourse as an emergency contraceptive. However, when the time of ovulation can be estimated, the Cu-IUD can be inserted beyond 5 days after intercourse, if necessary, as long as the insertion does not occur >5 days after ovulation. The eligibility criteria for interval Cu-IUD insertion also apply for the insertion of Cu-IUDs as emergency contraception (Box J1) (Table J1).

Classifications for emergency contraceptive pills (ECPs) are given for ulipristal acetate (UPA), levonorgestrel (LNG), and combined oral contraceptives (COCs). Cu-IUDs, UPA, LNG, and COCs do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

BOX J1. Categories for classifying emergency contraception

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

TABLE J1. Classifications for emergency contraception, including the copper-containing intrauterine device, ulipristal acetate, levonorgestrel, and combined oral contraceptives*

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD	UPA	LNG	COC	
Personal Characteristics and Reproductive History					
Pregnancy	4	NA	NA	NA	**Clarification (IUD):** The IUD is not indicated during pregnancy and should not be used because of the risk for serious pelvic infection and septic spontaneous abortion. **Clarification (ECPs):** Although this method is not indicated for a woman with a known or suspected pregnancy, no harm to the woman, the course of her pregnancy, or the fetus if ECPs are inadvertently used is known to exist. **Evidence:** Evidence suggests that poor pregnancy outcomes are rare among pregnant women who used ECPs during conception cycle or early in pregnancy *(1)*.
Breastfeeding	1	1	1	1	**Clarification (UPA):** Breastfeeding is not recommended for 24 hours after taking UPA because it is excreted in breast milk, with highest concentrations in the first 24 hours, and maximum maternal serum levels are reached 1–3 hours after administration. Mean UPA concentrations in breast milk decrease markedly from 0 to 24–48 hours and then slowly decrease over 5 days *(2)*. Breast milk should be expressed and discarded for 24 hours after taking UPA. **Evidence:** Breastfeeding outcomes do not seem to differ between women exposed to LNG and those who are not exposed. One pharmacokinetic study demonstrated that LNG passes to breast milk but in minimal quantities *(1)*.
Past ectopic pregnancy	1	1	1	1	—
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	1	1	1	1	—
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	1	1	1	1	**Comment:** Bariatric surgical procedures involving a malabsorptive component have the potential to decrease oral contraceptive effectiveness, perhaps further decreased by postoperative complications such as long-term diarrhea, vomiting, or both. Because of these malabsorptive concerns, an emergency IUD might be more appropriate than ECPs.

See table footnotes on page 94.

TABLE J1. (*Continued*) Classifications for emergency contraception, including the copper-containing intrauterine device, ulipristal acetate, levonorgestrel, and combined oral contraceptives*

Condition	Category				Clarifications/Evidence/Comments
	Cu-IUD	UPA	LNG	COC	
Cardiovascular Disease					
History of severe cardiovascular disease (ischemic heart disease, cerebrovascular attack, or other thromboembolic conditions) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	2	2	2	**Comment:** The duration of ECP use is less than that of regular use of COCs or POPs and thus would be expected to have less clinical impact.
Rheumatic Diseases					
Rheumatoid arthritis					
a. Receiving immunosuppressive therapy	2	1	1	1	—
b. Not receiving immunosuppressive therapy	1	1	1	1	—
Neurologic Conditions					
Migraine	1	1	1	2	**Comment:** The duration of ECP use is less than that of regular use of COCs and thus would be expected to have less clinical impact.
Gastrointestinal Conditions					
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	1	1	1	1	—
Severe liver disease (including jaundice) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	2	2	2	**Comment:** The duration of ECP use is less than that of regular use of COCs or POPs and thus would be expected to have less clinical impact.
Solid Organ Transplantation					
Solid organ transplantation This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).					
a. Complicated: graft failure (acute or chronic), rejection, or cardiac allograft vasculopathy	3	1	1	1	—
b. Uncomplicated	2	1	1	1	—
Other					
Repeated ECP use	1	1	1	1	**Clarification:** Recurrent ECP use is an indication that the woman requires further counseling about other contraceptive options. Frequently repeated ECP use might be harmful for women with conditions classified as 2, 3, or 4 for CHC or POC use. **Evidence:** In one case-control study, risk for ectopic pregnancy compared with intrauterine pregnancy did not increase after repeated use of LNG ECPs compared with nonuse *(1)*.
Sexual assault	2	1	1	1	**Clarification (IUD):** Women who have experienced sexual assault are at increased risk for STDs. According to CDC STD treatment guidelines, routine presumptive treatment of chlamydia, gonorrhea, and trichomonas is recommended after sexual assault *(3)*. Women with current purulent cervicitis or chlamydial infection or gonococcal infection should not undergo IUD insertion (category 4).
Obesity (BMI ≥30 kg/m^2)	1	2	2	2	**Clarification (ECPs):** ECPs might be less effective among women with BMI ≥30 kg/m^2 than among women with BMI <25 kg/m^2. Despite this, no safety concerns exist. **Evidence:** Limited evidence from secondary data analyses suggests that women with BMI ≥30 kg/m^2 experience an increased risk for pregnancy after use of LNG compared with women with BMI <25 kg/m^2. Two analyses suggest obese women might also experience an increased risk for pregnancy after use of UPA compared with nonobese women, although this increase was not significant in one study *(4)*.
CYP3A4 inducers (e.g., bosentan, carbamazepine, felbamate, griseofulvin, oxcarbazepine, phenytoin, rifampin, St. John's wort, topiramate, efavirenz, and lumacaftor)	1	2	2	2	**Clarification (ECPs):** Strong CYP3A4 inducers might reduce the effectiveness of ECPs. **Evidence:** According to labelling information, rifampin markedly decreases UPA levels by ≥90%, which might decrease its efficacy *(2)*. Therefore, theoretical concerns extend to use of other CYP3A4 inducers as well as to COC and LNG ECPs, which have metabolic pathways similar to those of UPA. A small pharmacokinetic study found that concomitant efavirenz use decreased LNG levels in women taking LNG ECPs (0.75 mg) by 56% compared with LNG ECPs alone *(5)*.

Abbreviations: BMI = body mass index; CHC = combined hormonal contraceptive; COC = combined hormonal contraceptive; Cu-IUD = copper-containing intrauterine device; ECP = emergency contraceptive pill; HIV = human immunodeficiency virus; IUD = intrauterine device; LNG = levonorgestrel; NA = not applicable; POC = progestin-only contraceptive; POP = progestin-only pill; STD = sexually transmitted disease; UPA = ulipristal acetate.

References

1. Jatlaoui TC, Riley H, Curtis KM. Safety data for levonorgestrel, ulipristal acetate and Yuzpe regimens for emergency contraception. Contraception 2016;93:93–112. http://dx.doi.org/10.1016/j.contraception.2015.11.001
2. Watson Pharmaceuticals. Ella [Prescribing information]. Morristown, NJ; 2010. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022474s000lbl.pdf
3. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(No. RR-03).
4. Jatlaoui TC, Curtis KM. Safety and effectiveness data for emergency contraceptive pills among women with obesity: a systematic review. Contraception 2016. Epub May 24, 2016. http://dx.doi.org/10.1016/j.contraception.2016.05.002
5. Carten ML, Kiser JJ, Kwara A, Mawhinney S, Cu-Uvin S. Pharmacokinetic interactions between the hormonal emergency contraception, levonorgestrel (Plan B), and efavirenz. Infect Dis Obstet Gynecol 2012;2012:137192.

Appendix K

Summary of Classifications for Hormonal Contraceptive Methods and Intrauterine Devices

Health-care providers can use the summary table as a quick reference guide to the classifications for hormonal contraceptive methods and intrauterine contraception to compare classifications across these methods (Box K1) (Table K1). See the respective appendix for each method for clarifications to the numeric categories, as well as for summaries of the evidence and additional comments. Hormonal contraceptives and intrauterine devices do not protect against sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV), and women using these methods should be counseled that consistent and correct use of the male latex condom reduces the risk for transmission of HIV and other STDs. Use of female condoms can provide protection from transmission of STDs, although data are limited.

BOX K1. Categories for classifying hormonal contraceptives and intrauterine devices

1 = A condition for which there is no restriction for the use of the contraceptive method.
2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
4 = A condition that represents an unacceptable health risk if the contraceptive method is used.

TABLE K1. Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs
Personal Characteristics And Reproductive History						
Pregnancy	4*	4*	NA*	NA*	NA*	NA*
Age	Menarche to <20 years: 2 ≥20 years: 1	Menarche to <20 years: 2 ≥20 years: 1	Menarche to <18 years: 1 18–45 years: 1 >45 years: 1	Menarche to <18 years: 2 18–45 years: 1 >45 years: 2	Menarche to <18 years: 1 18–45 years: 1 >45 years: 1	Menarche to <40 years: 1 ≥40 years: 2
Parity						
a. Nulliparous	2	2	1	1	1	1
b. Parous	1	1	1	1	1	1
Breastfeeding						
a. <21 days postpartum	—	—	2*	2*	2*	4*
b. 21 to <30 days postpartum						
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	—	—	2*	2*	2*	3*
ii. Without other risk factors for VTE	—	—	2*	2*	2*	3*
c. 30–42 days postpartum						
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	—	—	1*	1*	1*	3*
ii. Without other risk factors for VTE	—	—	1*	1*	1*	2*
d. >42 days postpartum	—	—	1*	1*	1*	2*

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs
Postpartum (nonbreastfeeding women)						
a. <21 days postpartum	—	—	1	1	1	4
b. 21–42 days postpartum						
i. With other risk factors for VTE (e.g., age ≥35 years, previous VTE, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, BMI ≥30 kg/m^2, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)	—	—	1	1	1	3*
ii. Without other risk factors for VTE	—	—	1	1	1	2
c. >42 days postpartum	—	—	1	1	1	1
Postpartum (including cesarean delivery)						
a. <10 minutes after delivery of the placenta						
i. Breastfeeding	1*	2*	—	—	—	—
ii. Nonbreastfeeding	1*	1*	—	—	—	—
b. 10 minutes after delivery of the placenta to <4 weeks (breastfeeding or nonbreastfeeding)	2*	2*	—	—	—	—
c. ≥4 weeks (breastfeeding or nonbreastfeeding)	1*	1*	—	—	—	—
d. Postpartum sepsis	4	4	—	—	—	—
Postabortion						
a. First trimester	1*	1*	1*	1*	1*	1*
b. Second trimester	2*	2*	1*	1*	1*	1*
c. Immediate postseptic abortion	4	4	1*	1*	1*	1*
Past ectopic pregnancy	1	1	1	1	2	1
History of pelvic surgery (see Postpartum [Including Cesarean Delivery] section)	1	1	1	1	1	1
Smoking						
a. Age <35 years	1	1	1	1	1	2
b. Age ≥35 years						
i. <15 cigarettes per day	1	1	1	1	1	3
ii. ≥15 cigarettes per day	1	1	1	1	1	4
Obesity						
a. BMI ≥30 kg/m^2	1	1	1	1	1	2
b. Menarche to <18 years and BMI ≥30 kg/m^2	1	1	1	2	1	2
History of bariatric surgery This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).						
a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, or laparoscopic sleeve gastrectomy)	1	1	1	1	1	1
b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass or biliopancreatic diversion)	1	1	1	1	3	COCs: 3 Patch and ring: 1
Cardiovascular Disease						
Multiple risk factors for atherosclerotic cardiovascular disease (e.g., older age, smoking, diabetes, hypertension, low HDL, high LDL, or high triglyceride levels)	1	2	2*	3*	2*	3/4*
Hypertension Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg are associated with increased risk for adverse health events as a result of pregnancy (Box 2).						
a. Adequately controlled hypertension	1*	1*	1*	2*	1*	3*

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs
b. Elevated blood pressure levels (properly taken measurements)						
i. Systolic 140–159 mm Hg or diastolic 90–99 mm Hg	1*	1*	1*	2*	1*	3*
ii. Systolic ≥160 mm Hg or diastolic ≥100 mm Hg	1*	2*	2*	3*	2*	4*
c. Vascular disease	1*	2*	2*	3*	2*	4*
History of high blood pressure during pregnancy (when current blood pressure is measurable and normal)	1	1	1	1	1	2
Deep venous thrombosis/ Pulmonary embolism						
a. History of DVT/PE, not receiving anticoagulant therapy						
i. Higher risk for recurrent DVT/PE (one or more risk factors) • History of estrogen-associated DVT/PE • Pregnancy-associated DVT/PE • Idiopathic DVT/PE • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	1	2	2	2	2	4
ii. Lower risk for recurrent DVT/PE (no risk factors)	1	2	2	2	2	3
b. Acute DVT/PE	2	2	2	2	2	4
c. DVT/PE and established anticoagulant therapy for at least 3 months						
i. Higher risk for recurrent DVT/PE (one or more risk factors) • Known thrombophilia, including antiphospholipid syndrome • Active cancer (metastatic, receiving therapy, or within 6 months after clinical remission), excluding nonmelanoma skin cancer • History of recurrent DVT/PE	2	2	2	2	2	4*
ii. Lower risk for recurrent DVT/PE (no risk factors)	2	2	2	2	2	3*
d. Family history (first-degree relatives)	1	1	1	1	1	2
e. Major surgery						
i. With prolonged immobilization	1	2	2	2	2	4
ii. Without prolonged immobilization	1	1	1	1	1	2
f. Minor surgery without immobilization	1	1	1	1	1	1
Known thrombogenic mutations (e.g., factor V Leiden; prothrombin mutation; and protein S, protein C, and antithrombin deficiencies) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1*	2*	2*	2*	2*	4*
Superficial venous disorders						
a. Varicose veins	1	1	1	1	1	1
b. Superficial venous thrombosis (acute or history)	1	1	1	1	1	3*
Current and history of ischemic heart disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	Initiation 2 Continuation 3	Initiation 2 Continuation 3	3	Initiation 2 Continuation 3	4

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs
Stroke (history of cerebrovascular accident) This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	2	Initiation: 2 Continuation: 3	3	Initiation: 2 Continuation: 3	4
Valvular heart disease Complicated valvular heart disease is associated with increased risk for adverse health events as a result of pregnancy (Box 2).						
a. Uncomplicated	1	1	1	1	1	2
b. Complicated (pulmonary hypertension, risk for atrial fibrillation, or history of subacute bacterial endocarditis)	1	1	1	1	1	4
Peripartum cardiomyopathy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).						
a. Normal or mildly impaired cardiac function (New York Heart Association Functional Class I or II: patients with no limitation of activities or patients with slight, mild limitation of activity) *(1)*						
i. <6 months	2	2	1	1	1	4
ii. ≥6 months	2	2	1	1	1	3
b. Moderately or severely impaired cardiac function (New York Heart Association Functional Class III or IV: patients with marked limitation of activity or patients who should be at complete rest) *(1)*.	2	2	2	2	2	4
Rheumatic Diseases						
Systemic lupus erythematosus This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation: 1* Continuation: 1*	3*	3*	Initiation: 3* Continuation: 3*	3*	4*
a. Positive (or unknown) antiphospholipid antibodies						
b. Severe thrombocytopenia	3* / 2*	2*	2*	3* / 2*	2*	2*
c. Immunosuppressive therapy	2* / 1*	2*	2*	2* / 2*	2*	2*
d. None of the above	1* / 1*	2*	2*	2* / 2*	2*	2*
Rheumatoid arthritis	Initiation / Continuation	Initiation / Continuation				
a. Receiving immunosuppressive therapy	2 / 1	2 / 1	1	2/3*	1	2
b. Not receiving immunosuppressive therapy	1	1	1	2	1	2
Neurologic Conditions						
Headaches						
a. Nonmigraine (mild or severe)	1	1	1	1	1	1*
b. Migraine						
i. Without aura (This category of migraine includes menstrual migraine.)	1	1	1	1	1	2*
ii. With aura	1	1	1	1	1	4*
Epilepsy This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1	1	1*	1*	1*	1*
Multiple sclerosis						
a. With prolonged immobility	1	1	1	2	1	3
b. Without prolonged immobility	1	1	1	2	1	1
Depressive Disorders						
Depressive disorders	1*	1*	1*	1*	1*	1*
Reproductive Tract Infections and Disorders						
Vaginal bleeding patterns		Initiation / Continuation				
a. Irregular pattern without heavy bleeding	1	1 / 1	2	2	2	1
b. Heavy or prolonged bleeding (includes regular and irregular patterns)	2*	1* / 2*	2*	2*	2*	1*

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs
Unexplained vaginal bleeding (suspicious for serious condition) before evaluation	Initiation: 4*	Continuation: 2*	Initiation: 4*	Continuation: 2*	3*	3*	2*	2*
Endometriosis	2		1		1	1	1	1
Benign ovarian tumors (including cysts)	1		1		1	1	1	1
Severe dysmenorrhea	2		1		1	1	1	1
Gestational trophoblastic disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).								
a. Suspected gestational trophoblastic disease (immediate postevacuation)								
i. Uterine size first trimester	1*		1*		1*	1*	1*	1*
ii. Uterine size second trimester	2*		2*		1*	1*	1*	1*
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)	Initiation	Continuation	Initiation	Continuation				
i. Undetectable/nonpregnant β-hCG levels	1*	1*	1*	1*	1*	1*	1*	1*
ii. Decreasing β-hCG levels	2*	1*	2*	1*	1*	1*	1*	1*
iii. Persistently elevated β-hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	2*	1*	2*	1*	1*	1*	1*	1*
iv. Persistently elevated β-hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	4*	2*	4*	2*	1*	1*	1*	1*
Cervical ectropion	1		1		1	1	1	1
Cervical intraepithelial neoplasia	1		2		2	2	1	2
Cervical cancer (awaiting treatment)	Initiation	Continuation	Initiation	Continuation				
	4	2	4	2	2	2	1	2
Breast disease Breast cancer is associated with increased risk of adverse health events as a result of pregnancy (Box 2).								
a. Undiagnosed mass	1		2		2*	2*	2*	2*
b. Benign breast disease	1		1		1	1	1	1
c. Family history of cancer	1		1		1	1	1	1
d. Breast cancer								
i. Current	1		4		4	4	4	4
ii. Past and no evidence of current disease for 5 years	1		3		3	3	3	3
Endometrial hyperplasia	1		1		1	1	1	1
Endometrial cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation: 4	Continuation: 2	Initiation: 4	Continuation: 2	1	1	1	1
Ovarian cancer This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1		1		1	1	1	1
Uterine fibroids	2		2		1	1	1	1
Anatomical abnormalities								
a. Distorted uterine cavity (any congenital or acquired uterine abnormality distorting the uterine cavity in a manner that is incompatible with IUD insertion)	4		4		—	—	—	—
b. Other abnormalities (including cervical stenosis or cervical lacerations) not distorting the uterine cavity or interfering with IUD insertion	2		2		—	—	—	—
Pelvic inflammatory disease								
a. Past PID	Initiation	Continuation	Initiation	Continuation				
i. With subsequent pregnancy	1	1	1	1	1	1	1	1
ii. Without subsequent pregnancy	2	2	2	2	1	1	1	1
b. Current PID	4	2*	4	2*	1	1	1	1

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs
Sexually transmitted diseases	Initiation	Continuation	Initiation	Continuation				
a. Current purulent cervicitis or chlamydial infection or gonococcal infection	4	2*	4	2*	1	1	1	1
b. Vaginitis (including *Trichomonas vaginalis* and bacterial vaginosis)	2	2	2	2	1	1	1	1
c. Other factors related to STDs	2*	2	2*	2	1	1	1	1
HIV								
	Initiation	Continuation	Initiation	Continuation				
High risk for HIV	2	2	2	2	1	1*	1	1
HIV infection For women with HIV infection who are not clinically well or not receiving ARV therapy, this condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	—	—	—	—	1*	1*	1*	1*
a. Clinically well receiving ARV therapy	1	1	1	1	—	—	—	—
b. Not clinically well or not receiving ARV therapy	2	1	2	1	—	—	—	—
Other Infections								
Schistosomiasis Schistosomiasis with fibrosis of the liver is associated with increased risk for adverse health events as a result of pregnancy (Box 2).								
a. Uncomplicated	1		1		1	1	1	1
b. Fibrosis of the liver (if severe, see Cirrhosis)	1		1		1	1	1	1
Tuberculosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation	Continuation	Initiation	Continuation				
a. Nonpelvic	1	1	1	1	1*	1*	1*	1*
b. Pelvic	4	3	4	3	1*	1*	1*	1*
Malaria	1		1		1	1	1	1
Endocrine Conditions								
Diabetes Insulin-dependent diabetes; diabetes with nephropathy, retinopathy, or neuropathy; diabetes with other vascular disease; or diabetes of >20 years' duration are associated with increased risk of adverse health events as a result of pregnancy (Box 2).								
a. History of gestational disease	1		1		1	1	1	1
b. Nonvascular disease								
i. Non-insulin dependent	1		2		2	2	2	2
ii. Insulin dependent	1		2		2	2	2	2
c. Nephropathy, retinopathy, or neuropathy	1		2		2	3	2	3/4*
d. Other vascular disease or diabetes of >20 years' duration	1		2		2	3	2	3/4*
Thyroid disorders								
a. Simple goiter	1		1		1	1	1	1
b. Hyperthyroid	1		1		1	1	1	1
c. Hypothyroid	1		1		1	1	1	1
Gastrointestinal Conditions								
Inflammatory bowel disease (ulcerative colitis or Crohn's disease)	1		1		1	2	2	2/3*
Gallbladder disease								
a. Symptomatic								
i. Treated by cholecystectomy	1		2		2	2	2	2
ii. Medically treated	1		2		2	2	2	3
iii. Current	1		2		2	2	2	3
b. Asymptomatic	1		2		2	2	2	2
History of cholestasis								
a. Pregnancy related	1		1		1	1	1	2
b. Past COC related	1		2		2	2	2	3

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD	LNG-IUD	Implants	DMPA	POP	CHCs	
Viral hepatitis						Initiation	Continuation
a. Acute or flare	1	1	1	1	1	3/4*	2
b. Carrier	1	1	1	1	1	1	1
c. Chronic	1	1	1	1	1	1	1
Cirrhosis Severe cirrhosis is associated with increased risk for adverse health events as a result of pregnancy (Box 2).							
a. Mild (compensated)	1	1	1	1	1	1	
b. Severe (decompensated)	1	3	3	3	3	4	
Liver tumors Hepatocellular adenoma and malignant liver tumors are associated with increased risk for adverse health events as a result of pregnancy (Box 2).							
a. Benign							
i. Focal nodular hyperplasia	1	2	2	2	2	2	
ii. Hepatocellular adenoma	1	3	3	3	3	4	
b. Malignant (hepatoma)	1	3	3	3	3	4	
Respiratory Conditions							
Cystic fibrosis This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	1*	1*	1*	2*	1*	1*	
Anemias							
Thalassemia	2	1	1	1	1	1	
Sickle cell disease This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	2	1	1	1	1	2	
Iron-deficiency anemia	2	1	1	1	1	1	
Solid Organ Transplantation							
Solid organ transplantation This condition is associated with increased risk for adverse health events as a result of pregnancy (Box 2).	Initiation	Continuation	Initiation	Continuation			
a. Complicated: graft failure (acute or chronic), rejection, or cardiac allograft vasculopathy	3	2	3	2	2	2	2	4
b. Uncomplicated	2	2	2	2	2	2	2	2*
Drug Interactions							
Antiretroviral therapy	Initiation	Continuation	Initiation	Continuation			
a. Nucleoside reverse transcriptase inhibitors (NRTIs)							
i. Abacavir (ABC)	1/2*	1*	1/2*	1*	1	1	1	1
ii. Tenofovir (TDF)	1/2*	1*	1/2*	1*	1	1	1	1
iii. Zidovudine (AZT)	1/2*	1*	1/2*	1*	1	1	1	1
iv. Lamivudine (3TC)	1/2*	1*	1/2*	1*	1	1	1	1
v. Didanosine (DDI)	1/2*	1*	1/2*	1*	1	1	1	1
vi. Emtricitabine (FTC)	1/2*	1*	1/2*	1*	1	1	1	1
vii. Stavudine (D4T)	1/2*	1*	1/2*	1*	1	1	1	1
b. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)							
i. Efavirenz (EFV)	1/2*	1*	1/2*	1*	2*	1*	2*	2*
ii. Etravirine (ETR)	1/2*	1*	1/2*	1*	1	1	1	1
iii. Nevirapine (NVP)	1/2*	1*	1/2*	1*	1	1	1	1
iv. Rilpivirine (RPV)	1/2*	1*	1/2*	1*	1	1	1	1
c. Ritonavir-boosted protease inhibitors							
i. Ritonavir-boosted atazanavir (ATV/r)	1/2*	1*	1/2*	1*	2*	1*	2*	2*
ii. Ritonavir-boosted darunavir (DRV/r)	1/2*	1*	1/2*	1*	2*	1*	2*	2*
iii. Ritonavir-boosted fosamprenavir (FPV/r)	1/2*	1*	1/2*	1*	2*	1*	2*	2*
iv. Ritonavir-boosted lopinavir (LPV/r)	1/2*	1*	1/2*	1*	1	1	1	1
v. Ritonavir-boosted saquinavir (SQV/r)	1/2*	1*	1/2*	1*	2*	1*	2*	2*
vi. Ritonavir-boosted tipranavir (TPV/r)	1/2*	1*	1/2*	1*	2*	1*	2*	2*

See table footnotes on page 103.

TABLE K1. (*Continued*) Summary of classifications for hormonal contraceptive methods and intrauterine devices

Condition	Cu-IUD		LNG-IUD		Implants	DMPA	POP	CHCs
d. Protease inhibitors without ritonavir								
i. Atazanavir (ATV)	1/2*	1*	1/2*	1*	1	1	1	2*
ii. Fosamprenavir (FPV)	1/2*	1*	1/2*	1*	2*	2*	2*	3*
iii. Indinavir (IDV)	1/2*	1*	1/2*	1*	1	1	1	1
iv. Nelfinavir (NFV)	1/2*	1*	1/2*	1*	2*	1*	2*	2*
e. CCR5 co-receptor antagonists								
i. Maraviroc (MVC)	1/2*	1*	1/2*	1*	1	1	1	1
f. HIV integrase strand transfer inhibitors								
i. Raltegravir (RAL)	1/2*	1*	1/2*	1*	1	1	1	1
ii. Dolutegravir (DTG)	1/2*	1*	1/2*	1*	1	1	1	1
iii. Elvitegravir (EVG)	1/2*	1*	1/2*	1*	1	1	1	1
g. Fusion inhibitors								
i. Enfuvirtide	1/2*	1*	1/2*	1*	1	1	1	1
Anticonvulsant therapy								
a. Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, and oxcarbazepine)	1		1		2*	1*	3*	3*
b. Lamotrigine	1		1		1	1	1	3*
Antimicrobial therapy								
a. Broad-spectrum antibiotics	1		1		1	1	1	1
b. Antifungals	1		1		1	1	1	1
c. Antiparasitics	1		1		1	1	1	1
d. Rifampin or rifabutin therapy	1		1		2*	1*	3*	3*
Psychotropic medications								
a. SSRIs	1		1		1	1	1	1
St. John's wort	1		1		2	1	2	2

Abbreviations: BMI = body mass index; COC = combined oral contraceptive; Cu-IUD = copper-containing IUD; DMPA = depot medroxyprogesterone acetate; DVT = deep venous thrombosis; hCG = human chorionic gonadotropin; HDL = high-density lipoprotein; HIV = human immunodeficiency virus.; IUD = intrauterine device; LDL = low-density lipoprotein; LNG-IUD = levonorgestrel-releasing IUD; NA = not applicable; PE = pulmonary embolism; PID = pelvic inflammatory disease; POP = progestin-only pill; SSRI = selective serotonin reuptake inhibitor; STD = sexually transmitted disease.
* Consult the appendix for this contraceptive method for a clarification to this classification.

References

1. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Little, Brown & Co; 1994.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR*'s free subscription page at *http://www.cdc.gov/mmwr/mmwrsubscribe.html*. Paper copy subscriptions are available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

Readers who have difficulty accessing this PDF file may access the HTML file at http://www.cdc.gov/mmwr/volumes/65/rr/rr6503a1.htm?s_cid=rr6503a1_w. Address all inquiries about the *MMWR* Series, including material to be considered for publication, to Executive Editor, *MMWR* Series, Mailstop E-90, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30329-4027 or to *mmwrq@cdc.gov.*

All material in the *MMWR* Series is in the public domain and may be used and reprinted without permission; citation as to source, however, is appreciated.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of these sites. URL addresses listed in *MMWR* were current as of the date of publication.

ISSN: 1057-5987 (Print)