



USAID
FROM THE AMERICAN PEOPLE

Hormonal Contraception and HIV: What is going on?

**Jen Mason &
Tabitha Sripipatana**

**PRH Open Staff
April 14, 2016**



USAID
FROM THE AMERICAN PEOPLE

Two Different Questions and Two Different Populations

HIV-positive (+)
women taking ART
and HC

Do certain ARVs interact
with hormonal
contraceptives?

HIV-negative (-)
women taking HC

Do certain hormonal
contraceptives increase
the risk of HIV
acquisition?



USAID
FROM THE AMERICAN PEOPLE

HIV-negative (-)
women taking HC

Do certain hormonal
contraceptives increase the
risk of HIV acquisition?



WHO, Medical Eligibility Criteria (MEC)

- Provides evidence based guidance on who can safely use contraceptive methods
- 2014 MEC expert group reviewed evidence on hormonal contraception and HIV acquisition
 - Commissioned systematic review of relevant studies



Summary of Evidence, Acquisition

(C.Polis, 2014)

Method	Acquisition
Patches, Rings, EC	No Data
LNG-IUD	No Data
OCPs	No Current Concern
Implants	No Current Concern
NET-EN	Some Concern (limited data)
DMPA	Concern

Systematic review concluded that the relationship between injectable HC and HIV risk is inconclusive (22 studies)



- 2014 MEC expert panel reviewed evidence, recommended no restriction on any HC method for women at high risk of HIV, but with a clarification



World Health Organization

Hormonal contraceptive methods for women at high risk of HIV and living with HIV

2014 guidance statement

Recommendations concerning the use of hormonal contraceptive methods by women at high risk of HIV and women living with HIV



Photo: UNMIS/J. Naar

Women at high risk of HIV infection should be informed that progestogen-only injectables may or may not increase their risk of HIV acquisition. Women and couples at high risk of HIV acquisition considering progestogen-only injectables should also be informed about and have access to HIV preventive measures, including male and female condoms.



Why hasn't the research determined if the association between DMPA and HIV is causal?

- All observational data
 - Varying quality of the research
 - Secondary analysis: HIV acquisition was not the primary question driving study design
 - Problem of confounding factors
 - Condom use
 - Other unknown factors





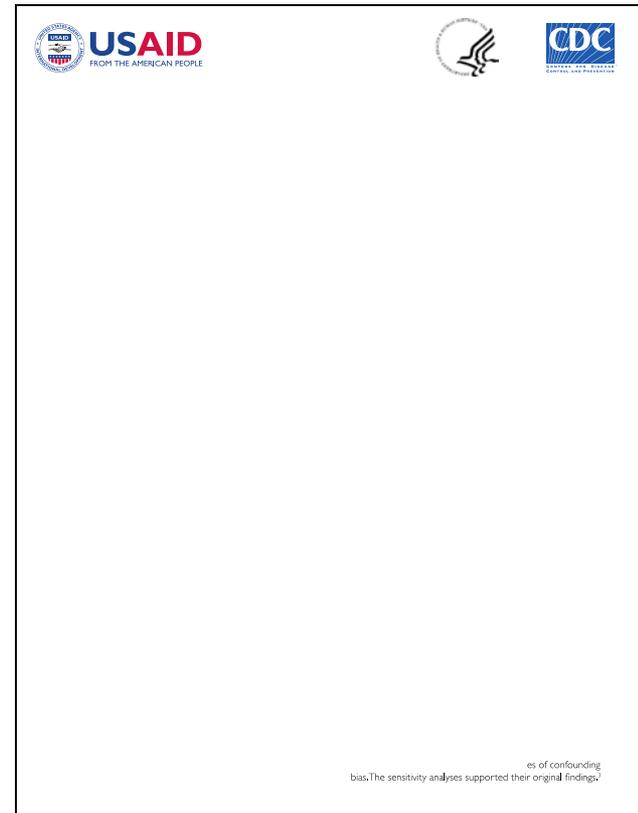
- No clear answers about hormonal contraception and HIV acquisition
- The global health community must do the best to assist women and couples who wish to prevent pregnancy
 - Make an informed decision about the contraceptive method that best fits their needs
 - People have a right to receive information about the risks and benefits of all contraceptive methods
 - Importance of dual protection
- The potential risk with DMPA must be balanced against risks of unintended pregnancy, including:
 - Maternal morbidity and mortality
 - Unsafe abortion
 - Infant mortality
 - Increase in risk of HIV acquisition which may possibly be associated with pregnancy itself



USAID
FROM THE AMERICAN PEOPLE

What is USAID doing?

- PRH/OHA activities to provide guidance to USAID missions, partners and MOH counterparts.
 - USG and USAID Briefs on Hormonal Contraception and HIV
 - Strategic Communication Framework for Hormonal Contraception Methods and HIV Related Risks
 - Plan to evaluate roll out of HC-HIV messages in Malawi
 - Method mix analysis (Net-En)
 - Support to USG partners, USAID missions and implementing partners in integrating HC-HIV messages into HIV and FP programming
 - Collaboration with WHO and UNFPA to disseminate information to MOH and UN offices





HIV-positive (+)
women taking ART and
HC

Do certain ARVs interact
with hormonal
contraceptives?

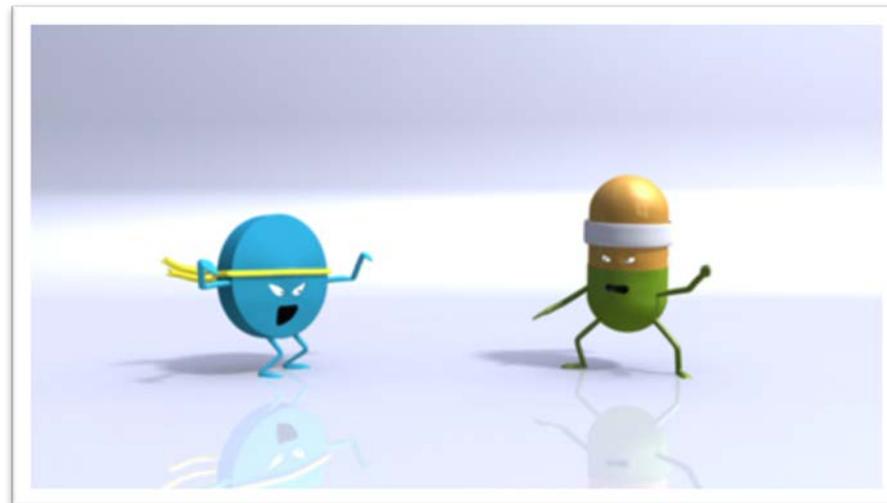


USAID

FROM THE AMERICAN PEOPLE

What is a drug to drug interaction (DDI) ?

- A pharmacokinetic drug interaction occurs when a drug interferes (in a positive or negative way) with another drug, resulting in higher or lower levels of either drug in the body
- Certain hormonal contraceptive methods and certain ARVs have the potential to interact with each other and, in theory, to lead to decreases in efficacy of either medication or to increased side effects or toxicity





USAID
FROM THE AMERICAN PEOPLE

Do hormonal contraceptive methods reduce the efficacy of ART?

- While data are limited, ART efficacy does not appear to be impacted by use of hormonal contraceptive methods





USAID
FROM THE AMERICAN PEOPLE

Do specific ARVs reduce the efficacy of hormonal contraceptive methods?

Contraceptive Method	Evidence
Combined oral contraceptives	Efavirenz and boosted PIs see reduced blood progestin levels of COCs. No efficacy data are available, however, reduced progestin could lead to unintended pregnancies.
Progestin only pills	No efficacy data are available; and data on POP levels when used with efavirenz or nevirapine are not available
Progestin-only injectables	Levels of DMPA do not appear to be reduced by ARVs. Studies on Net-En when used with ART are not available.
Emergency contraception	Limited evidence suggests that levonorgestrel levels are significantly reduced among women using LNG ECPs and efavirenz, but no efficacy data are available.
Levonorgestrel-releasing IUD	Limited evidence suggests that efficacy of the levonorgestrel-releasing IUD is unlikely to be affected by ART.
Implants	Data review on next slides



USAID
FROM THE AMERICAN PEOPLE

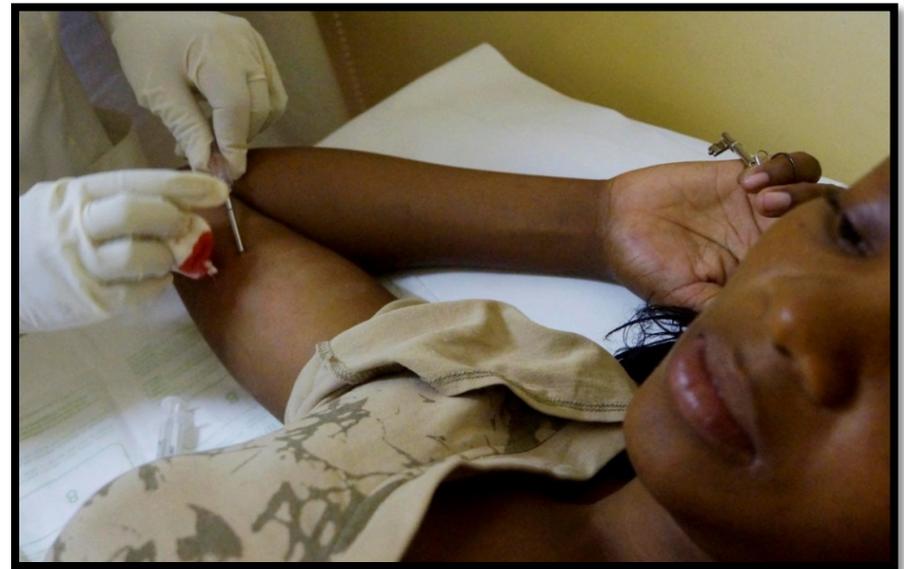
Contraceptive Implants

There are two distinctly different types of progestin based hormonal contraceptive subdermal implants available:

- Implanon (etonogestrel) 1 rod
- Jadelle (levonorgestrel) 2 rods

These implants differ in their hormonal formulations, mechanisms of action to prevent pregnancy, and duration of effectiveness (three versus five years, respectively)

Expected failure rate is less than 1%





USAID
FROM THE AMERICAN PEOPLE

How much is out there?

- Implants are the fastest growing method of contraception in Sub-Saharan Africa
- In 2014, USAID's Deliver Project shipped 1.9 million implants to 10 countries
- Efavirenz are WHO first line therapy
- 13 million women in Sub-Saharan Africa living with HIV are candidates for efavirenz use
- USAID shipped over 10 million units of efavirenz containing medication in 2014

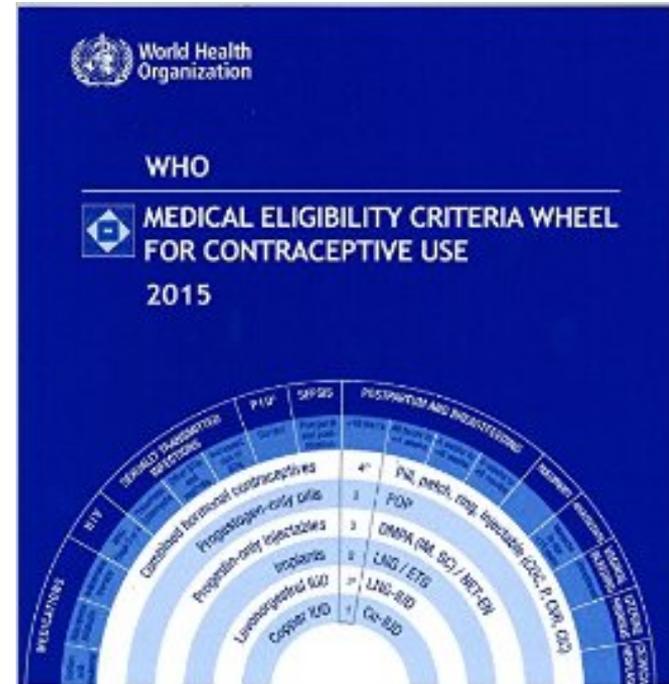




USAID
FROM THE AMERICAN PEOPLE

What is the MEC Guidance?

- Use of implants by HIV-positive women who use certain ART regimens are classified by the WHO via their medical eligibility criteria guidance as category 2:
 - The advantage of using the method generally outweigh the theoretical or proven risks





So....

- Reported increase in contraceptive failures with concomitant Jadelle and efavirenz use
- Despite an apparent decrease in contraceptive efficacy for women using implants and an EFV-based ART regimen, ***the data from the Kenya study suggest that implants are still more effective in preventing unintended pregnancy than shorter-acting contraceptive methods***, such as the DMPA injection, pills or condoms
- Data needed to support alternative strategies for optimizing the effectiveness of contraceptive implants in combination with efavirenz





USAID
FROM THE AMERICAN PEOPLE

Take Home Messages

- Implants still appear to be more effective in preventing unintended pregnancy than many other contraceptive methods used



© 2012 Akintunde Akinleye/NURHI, Courtesy of Photoshare

- HIV programs and providers need to actively engage women in conversations about the potential risks and benefits of each contraceptive method



USAID
FROM THE AMERICAN PEOPLE

What is USAID doing?

- PRH/OHA activities to provide guidance to USAID missions, partners and MOH counterparts.
 - USG/USAID Briefs
 - Research (MCSP and Envision)
 - Prospective PK/PD study – ETG (is ETG better than LNG – for how long?)
 - Retrospective chart review
 - Method Choice support



TECHNICAL ISSUE BRIEF

DRUG INTERACTIONS BETWEEN HORMONAL CONTRACEPTIVE METHODS AND ANTI-RETROVIRAL MEDICATIONS USED TO TREAT HIV

October 2014

BACKGROUND

This brief was produced in collaboration with the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the Office of Population and Reproductive Health at the U.S. Agency for International Development (USAID), with technical input from FHI 360.

What is the purpose of this brief?

This brief summarizes what is known on potential drug interactions between certain hormonal contraceptive methods and certain antiretrovirals (ARVs) used to treat HIV and to discuss recommendations and programmatic implications. This issue has been highlighted recently by the publication of a retrospective chart review that suggested a higher rate of pregnancy among women using levonorgestrel-releasing contraceptive implants (Jadelle) and efavirenz-based antiretroviral therapy (ART) compared with women taking non-efavirenz-based ART regimens.¹

What is a drug interaction?

A pharmacokinetic drug interaction occurs when a drug interferes (in a positive or negative way) with another drug, resulting in higher or lower levels of either drug in the body. Such changes in drug levels could have an impact on the effectiveness or side effects of either drug.

Why is this issue important for women living with HIV who use ART and a hormonal contraceptive method?

Certain hormonal contraceptive methods and certain ARVs have the potential to interact with each other and, in theory, to lead to decreases in efficacy of either medication or to increased side effects or toxicity. Any potential decrease in efficacy of a hormonal contraceptive method could increase risk of unintended pregnancy and associated negative health outcomes; any potential decrease in efficacy of ART could increase risk of treatment failure, development of viral resistance, and potential transmission to HIV-negative sex partners and infants. Increases in side effects can have an impact on the health and quality of life of the person living with HIV and may affect treatment adherence. Certain ARVs for which some concern about potential drug interaction exists, such as efavirenz, are becoming even more widely used following recent updates to WHO guidance on ART use.²

Who should read this brief?

- National policymakers responsible for HIV and/or family planning programming

- U.S. Government family planning and HIV program managers at headquarters and in the field
- HIV and family planning implementing partners, practitioners, researchers, and professional societies

TYPES OF HORMONAL CONTRACEPTIVES AND ART MEDICATIONS

What are some common hormonal contraceptive methods?

Common hormonal contraceptive methods include combined (estrogen/progestin) oral contraceptive pills (COCs, e.g., Microgynon*), progestin-only pills (POPs, e.g., Microlut*), injections (e.g., depot medroxyprogesterone acetate [DMPA] or Net-En), implants containing either levonorgestrel (e.g., Jadelle*) or etonogestrel (e.g., Implanon*), and levonorgestrel-releasing intrauterine devices (e.g., Mirena*). Emergency contraceptive pills (ECp) may contain levonorgestrel (LNG ECp), ulipristal acetate (UPA ECp), or combined estrogen and progestin (Yuzpe regimen).

What types of ARVs exist?

Five basic classes of ARV drugs exist: (1) nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs); (2) non-nucleoside reverse transcriptase inhibitors (NNRTIs); (3) protease inhibitors (PIs); (4) entry inhibitors; and (5) integrase inhibitors. Each class contains several different individual medications. In addition to individual medications, "fixed dose combination" drugs also exist; these combine two or more medications. A complete list of ARV medications approved by the U.S. Food and Drug Administration (FDA) is available at <http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119231.htm>.

Which ART regimens are commonly used?

The World Health Organization recommends that a first-line ART regimen for adults and adolescents should contain an NNRTI plus two NRTIs. The current recommended first-line regimen is efavirenz (EFV), tenofovir (TDF), and either lamivudine (3TC) or emtricitabine (FTC), provided in a fixed-dose combination.³ If this regimen

¹ Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Government. In addition, this is not an exhaustive list of hormonal contraceptive methods but represents some commonly used methods in U.S. Government-supported foreign assistance programs.



What is USAID doing?

- APC/Envision work on updating HC DDI chart and provider information
- Support to USG partners, USAID missions and implementing partners in integrating HC-HIV messages into HIV and FP programming
- Collaboration with WHO and UNFPA to disseminate information to MOH and UN offices



USAID
FROM THE AMERICAN PEOPLE

Key Considerations for HC-HIV: Rights Based Approach

Women and couples should retain the right to make an informed decision about their contraceptive and reproductive health options





USAID
FROM THE AMERICAN PEOPLE

Key Considerations for HC-HIV: Counseling & Access

- FP and HIV Providers must be trained on potential HC-HIV acquisition and interactions issues and on counseling approaches
- Women at risk for HIV/STIs should be counseled on dual method use in FP, HIV and MNCH settings.
- Women at risk for HIV should be counseled that there is a potential increased risk for HIV acquisition when using DMPA.
- Implant users (Jadelle or Implanon) who are living with HIV and using ART should be informed about the possibility of decreased contraceptive effectiveness
- FP/MNCH services should be strengthened to better serve the needs of PLHIV; including counseling on HC-ART interactions



USAID
FROM THE AMERICAN PEOPLE

Key Considerations for HC-HIV: Expanding Method Choice

- Every effort should be made to ensure that women and couples have access to a wide variety of contraceptive methods
- There are real/significant reasons for current method mix that are not easily shifted
- Reliance on DMPA/injectables and lack of access to LARC in Southern Africa is limiting women's ability to make choices regarding FP use.
- Alternative FP methods should be available for women who choose not to use DMPA or implants.





USAID
FROM THE AMERICAN PEOPLE

Key Considerations for HC-HIV: Integrated Service Delivery

Integrating FP services into HIV platforms provides important opportunities for providers to reach women and their partners with information about how their medications may interact





- Counseling Framework : <http://healthcommcapacity.org/hc3resources/strategic-communication-framework-for-hormonal-contraceptive-methods-and-potential-hiv-related-risks/>
- Hormonal contraceptive methods for women at high risk of HIV and living with HIV 2014 Guidance statement, WHO:http://www.who.int/reproductivehealth/publications/family_planning/HC_and_HIV_2014/en/
- **USG HC-HIV Technical Brief:** <http://www.usaid.gov/sites/default/files/documents/1864/hormonal-contraception-and-HIV.pdf>
- **HC/HIV Acquisition Update:** http://www.usaid.gov/sites/default/files/documents/1864/HC-HIV-BriefUpdate.pdf?utm_source=March+6%2C+2015&utm_campaign=2015.02.27&utm_medium=email
- **USG HC-ART Drug Interactions Brief:** http://www.usaid.gov/sites/default/files/documents/1864/HC_ART-brief.pdf



USAID
FROM THE AMERICAN PEOPLE

Thank you!

