

Hormonal Contraception and HIV: The WHO Responds

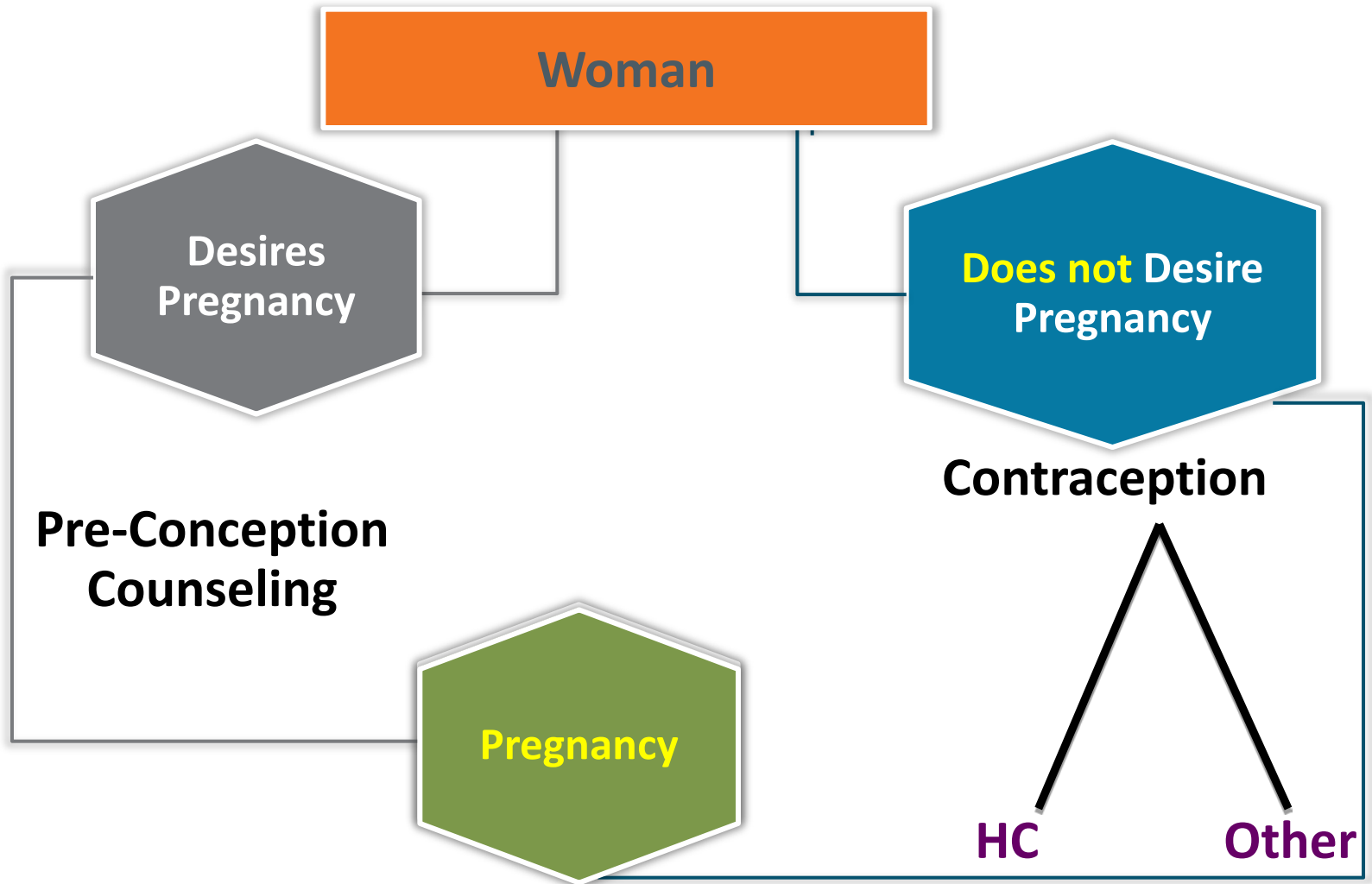
Ward Cates
MTN Annual Meeting
February 21, 2012

Acknowledgments

Colleagues from:

- FHI 360
- The MTN
- USAID
- University of Washington
- WHO
- And many more...

Woman's Fertility Intentions



Today's Talk

- **The History of an Hypothesis**
- **The WHO MEC Process**
- **The WHO Recommendations**
- **“So What” for the MTN?**

Hormones and HIV Possible Mechanisms

- **Vaginal and cervical epithelium (ectopy, etc.)**
- **Cervical mucus**
- **Menstrual patterns**
- **Vaginal and cervical immunology**
- **Viral (HIV) replication**
- **Acquisition of other STI**

HC/HIV Acquisition Research Timeline

- **1987** – **Plummer IAS presentation**
- **1988-on** – **Multiple secondary analyses**
- **1996** – **Marx monkey model/NIH review**
- **2008** – **1st WHO HC/HIV Consultation**

WHO Conclusions - 2008

- **“Intermediate” level of evidence**
- **COC – Category 1 - “No Restriction”**
- **DMPA – Category 1 for women at risk of HIV**
 - **Category 2 for youth (bone concerns)****“Advantages Outweigh Risks”**

Source: WHO Medical Eligibility Criteria (2008)

HC/HIV Acquisition Research Timeline

- **July 2011 – University of Washington HC/HIV study presented at IAS, Rome**
- **1st Week Oct 2011 – The Week That Was:**
 - **University of Washington HC/HIV study published in *Lancet Infectious Diseases***
 - ***New York Times* front page**
 - **Global “viral” media reaction**

BOOSTER SHOTS: ODDITIES, MUSINGS AND NEWS FROM THE HEALTH WORLD

Africa study suggests hormonal contraceptive tie to HIV infection



13 hours 44 min ago - health

Female hormonal contraceptive linked to higher HIV risk



Women who use hormonal control are roughly twice as likely to become infected with HIV or pass on the AIDS virus to their partner, according to a study published on Tuesday. The research was carried out among 3,700 heterosexual couples in Africa where one partner had the human immunodeficiency virus (HIV) and the other was uninfected.

Birth control method blamed for HIV risk



PHOTOFILE Last week, the US Federal Drug Administration warned over the potentially high risk of blood clots in women using birth control pills containing the hormonal chemical called estrogen. It is marketed under various brand names in Kenya. Such a product is registered with the Pharmacy and Poisons Board as well.

Health

Contraceptive Used in Africa May Double Risk of H.I.V.

By PAM BELLUCK
Published: October 3, 2011

The most popular contraceptive for women in eastern and southern Africa, a hormone shot given every three months, appears to double the risk the women will become infected with [H.I.V.](#), according to a large study published Monday. And when it is used by H.I.V.-positive women, their male partners are twice as likely to become infected than if the women had used no [contraception](#).

- RECOMMEND
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World news

HIV could spread if birth control injections increase, warn scientists

Researchers call for new guidelines for women using family planning services in Aids-hit areas

Miguna Miguna

Uhuru won propaganda war but lost legal battle



Comment: Page 24

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Nairobi Council starts e-Construction permits

Property: Page 38

the STAR

CONTRACEPTIVES DOUBLE HIV RISK

BY JOHN MUCHANGI

THE most popular contraceptive in Kenya doubles the risk of women becoming infected with HIV, a new study shows. Use of the injectable contraceptive also increases the risk of HIV-positive women infecting their male partners. The results present a predicament for

women because injectables and the pill are Kenya's most popular contraceptives, in part because women can keep them secret. The study was published in the respected *Lancet Infectious Diseases* journal on Monday and involved 3,800 couples from Kenya, Uganda, Tanzania, Botswana, Rwanda, South Africa and Zambia. It was led by University of Washington

but also included researchers from Kenyatta National Hospital, University of Nairobi and Moi University. The study has prompted the World Health Organisation to convene a meeting next January to consider if evidence is now strong enough to advise women against injectable contraceptives. Two past studies showed similar results

but researchers yesterday said the study is the strongest. "We want to make sure that we when there is a real need to warn, but the same time we don't want to con with a hasty judgement that would far-reaching severe consequences fo

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Contraceptives double HIV risk

FROM PAGE 1

sexual and reproductive health of women," said Mary Lyn Gaffield, an epidemiologist in the World Health Organisation's department of reproductive health and research quoted in the *New York Times*.

Kenya's Ministry of Public Health says they are waiting for direction from the WHO.

There may however be a policy change to promote alternative family planning solutions for women.

Injectables have been the most popular form of contraception in Kenya and are used by 48 percent of married women, according to the 2008 Kenya Demographic and Health Survey.

About 16% of total users prefer the pill while women using implants account for about 14 percent of total users.

The *Lancet* study says that women using hormonal contraception through injectables became infected at a rate of 6.61 per 100 person-years, compared with 3.78 for those not using them.

Transmission of HIV to men occurred at a rate of 2.61 per 100 person-years for women using hormonal contraception compared with 1.51 for those who did not.

Researchers have been trying to explain the link between contraceptive use and HIV infection.

They said it is possible

hormonal contraception causes biological changes, such as changes to the cells that line the vagina or cervix and that influence susceptibility to HIV.

Renée Heffron, an epidemiologist and co-author of the study, however said research examining whether the hormone changes genital tissue or vaginal mucous had been inconclusive.

"It could be that progestin in injectables causes immunologic changes in the vagina and cervix or could increase the HIV's ability to replicate," Charles Morrison, senior director of clinical sciences at FHI 360, an NGO whose work includes researching the intersection of family planning and HIV told the US media.

The study however recorded condom use, thus excluding the possibility that increased infection occurred because couples using contraceptives were less likely to use condoms.

Injectable contraceptives in Kenya include Depo Provera. Pfizer, the US-based manufacturer of the branded version of Depo-Provera, declined to comment to the *New York Times* on the study, saying officials had not yet read it.

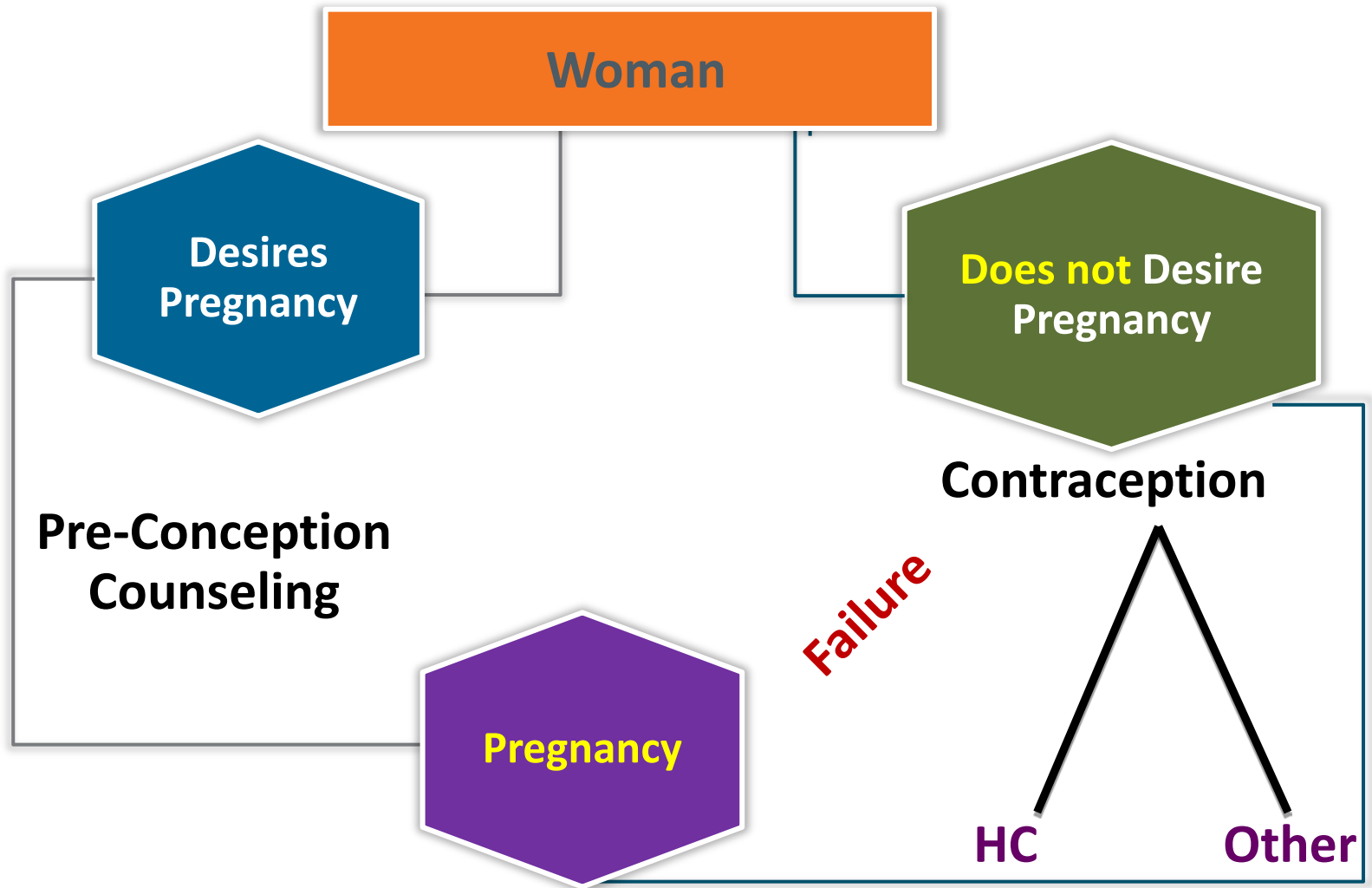
The study's authors however said the injectables used by the African women were probably generic versions.

Depo Provera has never been approved for use as a contraceptive in the US. It is controversial because it reportedly can cause heavy bleeding, weight gain, headaches, nervousness and depression.



RISKY: A nurse shows one of the most widely used contraceptives

Hormonal Contraception In Context



So...What's An **Uninfected** Woman To Do?

- If she uses DMPA,
 - Less risk of pregnancy
 - More risk of HIV acquisition
- If she becomes pregnant,
 - More risk of HIV acquisition
 - More risk of pregnancy M&M
- Tradeoffs

So...What's An **Infected** Woman To Do?

- If she uses hormonal contraception,
 - Less risk of pregnancy
 - More risk of HIV transmission to partner
- If she becomes pregnant,
 - More risk of HIV transmission to partner
 - Potential for transmission to infant
 - More risk of pregnancy M&M to self
- Tradeoffs

The WHO Recommendations

Developing Reference Documents

Research is conducted



Scientific evidence is obtained



The evidence is used to develop international recommendations



International recommendations are used as reference for national guidelines



Job aids (tools) are developed

Eligibility Criteria: WHO Classifications

Classification of Known Conditions	Definition
1	No restriction on use
2	Benefits generally outweigh risks
3	Risks generally outweigh benefits
4	Unacceptable health risk

Contraceptive Options for Youth

Age and Parity	Combined Hormonal Methods (Pills and Injectables), Condoms, Spermicides	Progestin-only Methods (Pills, Injectables and Implants)	IUDs	NFP, LAM
Under 18	No restriction	No restriction	Can generally use	No restriction
18-20				
Over 20				
Nulliparous	No restriction		Can generally use	No restriction

Source: WHO, 2008.

The WHO Consultation – The Setting

- **Jan 31 – Feb 2, 2012 in Geneva**
- **75 participants from 18 countries**
- **Days 1 & 2 review evidence**
- **Day 3 identify programmatic and research implications**

WHO Consultation – The Agenda

- **Synthesis of published literature on hormonal contraception/HIV**
 - Acquisition
 - Transmission
 - Progression
- **GRADE rating of the evidence**
- **Discussion of MEC criteria**

WHO Consultation – GRADE Process

- **Goal - To achieve transparency, standardization and rigor in summarizing evidence**
- **Adapted by many groups – WHO, ACP, USPSTF, CDC, et.al.**
- **Starting points**
 - **RCTs = “high quality”**
 - **Observational = “low quality”**

WHO Consultation – GRADE Rating

- **HC/HIV acquisition evidence**
 - 8 cohort studies met minimum quality criteria
 - Serious limitations
 - Rated “low overall quality”
- **HC/HIV progression evidence**
 - 1 RCT, 6 cohort studies
 - Rated “low overall quality”
- **HC/HIV transmission evidence**
 - Rated “low overall quality”

WHO Consultation – The Dilemma

- **WHO focused on the MEC category 1 for DMPA and condition “women at risk of HIV”**
- **Did the new evidence justify a change?**
 - If left an MEC 1 – no change implies DMPA has a clean bill of health
 - If moved to MEC 2 – a change implies evidence is strong enough to taint DMPA
- **Bell-shaped curve of opinion**

The WHO Statement – Feb 16

WHO/RHR/12.08

Hormonal contraception and HIV

Technical statement

Executive summary

Following new findings from recently published epidemiological studies, the World Health Organization (WHO) convened a technical consultation regarding hormonal contraception and HIV acquisition, progression and transmission. It was recognized that this issue was likely to be of particular concern in countries where women have a high lifetime risk of acquiring HIV, where hormonal contraceptives (especially progestogen-only injectable methods) constitute a large proportion of all modern methods used and where maternal mortality rates remain high. The meeting was held in Geneva between 31 January and 1 February 2012, and involved 75 individuals representing a wide range of stakeholders. Specifically, the group considered whether the guideline *Medical eligibility criteria for contraceptive use, Fourth edition 2009* (MEC) should be changed in light of the accumulating evidence.

After detailed, prolonged deliberation, informed by systematic reviews of the available evidence and presentations on biological and animal data, GRADE profile summaries on the strength of the epidemiological evidence, and analysis of risks and benefits to country programmes, the group concluded that the World Health Organization should continue to recommend that there are no restrictions (MEC Category 1) on the use of any hormonal contraceptive method for women living with HIV or at high risk of HIV. However, the group recommended that a new clarification (under Category 1) be added to the MEC for women using progestogen-only injectable contraception at high risk of HIV as follows:

Some studies suggest that women using progestogen-only injectable contraception may be at increased risk of HIV acquisition, other studies do not show this association. A WHO expert group reviewed all the 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 of HIV acquisi-

Technical statement on hormonal contraception and HIV

The World Health Organization (WHO) has concluded that women living with HIV or at high risk of HIV can safely continue to use hormonal contraceptives to prevent pregnancy. The recommendation follows a thorough review of evidence about links between hormonal contraceptive use and HIV acquisition.

[Technical statement](#)

8 pages, 6 February 2012

http://www.who.int/reproductivehealth/publications/family_planning/9789241563888/en/index.html

Statement
Statement



WHO Consultation – The Solution

- Recommendation – **MEC Category 1** (no restrictions)
- **1* Clarification** – “women using progestogen-only injectable strongly advised to also always use condoms”

WHO Consultation – Programmatic Recommendations

- **Withdrawal of hormonal contraception from FP programs is not warranted**
- **Contraceptive method mix needs to be expanded, especially for women at risk of HIV**
- **Condoms must be strongly emphasized**
- **FP and HIV programs should be integrated**

WHO Consultation – Research Recommendations

- Higher quality clinical studies are needed to improve the HC/HIV acquisition evidence
- Developing new multipurpose technologies to prevent both HIV and unintended pregnancy – a high level priority
- Understanding the biology of HC/HIV interactions essential

What Does This Mean For The MTN? (A Tale of 3 Enigmas)

The Etiologic Enigma

- All previous studies observational – selection/confounding biases likely
- Macaque studies continue to find increased SIV transmission with DMPA
- HIV prevention trials have high HIV rates among young women; most using DMPA
- Recent HC/HIV findings have raised visibility
- We need to resolve this important global health issue once and for all

The Programmatic Enigma

- **Is evidence sufficient to withdraw DMPA or other hormonal methods from national FP programs?**
- **How to seize an opportunity to increase contraceptive method mix within national programs?**
- **Can this issue accelerate FP/HIV program integration?**

The Ethical Enigma

- **Should participants in an HIV prevention trial be required to use a contraceptive which might increase the risks of acquiring HIV?**
- **Should trial participants choosing DMPA for contraception have access to additional HIV prevention measures beyond those available in their communities?**

HC/HIV: Ward's Conclusions

- **Recent DMPA findings concerning**
- **Intriguing pregnancy results**
- **Reproductive choice tradeoffs**
- **WHO's 1* clarification**
- **Women need contraceptive options**
- **Stay tuned**