The Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial: Primary Results

The ECHO Trial Consortium

9th SA AIDS Conference, Durban, South Africa

13 June 2019

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Evidence for Contraceptive Options & HIV Outcomes

Introductions & agenda

- **Introduction to the ECHO Study – Prof Helen Rees**, Executive Director, Wits RHI and Personal Professor, Obstetrics and Gynaecology, University of Witwatersrand, Johannesburg, SA
- **Hormonal contraception and HIV acquisition: The need for ECHO – Dr Nelly Mugo**, Head of the Sexual, Reproductive, Adolescent and Child Health Research Programme, Kenya Medical Research Institute, Nairobi, Kenya, and Research Associate Professor, Department of Global Health, University of Washington, Seattle, USA
- **Recognition of Dr Ward Cates – Dr Timothy Mastro**, Chief Science Officer, FHI 360, Durham, NC, USA
- **Results** – **Dr Jared Baeten**, Professor and Vice Chair, Department of Global Health, University of Washington Schools of Medicine and Public Health, Seattle, WA, USA
- **Next Steps – Dr James Kiarie**, Coordinator, Human Reproduction Team, Department of Reproductive Health and Research, World Health Organization, Geneva, SUI

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Starting point

Safe and effective contraception is essential to the health and development of women, children and communities worldwide

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Context

- Women represent over half of the 37 million persons currently living with HIV; nearly 600,000 new HIV infections occur yearly among adolescent girls and women in Africa.
- Modern contraceptive methods are used by >700 million women worldwide, including >58 million African women.
- Use of these methods substantially improves the health of women and children by averting unintended pregnancy and sequelae and contributes to women's empowerment and to economic and social development.

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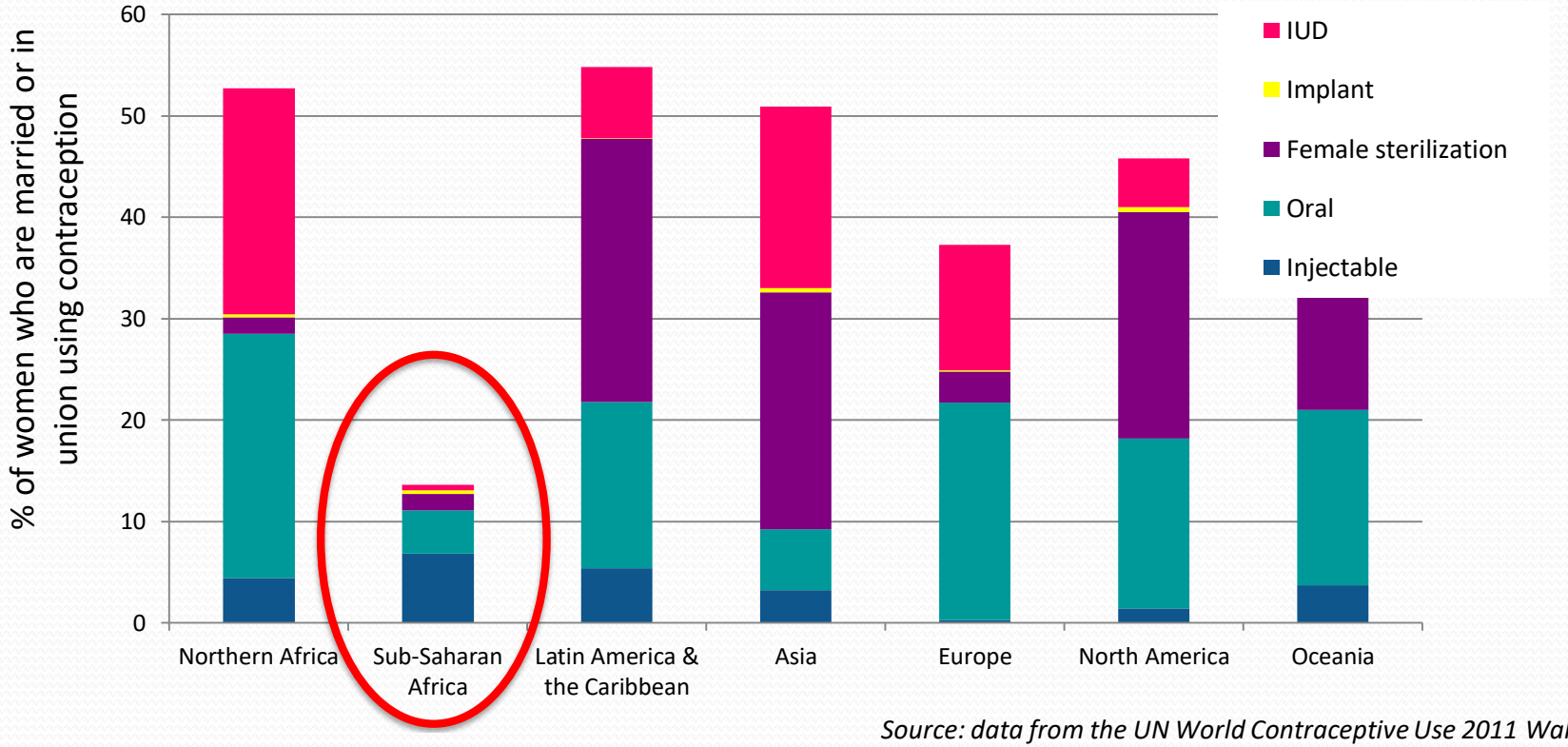
Unmet need and contraceptive choices

- For African women, unmet contraceptive need is high, contraceptive choices are often limited, and injectable methods are the most commonly used.



Source: data from the UN World Contraceptive Use 2011 Wall Chart

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30 years of unresolved questions

Progesterone implants enhan
transmission and early vi

PRESTON A. MARX[1,2], ALEXANDER I. SPIRA[1,2], AGEGNEHU GETTIE
RONALD S. VEAZEY[4], AND
LEE E. CL

PLOS | MEDICINE

RESEARCH ARTICLE

Hormonal
Acquisition
Meta-analy

Charles S. Morrison[1]*, P
Angela M. Crook[5], Lut Va
Barbara A. Friedland[9], Ri
Abdool Karim[10], Stephani
Sheena McCormack[4], Nua
Straten[15], Deborah Watson
Nicola Low[18]

Los Angeles Times | BOOSTER SHOT

LOCAL U.S. WORLD BUSINESS SPORTS ENTERTAINMENT HEALTH LIVING TRA

BOOSTER SHOTS | MEDICINE | FITNESS & NUTRITION | MENTAL HEALTH | HEALTH REPO

HEALTH TOPICS: TAINTED CANTALOUPES | COLON CANCER | CAFFEINE & WOMEN'S DEPRESSION

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

Africa study suggests hormonal contraceptive tie to HIV infection

HIV transmission rates may be increased by hormone contracepti

FRANCE 24 INTERNATIONAL NEWS 24H/7

FR - EN - AR

04 October 2011 12:20 PM GMT

NEWS | WIRES

13 hours 44 min ago - health

Female hormonal contraception linked to higher HIV risk

Miguna Miguna

Uhuru won propaganda war but lost legal battle

Comment: Page 24

Building online

Nairobi Council starts e-Construction permits

Property: Page 38

FRESH, INDEPENDENT, DIFFERENT

NO: 1287
WEDNESDAY, OCTOBER 5, 2011
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Ksh40/00

theSTAR

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 Organization 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 current study is the strongest.

"We want to make sure that we warn when there is a real need to warn, but at the same time we don't want to come up with a hasty judgement that would have far-reaching severe consequences for the

CONTINUED ON PAGE 6

DAILY NATION

Wednesday, October 5, 2011

Mobile Site | Nation Media Group | Nation Careers | Africa Review | The EastAfrican | Business Daily | NTV | NTV Uganda

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Birth control method blamed for HIV risk

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LE Last week, the US Federal Drug Administration warned over the potentially high risk of blood clots in women using birth ile containing the hormonal chemical called drospirenone. It is marketed under various brand names. In Kenya, such a product is with the Pharmacy and Poisons Board as Yasmin, and is sold in the form of tablets.

NTV

THE NEW YORKER

NEWS & TECH | BUSINESS | HUMOR | CARTOONS | MAGAZINE | AUDIO

OBER 4, 2011

AIDS AND CONTRACEPTIVES: BAD CHOICES IN AFRICA

BY MICHAEL SPECTER

World Health Organization

Statement on the Heffron et al study on the safety of using hormonal contraceptives for women at risk of HIV infection

October 2011

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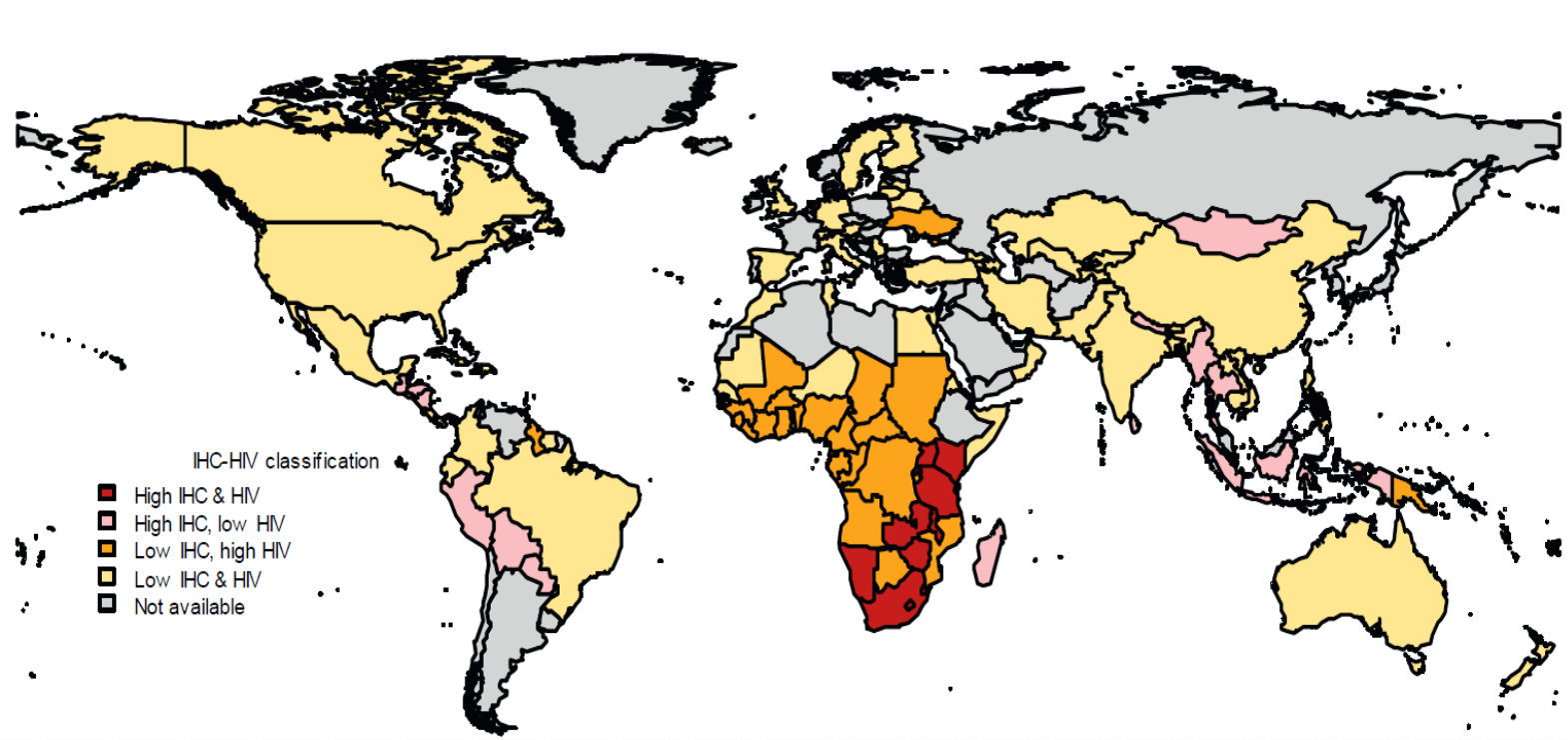
Injectable contraceptive use and HIV

- In many settings in Africa where HIV incidence is high, the intramuscular injectable progestin depot medroxyprogesterone acetate (DMPA-IM) is the predominant contraceptive used.



Source: Butler et al., AIDS 2013

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ECHO Trial Consortium

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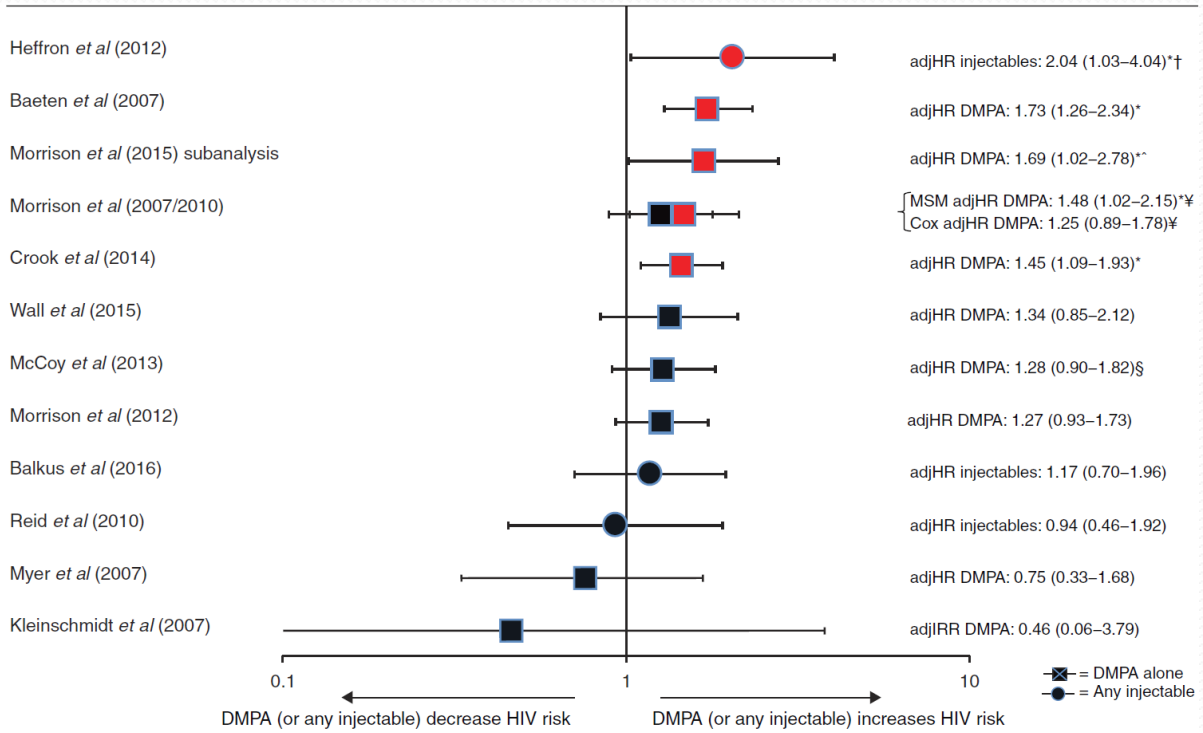
Prior evidence

- 30 years of epidemiologic and laboratory studies have tried to determine whether there is truly increased risk of HIV acquisition associated with use of hormonal contraception.
- Some studies showed that progestin-only injectables, particularly the intramuscular injectable depot medroxyprogesterone acetate (DMPA-IM), were linked to increased HIV risk, but other studies did not show this result.
  - In meta-analyses, the magnitude of increased HIV risk was approximately 40-50% (i.e., hazard ratios of 1.4-1.5)



Source: Polis et al., AIDS 2016

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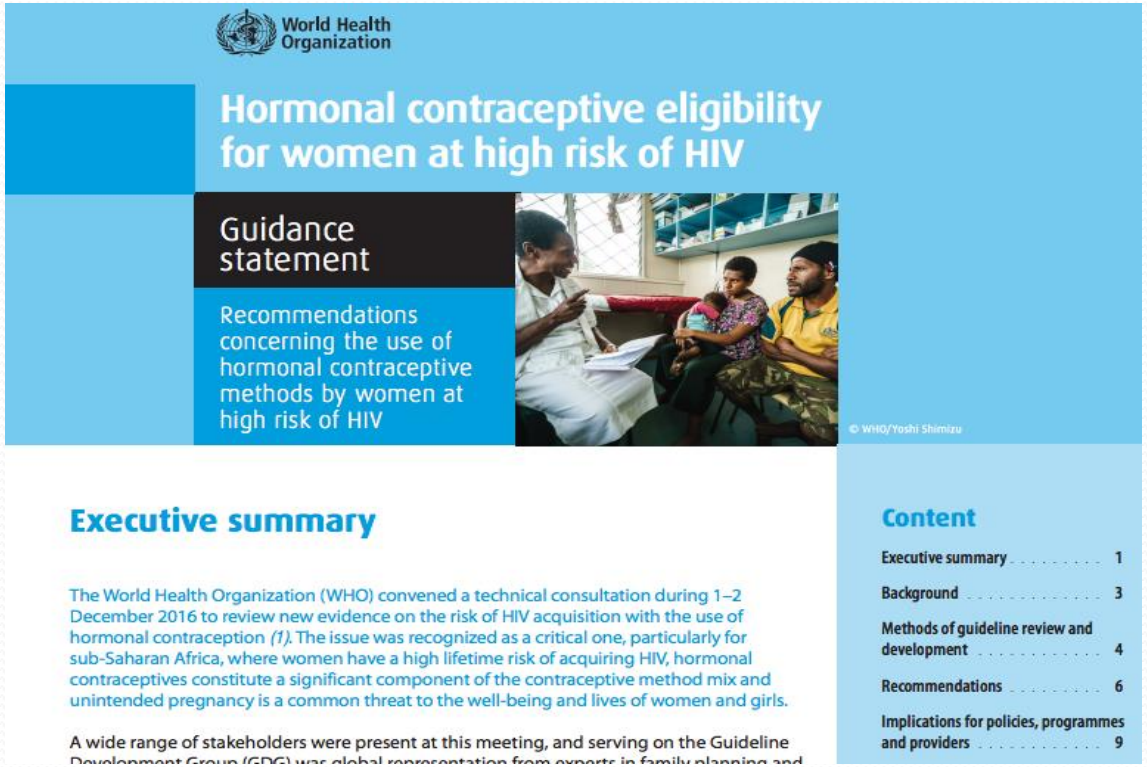
Prior evidence

- Very few research studies have looked at HIV risk for other highly effective contraceptives, such as intrauterine devices (IUDs) and hormonal implants, including levonogestrel (LNG) implants.

WHO guidance

- Over the past decade, WHO has repeatedly reviewed the evidence relating hormonal contraceptive use to HIV risk.

- In 2017, WHO guidance summarized that women at risk for HIV can use progestin-only injectables but should be advised about:
  - Concerns about possible ↑ risk of HIV
  - Uncertainty about causal relationship
  - How to minimize their risk



World Health Organization

Hormonal contraceptive eligibility for women at high risk of HIV

Guidance statement

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

© WHO/Yoshi Shimizu

Executive summary

The World Health Organization (WHO) convened a technical consultation during 1–2 December 2016 to review new evidence on the risk of HIV acquisition with the use of hormonal contraception *(1)*. The issue was recognized as a critical one, particularly for sub-Saharan Africa, where women have a high lifetime risk of acquiring HIV, hormonal contraceptives constitute a significant component of the contraceptive method mix and unintended pregnancy is a common threat to the well-being and lives of women and girls.

A wide range of stakeholders were present at this meeting, and serving on the Guideline

Content

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Women's right to know

- Women need to know whether certain contraceptives increase their chances of getting HIV.
- This information will help them make informed choices about which contraceptive they want to use and which HIV prevention methods they need.

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Rationale for a randomised trial

Injectable, intrauterine, and implantable contraceptives have been prioritised for programmatic delivery because they offer high contraceptive efficacy and safety.

A randomised trial provides the highest quality evidence to enable women to make fully informed choices, inform clear counselling messages for clinicians, and offer guidance for policymakers and programs.

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ECHO

- ECHO was a multicentre, open-label, randomised clinical trial comparing HIV incidence and contraceptive benefits in women living in areas of high HIV incidence and using one of three highly-effective, licensed contraceptive methods:
  - intramuscularly-delivered depot medroxyprogesterone acetate (DMPA-IM)
  - a copper intrauterine device (IUD)
  - and a levonorgestrel (LNG) implant

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Objectives

- **The primary objective was to compare HIV incidence among women randomised to DMPA-IM, a copper IUD, or an LNG implant.**

- Secondary objectives included comparison by randomised method of rates of pregnancy, contraceptive method continuation, and serious adverse events and adverse events leading to method discontinuation.

- The trial began in December 2015 and concluded in October 2018.

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Contraceptive methods rationale

DMPA-IM

Copper IUD

LNG implant

- **DMPA-IM** was included in the trial because it is the contraceptive that observational data suggested could increase HIV susceptibility and is commonly used in many African settings that have high HIV prevalence.
- We included the **copper IUD** to have a highly-effective non-hormonal comparator.
- The **LNG implant** was included to represent another progestin-based contraceptive and because use of long-acting reversible methods like implants is rapidly increasing in Africa. LNG is also a part of many oral contraceptive pills and multipurpose prevention technologies in development.

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Trial sites

- The trial was undertaken in 12 sites in 4 countries: Eswatini (1), Kenya (1), South Africa (9), and Zambia (1)

The Aurum Institute
Klerksdorp, South Africa

Effective Care Research Unit
East London, South Africa

Emavundleni Research Centre
Cape Town, South Africa

Madibeng Centre for Research
Brits, South Africa

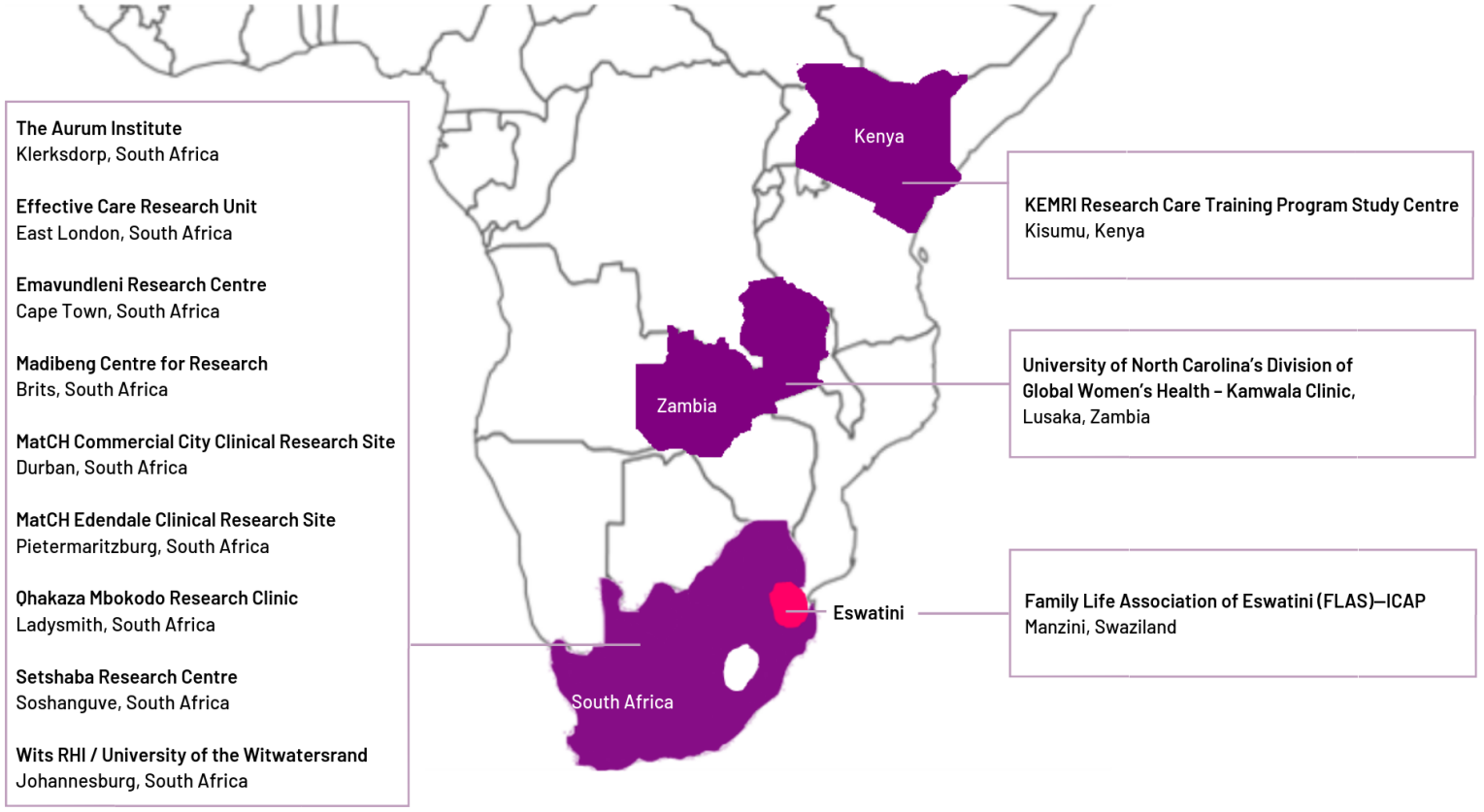
MatCH Commercial City Clinical Research Site
Durban, South Africa

MatCH Edendale Clinical Research Site
Pietermaritzburg, South Africa

Qhakaza Mbokodo Research Clinic
Ladysmith, South Africa

Setshaba Research Centre
Soshanguve, South Africa

Wits RHI / University of the Witwatersrand
Johannesburg, South Africa



KEMRI Research Care Training Program Study Centre
Kisumu, Kenya

University of North Carolina's Division of Global Women's Health – Kamwala Clinic,
Lusaka, Zambia

Family Life Association of Eswatini (FLAS)–ICAP
Manzini, Swaziland

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Screening

- Eligibility criteria:
  - desired effective contraception,
  - not pregnant,
  - HIV seronegative,
  - aged 16-35 years,
  - agreed to use the assigned method for 18 months,
  - reported not using injectable, intrauterine, or implantable contraception for the prior six months, and
  - able to provide written, informed consent.

Women were recruited for this trial based on residing in geographies that had high risk of HIV but not individual characteristics of HIV risk, such as transactional sex, history of STIs, or self-reported high-risk behaviours.

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Randomisation and contraceptive methods

- At enrolment, women were assigned in a 1:1:1 ratio to receive either:
  - DMPA-IM (150 mg/1 mL, Depo Provera, Pfizer),
  - copper IUD (Optima TCu380A, Injeflex), or
  - LNG implant (Jadelle, Bayer),

  using variable block size randomization, stratified by site.

- DMPA-IM was provided on site every 3 months
- LNG implant placement was confirmed at every visit
- Copper IUD placement was confirmed at one month, when clinically indicated, and at the final visit.

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Follow-up

- Study follow-up occurred at one month to address contraceptive side effects, then quarterly for up to 18 months, including HIV testing, contraceptive counselling, and safety monitoring.
  - Women were counselled that they could at any time choose to discontinue their randomised method, choosing another trial method, a different contraceptive method, or no method.
    - Women discontinuing their randomised method were retained in the trial.
  - In 2017, all women were provided updated information based on WHO guidance.

HIV prevention

- At every visit, participants received a comprehensive package of HIV prevention services, including HIV risk reduction counselling, partner and participant HIV and STI testing and management, condoms, and, as it became a part of national standard of prevention, pre-exposure prophylaxis (PrEP).
- HIV counselling messages were implemented consistently for all participants and emphasized that none of the three contraceptive methods used in the study provided protection against HIV or STIs.

ECHO oversight

- Ethics reviews for each trial site
- Periodic reviews by qualified independent clinical monitors
- A safety oversight committee, available 24/7 for clinical advice
- Global Community Advisory Group & Community Advisory Boards at each site, with Good Participatory Practice plans
- An independent Data and Safety Monitoring Board, which met twice yearly

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The ECHO Trial

is dedicated to the memory of

Dr. Ward Cates

1942 - 2016

President – Research

FHI 360

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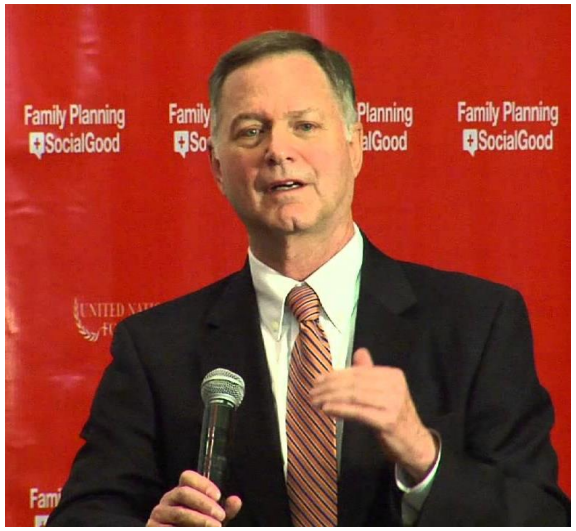
Ward – one of a kind!



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Why ECHO was important for Ward

- A champion for the integration of women's reproductive health and HIV prevention: FP-HIV
- A rigorous scientist – "follow the data"
- Effectively made the case for an RCT to provide high-quality data on the questions behind ECHO
- Was key to mobilizing the resources for ECHO
- Always looked for a "Win – Win" outcome
- An inspirational mentor
- ECHO is an important part of Ward's legacy

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Ward would have loved to see the data!

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ECHO results

ECHO performance metrics

To do the ECHO trial well, the team, funders, and DSMB agreed prior to initiation that a key operational metrics would be reviewed continually during the study and if not met would trigger careful reevaluation of whether to stop the trial:

ECHO Performance Standard	Target (*=overall and at each site)
#1 Accrual	Achieve target sample within ~18 months
#2 Method refusal	<5% of subjects*
#3 Retention	Per-visit completion of ≥90% and ≤10% of expected person-years lost*
#4 Method discontinuation	≤10% of all person-time off assigned method*
#5 HIV incidence	*sufficient to meet the study objectives (≥3.5%/year)*
#6 Ineligible enrollments	<1-2% of total*
#7 HIV endpoint adjudication	up-to-date for each DSMB review*
#8 Data quality	current for each DSMB, QC ≤5/100 CRFs, fax time ≤7d*

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Statistical design

- The trial was designed with 80% power to detect a 50% increase in the hazard of HIV for each contraceptive method compared to each of the others

DMPA-IM vs copper IUD | DMPA-IM vs LNG implant | copper IUD vs LNG implant

  - *We chose a 50% increase in HIV risk based on formative work with stakeholders to determine a meaningful difference that would inform policy change.*

- Assumptions:
  - underlying HIV incidence of 3.5 per 100 woman-years
  - a two-sided type I error rate of 0.04 for each comparison
  - 10% loss to follow-up & 10% dilution of treatment effect due to method discontinuation

- Under these assumptions, a minimum of 250 HIV acquisition events per comparison was required, and a total sample size of 7800 was planned.

Enrolment and randomised assignments

7829 women ages 16-35 desiring contraception and willing to be randomised

Randomise (1:1:1 ratio)

- **DMPA–IM (2609 women)**
- **Copper IUD (2607 women)**
- **LNG implant (2613 women)**

Eswatini	Kenya	South Africa	Zambia
502	901	5768	658

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Participant characteristics

Average age 23 (range 16-35), 63% <25 years of age

Most (81%) were not married & most (81%) had previously been pregnant at least once

Half did not use a condom with their last sex act, but only 7% reported >1 partner in the prior 3 months

STIs were common: 18% had *C. trachomatis,* 5% *N. gonorrhoeae*, and 38% HSV-2

MPA levels in blood samples were tested in a subset of participants from the enrolment visit – 13% had levels suggesting potential use in the prior 6 months

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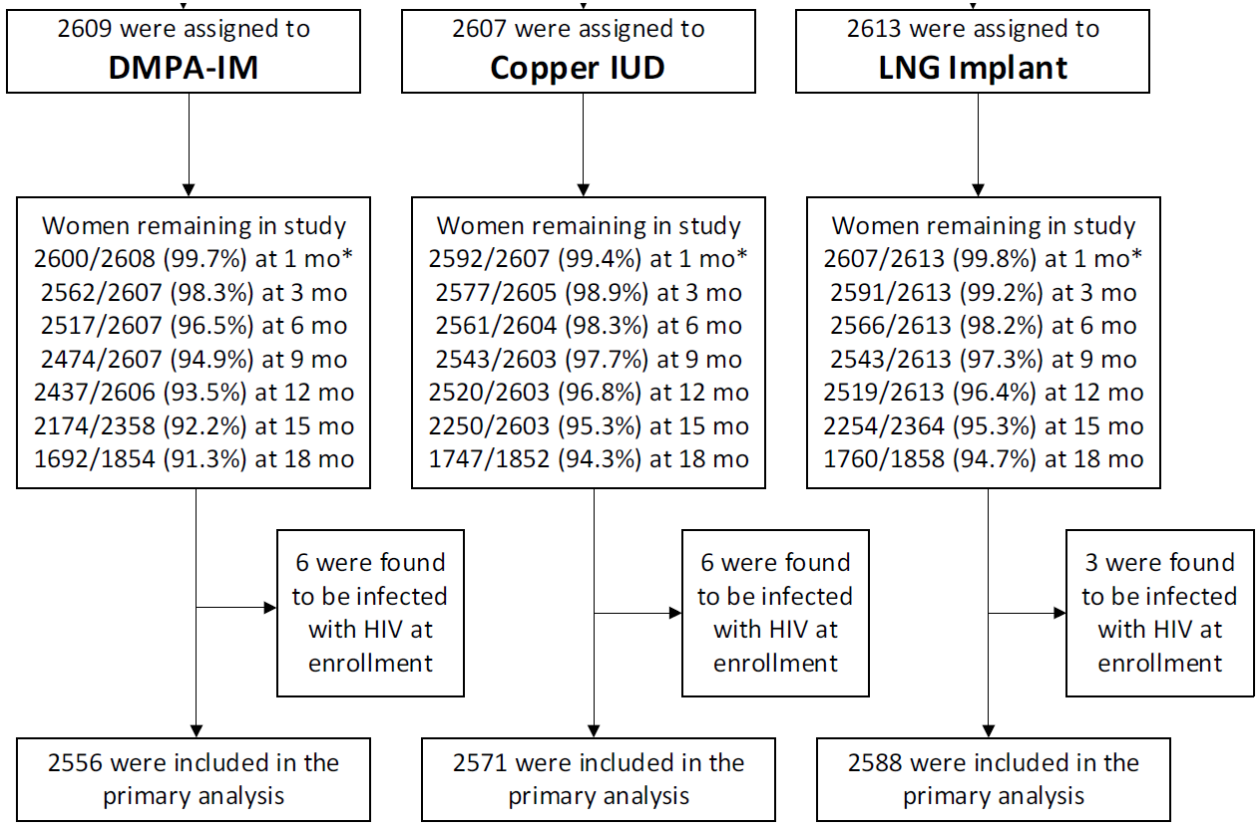
Follow-up

- 7715 (99%) completed at least one post-randomization HIV test
- Retention was 93.6% at the final study visit & >91% at each visit in all groups
- A total of 10,409 woman-years of follow-up time were accrued



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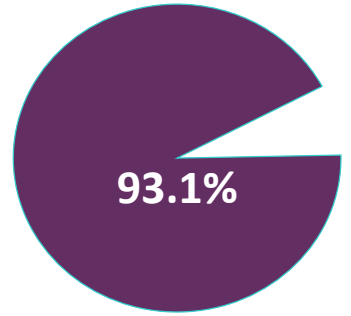
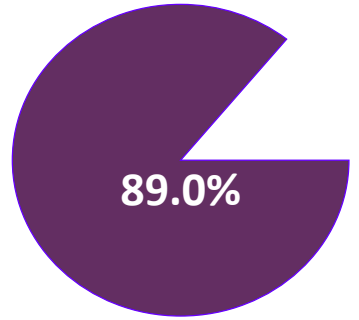
Contraceptive Method Use

- 7785 / 7829 women (99.4%) accepted their randomised method at enrolment.
  - Of the 44 who initially declined, 0 were assigned DMPA-IM, 36 (1.4%) copper IUD, 8 (0.3%) LNG implant
- **Participants used their methods for 92% of the time they were in the study**
- For DMPA-IM, 99.2% of injections were provided on-site

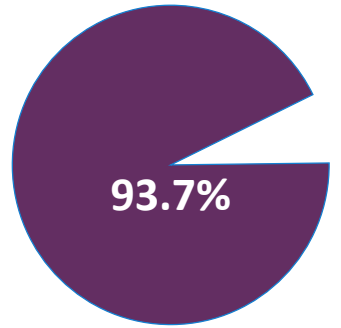
DMPA-IM



Copper IUD



LNG implant



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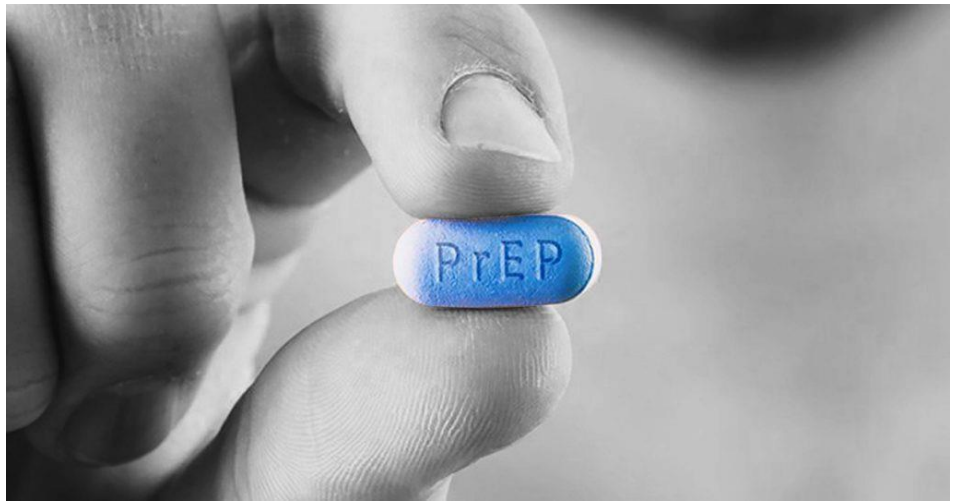
PrEP

- PrEP became available relatively late into the course of the trial

- 622 women used PrEP
  - 188 DMPA-IM
  - 216 copper IUD
  - 218 LNG implant

- PrEP use overlapped with 195 woman-years in the trial (2% of total follow-up)



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Rate of new HIV infections

- In total, **397 of the 7829** women acquired HIV during the study
- The overall rate of new HIV infections was 3.81% per year (95% CI 3.45-4.21).

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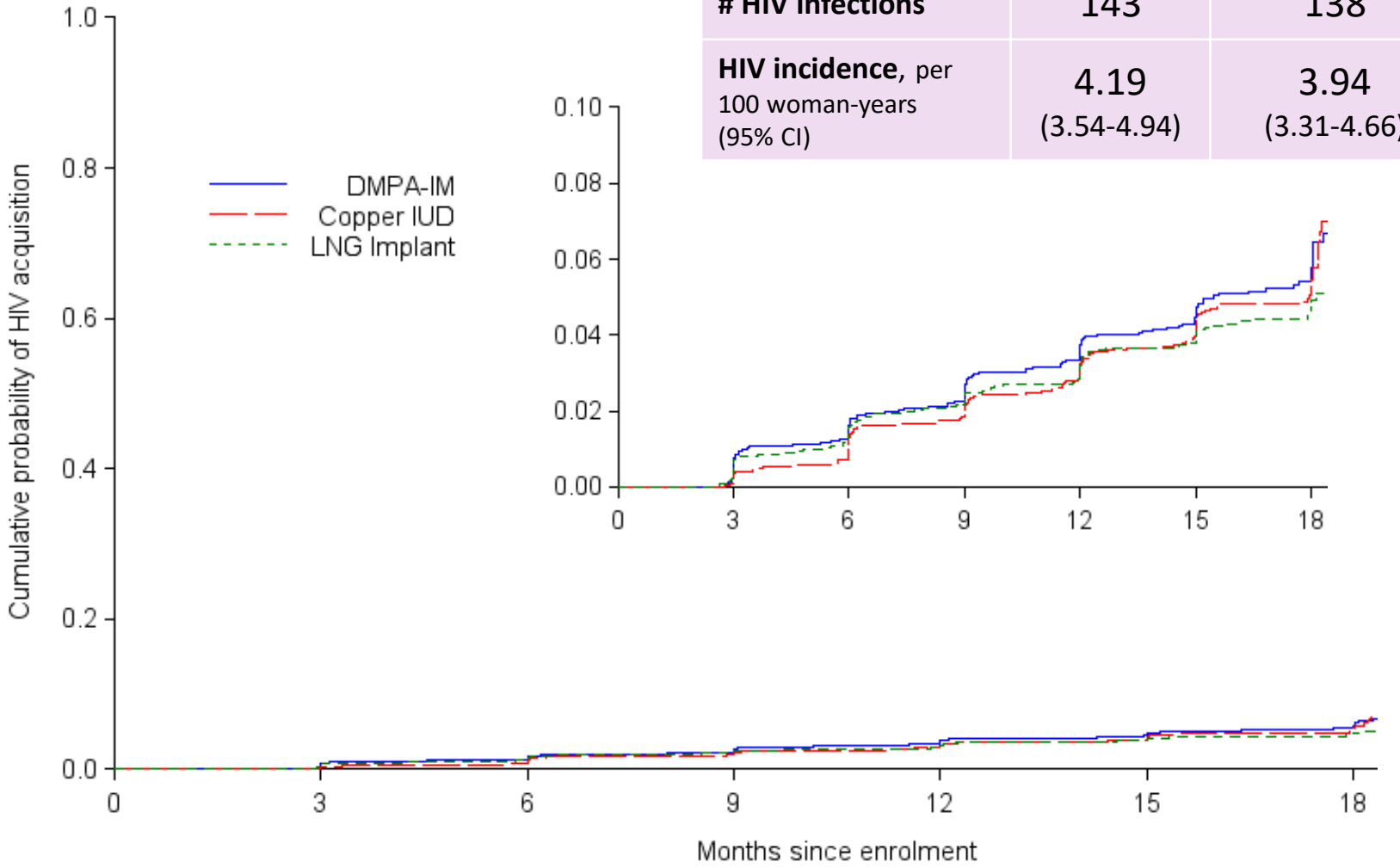
HIV incidence

Intention-to-treat analysis			
	DMPA-IM	Copper IUD	LNG Implant
# HIV infections	143	138	116
HIV incidence, per 100 woman-years (95% CI)	4.19 (3.54-4.94)	3.94 (3.31-4.66)	3.31 (2.74-3.98)



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HIV incidence – intention-to-treat analysis

Intention-to-treat analysis			
	DMPA-IM	Copper IUD	LNG Implant
# HIV infections	143	138	116
HIV incidence, per 100 woman-years (95% CI)	4.19 (3.54-4.94)	3.94 (3.31-4.66)	3.31 (2.74-3.98)

DMPA-IM vs. Copper IUD
HR = 1.04
96% CI = 0.82-1.33
p = 0.72

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HIV incidence – intention-to-treat analysis

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DMPA-IM vs. Copper IUD	DMPA-IM vs. LNG Implant
HR = 1.04	HR = 1.23
96% CI = 0.82-1.33	96% CI = 0.95-1.59
p = 0.72	p = 0.097

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HIV incidence – intention-to-treat analysis

Intention-to-treat analysis			
	DMPA-IM	Copper IUD	LNG Implant
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DMPA-IM vs. Copper IUD	DMPA-IM vs. LNG Implant	Copper IUD vs. LNG Implant
HR = 1.04	HR = 1.23	HR = 1.18
96% CI = 0.82-1.33	96% CI = 0.95-1.59	96% CI = 0.91-1.53
p = 0.72	p = 0.097	p = 0.19

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Subgroup and sensitivity analyses

- Subgroup analyses – including defined by age (< & ≥25 years) and HSV-2 serostatus – results were similar to the overall findings
- Sensitivity analyses were done limiting to time up until the first discontinuation of randomised method, using causal analysis methods + inverse probability weighting + adjustment for baseline and time-dependent covariates. Those results were consistent with the primary intention-to-treat analyses.

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HIV incidence – South Africa (post hoc)

Intention-to-treat analysis			
	DMPA-IM	Copper IUD	LNG Implant
# HIV infections	124	118	103
HIV incidence, per 100 woman-years (95% CI)	4.94 (4.11-5.89)	4.58 (3.79-5.49)	4.02 (3.28-4.87)

DMPA-IM vs. Copper IUD	DMPA-IM vs. LNG Implant	Copper IUD vs. LNG Implant
HR = 1.05	HR = 1.19	HR = 1.13
96% CI = 0.82-1.36	96% CI = 0.91-1.55	96% CI = 0.87-1.47
p = 0.69	p = 0.20	p = 0.37

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Pregnancy

Primary intention-to-treat analysis			
	DMPA-IM	Copper IUD	LNG Implant
# Pregnancies	61	116	78
Pregnancy incidence, per 100 woman-years	1.75	3.27	2.19

Continuous use analysis			
	DMPA-IM	Copper IUD	LNG Implant
# Pregnancies	18	35	21
Pregnancy incidence, per 100 woman-years	0.61	1.11	0.63

- Pregnancy rates were low, in all three groups, and most pregnancies (71%) occurred among women who had previously discontinued their randomised method.
- All methods had high contraceptive effectiveness – the two hormonal methods had lower pregnancy rates than the IUD.

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Safety

- Serious adverse events were rare across all groups

- Adverse events that resulted in method discontinuation were relatively uncommon (7% of women overall) and more common among women randomised to the copper IUD or LNG implant compared to DMPA-IM

	DMPA-IM	Copper IUD	LNG Implant
SAE	49 (1.88%)	92 (3.53%)	78 (2.99%)
AE resulting in method discontinuation	109 (4.18%)	218 (8.36%)	226 (8.65%)

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ECHO Summary

- This multi-country randomised trial measured HIV incidence among African women assigned to one of three highly-effective contraceptive methods.
- Acceptance of randomised method, contraceptive continuation, and retention were very high across all methods.
- All three methods were effective at preventing pregnancy and were well tolerated.
- HIV incidence was high for all three groups.

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Discussion – HIV risk

- We designed this trial to detect a 50% increase in HIV incidence for each of the contraceptive methods compared to each of the others. None of the comparisons showed a 50% increase in HIV incidence.

Discussion – HIV risk

- We designed this trial to detect a 50% increase in HIV incidence for each of the contraceptive methods compared to each of the others. None of the comparisons showed a 50% increase in HIV incidence.

- Results from the primary intention-to-treat, analyses among pre-defined subgroups, and sensitivity analyses limited to continuous use of the randomised method (and using causal analysis methods) all had consistent findings for all comparisons.

Discussion – HIV risk

- We designed this trial to detect a 50% increase in HIV incidence for each of the contraceptive methods compared to each of the others. None of the comparisons showed a 50% increase in HIV incidence.

- Under the design of this study an observed approximately 30% increase in HIV incidence would have been found to be statistically significant, and hazard ratios less than approximately 1.17 would have excluded a 50% increase in risk from the confidence interval.

Discussion – HIV risk

- We designed this trial to detect a 50% increase in HIV incidence for each of the contraceptive methods compared to each of the others. None of the comparisons showed a 50% increase in HIV incidence.

- DMPA-IM and copper IUD had comparable HIV risk.

DMPA-IM vs. Copper IUD
HR = 1.04
96% CI = 0.82-1.33
p = 0.72

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Discussion – HIV risk

- We designed this trial to detect a 50% increase in HIV incidence for each of the contraceptive methods compared to each of the others. None of the comparisons showed a 50% increase in HIV incidence.

- DMPA-IM and copper IUD had point estimates >1.17 & <1.30 compared to LNG implant, with CIs that included both no difference and a 50% increase.

DMPA-IM vs. LNG Implant	Copper IUD vs. LNG Implant
HR = 1.23	HR = 1.18
96% CI = 0.95-1.59	96% CI = 0.91-1.53
p = 0.097	p = 0.19

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Discussion – HIV risk

- We designed this trial to detect a 50% increase in HIV incidence for each of the contraceptive methods compared to each of the others. None of the comparisons showed a 50% increase in HIV incidence.

- For individual women at very high HIV risk, we acknowledge that even a relatively small effect might be important in contraceptive and HIV prevention decision-making.

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Discussion – safety and pregnancy

- All three contraceptive methods were well-tolerated. Adverse events resulting in method discontinuation were generally within the spectrum of common side effects for these methods.
- All three methods had high contraceptive effectiveness, with pregnancy rates approximately 1% or less per year when in use.
- Fewer women using DMPA-IM discontinued their method due to adverse events compared with women using either the copper IUD or the LNG implant, and the pregnancy rate for DMPA-IM users was the lowest.

Discussion – other methods

- For logistical and financial feasibility, we chose to include three highly-effective contraceptive methods available in the African region, including one non-hormonal and two different progestin-only methods.
- Our results cannot be generalized to other contraceptive methods not included in the study (e.g., NET-En, DMPA-SC, hormone-containing IUDs, etc.)
- We enrolled women who desired effective contraception and did not include a placebo or no contraceptive group in this trial. The salient question is weighing the relative risks and benefits of different methods, not no method.

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Discussion – services

- We recognise that regular counseling, scheduled follow-up, on-site contraceptive delivery, and clinical management of contraceptive side effects in this study contributed to high method continuation.

- This trial demonstrates that delivery of high-quality services to support the use of the copper IUD and the LNG implant across multiple African settings is possible with appropriate investment in training, assurance of provider clinical competency, adequate human resources for counselling and management of side effects, and necessary logistical support including management of commodities.

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Discussion – HIV incidence

- In spite of an individualized HIV prevention package provided to all participants throughout follow-up and country-wide HIV treatment and prevention programmes, HIV incidence was alarmingly high in this population throughout the course of the trial and STI prevalence at baseline was also very high.

- Our results strongly emphasize the need for more aggressive HIV and STI prevention and management efforts for African women, including PrEP and HIV prevention integrated with contraceptive services.

Conclusions

- Many women in Africa are at high risk for HIV infection and for morbidity and mortality from unintended pregnancy.
- This well-executed randomised trial did not find a substantial difference in HIV risk among the methods evaluated, and all methods were safe and highly effective.
- These results underscore the importance of continued and increased access to these three contraceptive methods, as well as expanded contraceptive choices, complemented by high-quality HIV and STI prevention services.

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Conclusions

Women's informed choice in sexual and reproductive health services is essential. This evidence will enhance women's contraceptive decision-making and assist providers and policymakers in delivering high-quality, rights-based contraceptive care.

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Acknowledgements

- We thank the women who participated in this study for their motivation and dedication and the communities that supported this work. We are grateful to the members of the trial's Data and Safety Monitoring Board, Global Community Advisory Group and local community advisory boards at each trial site, and overseeing ethics review committees for their expertise and guidance.

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We thank the funders of the ECHO Trial who had the confidence to invest in this globally-important study

Contraceptive supplies donated by USAID and the Republic of South Africa

ECHO Trial Consortium

Caitlin W Scoville	Kathleen Shears
Charles S Morrison	Kavita Nanda
Cheryl Louw	Khatija Ahmed
Deborah Donnell	Linda-Gail Bekker
Douglas Taylor	Mags Beksinska
Elizabeth A Bukusi	Mandisa Singata-Madliki
G Justus Hofmeyr	Margaret Phiri Kasaro
Gonasagrie Nair	Maricianah Onono
Helen Rees	Melanie Pleaner
James Kiarie	Nelly R Mugo
Jared M Baeten	Peter B Gichangi
Jeffrey Stringer	Petrus S Steyn
Jenni Smit	Raesibe Agnes Pearl Selepe
Jessica Justman	Sydney Sibiya
Julia D Welch	Thesla Palanee-Phillips
Kate B Heller	Timothy D Mastro
Katherine K Thomas	Zelda Nhlabatsi

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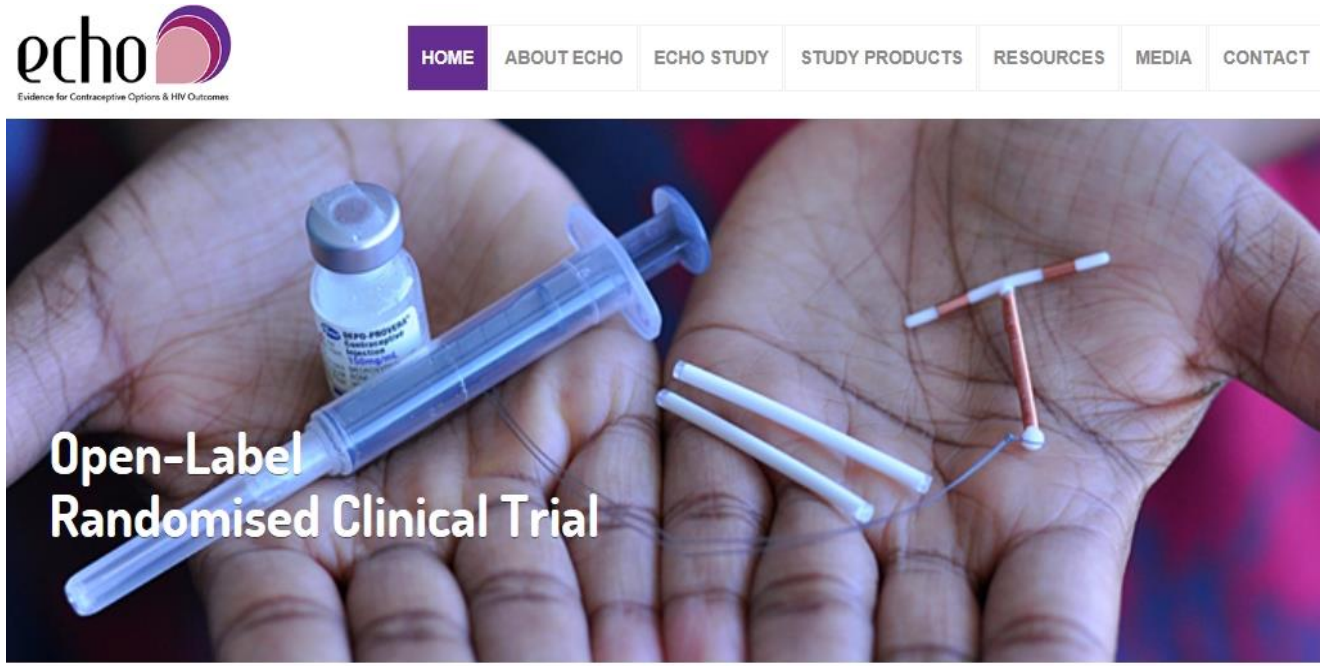
Website - www.echo-consortium.com



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Durban, South Africa, June 13th 2019

WHO perspectives and next steps

James Kiarie
Coordinator, Human Reproduction Team
Department of Reproductive Health and Research

World Health Organization

human reproduction programme hrp
research for impact
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What Has ECHO Told Us

- Each method had high levels of safety and effectiveness in preventing pregnancy
- All methods well-accepted
- No statistically significant differences in HIV infection rates

  (Observed differences if any less than 30%)
- The incidence of HIV infections was high

Key Considerations in WHO Response to ECHO Trial

- Access to preferred contraceptive methods should be maximized, while protecting women's health
- Women have the right to the latest and best information and to access a broad range of effective and acceptable methods
- Current levels of contraceptive unmet need in many developing countries are not acceptable
- Need to step up HIV prevention efforts, particularly in high-burden countries and for young women.

This is a long standing question For The Medical Eligibility Criteria

2012: Category 1*

Programmes can continue to offer all methods of hormonal contraception.

- none of these methods protects against HIV,
- Use HIV preventive measures strongly recommended

2014: Category 1*

Women at high risk of HIV infection should be informed that Progesterone only Injectables may or may not increase their risk of HIV acquisition

2016: Category 2

Women can use progestogen-only injectables but should be advised about:

- Concerns about possible ↑ risk of HIV
- Uncertainty about causal relationship
- How to minimize their risk

ECHO Data is the Most Robust

- ❑ Randomized, high retention and high method continuation
- ❑ High standard of measuring method exposure
- ❑ Enrolled women who wanted to use contraception
- ❑ The methods studied different in the way they act

How Will WHO Addresses New Evidence Presented by ECHO

Evidence Synthesis

- Values and Preferences
- Additional studies after 2016 review
- What does ECHO study add to the current evidence

Guideline development

- Guideline Development Group advertised
- GDG meeting 29-31 July 2019
- Revised recommendations anticipated August 2019

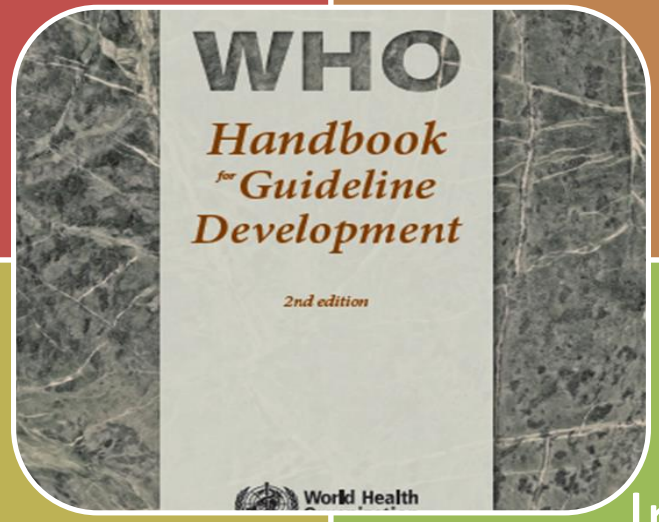
Technical support

- Communicating results and immediate policy responses
- Strengthening HIV/SRH integration
- Continuing access to method options and choice

WHO Guidelines

Focus on end-users' needs

Are based on highest-quality evidence



All judgments and decision-making are transparent and explicit

Incorporate multiple processes to minimize bias

Global Leadership

- Resources available to support response to the ECHO trial results
  - WHO statement in response to the ECHO study results
  - Responses to frequently asked questions
  - Current WHO recommendations
  - Key messages for policy makers, providers and women for high and low HIV prevalence countries
- The World Health Organization (WHO) Director-General has established the WHO Advisory Group of Women Living with HIV
- Convening of 14 countries with High HIV prevalence in Lusaka on 10-11 July 2019
  - Expansion of method mix and promotion of choice
  - Strengthening HIV prevention in family planning services

Department of Reproductive Health and Research (RHR) *including* the UNDP/UNFPA/UNICEF/WHO/World Bank Special programme of research, development and research training in human reproduction (HRP)

Follow us on Twitter **@HRPresearch**

Visit our website **who.int/reproductivehealth/hc-hiv**

Panel discussion

Facilitated Panel Discussion Chaired by Prof Helen Rees, Wits RHI

Panellists in addition to above speakers:

- **Dr Maricianah Onono,** Site Investigator Kenya Medical Research Institute
- **Dr Yogan Pillay,** Deputy Director General, Department of Health, South Africa
- **Ms Yvette Raphael,** Advocacy for Prevention of HIV and AIDS, ECHO Global Community Advisory Group (GCAG) Representative

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