

South Africa - Effects of injectable contraception with depot medroxyprogesterone acetate or norethisterone enanthate on estradiol levels and menstrual, psychological and behavioral measures relevant to HIV risk: the WHICH randomized trial

Mandisa Singata-Madliki, Jenni Smit, Mags Beksinska, Yusementha Balakrishna, Chanel Avenant, Ivana Beesham, Ishen Seocharan, Joanne Batting, Janet P. Hapgood, G Justus Hofmeyr

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Overview

Identification

ID NUMBER

EffectsOfInjectableContraceptive

Overview

ABSTRACT

Background

Observational data suggest lower HIV risk with norethisterone enanthate (NET-EN) than with depo-medroxyprogesterone acetate intramuscular (DMPA-IM) injectable contraceptives. If confirmed, a switch between these similar injectable methods would be programmatically feasible and could impact the trajectory of the HIV epidemic. We aimed in this paper to investigate the effects of DMPA-IM and NET-EN on estradiol levels, measures of depression and sexual activity and menstrual effects, relevant to HIV risk; and to ascertain whether these measures are associated with estradiol levels.

Methods

This open-label trial conducted at two sites in South Africa from 5 November 2018 to 30 November 2019, randomized HIV-negative women aged 18-40 to DMPA-IM 150 mg intramuscular 12-weekly (n=262) or NET-EN 200 mg intramuscular 8-weekly (n=259). Data were collected on hormonal, behavioral and menstrual effects at baseline and at 25 weeks (25W).

Results

At 25W, median 17β estradiol levels were substantially lower than at baseline ($p<0.001$) for both methods: 76.5 pmol/L (interquartile range (IQR) 54.1 to 104.2) in the DMPA-IM group (n=222), and 69.8 pmol/L (IQR: 55.1 to 89.3) in the NET-EN group (n=225), with no statistical difference between the two methods ($p=0.450$). Compared with DMPA-IM, NET-EN users reported significantly less amenorrhoea, fewer sexual acts, fewer users reporting at least one act of unprotected sex, more condom use with steady partner, more days with urge for sexual intercourse, more days feeling partner does not love her, and more days feeling sad for no reason. We did not find a clear association between estradiol levels and sexual behavior, depression and menstrual effects. Behavioral outcomes suggest less sexual exposure with NET-EN than DMPA-IM. The strength of this evidence is high due to the randomized study design and the consistency of results across the outcomes measured.

Conclusions

Estradiol levels were reduced to postmenopausal levels by both methods. Secondary outcomes suggesting less sexual exposure with NET-EN are consistent with reported observational evidence of less HIV risk with NET-EN. A randomized trial powered for HIV acquisition is feasible and needed to answer this important question.

Producers and Sponsors

PRIMARY INVESTIGATOR(S)

Name	Affiliation
Mandisa Singata-Madliki	Effective Care Research Unit, Eastern Cape Department of Health/Universities of the Witwatersrand and Fort Hare, East London, South Africa
Jenni Smit	Wits MRU (MatCH Research Unit), Department of Obstetrics and Gynecology, Faculty of Health Sciences, University of the Witwatersrand, Durban, South Africa
Mags Beksinska	Wits MRU (MatCH Research Unit), Department of Obstetrics and Gynecology, Faculty of Health Sciences, University of the Witwatersrand, Durban, South Africa
Yusentha Balakrishna	Biostatistics Research Unit, South African Medical Research Council, Durban, South Africa
Chanel Avenant	Department of Molecular and Cell Biology, University of Cape Town, Cape Town, South Africa

Ivana Beesham	Wits MRU (MatCH Research Unit), Department of Obstetrics and Gynecology, Faculty of Health Sciences, University of the Witwatersrand, Durban, South Africa
Ishen Seocharan	Biostatistics Research Unit, South African Medical Research Council, Durban, South Africa
Joanne Batting	Effective Care Research Unit, Eastern Cape Department of Health/Universities of the Witwatersrand and Fort Hare, East London, South Africa
Janet P. Hapgood	Department of Molecular and Cell Biology, University of Cape Town, Cape Town, South Africa
G Justus Hofmeyr	Effective Care Research Unit, Eastern Cape Department of Health/Universities of the Witwatersrand and Fort Hare, East London, South Africa

Sampling

No content available

Questionnaires

No content available

Data Collection

Data Processing

No content available

Data Appraisal

No content available

File Description

Variable List

WHICH_demo_estradiol_behaviour

Content

Cases	972
Variable(s)	25
Structure	Type: Keys: ()
Version	
Producer	
Missing Data	

Variables

ID	NAME	LABEL	TYPE	FORMAT	QUESTION
V1	ID	ID	contin	numeric	
V2	site	site	discrete	character	
V3	ITT_arm	ITT_arm	discrete	character	
V4	PP_arm	PP_arm	discrete	character	
V5	visit_code	visit_code	discrete	character	
V6	age	age	contin	numeric	
V7	ethnicity	ethnicity	discrete	character	
V8	marital	marital	discrete	character	
V9	education1	education1	discrete	character	
V10	income	income	discrete	character	
V11	dmpa	dmpa	discrete	character	
V12	neten	neten	discrete	character	
V13	asex_score	asex_score	discrete	numeric	
V14	sexual_dysfunction	sexual_dysfunction	discrete	character	
V15	bdi_score	bdi_score	contin	numeric	
V16	any_depression	any_depression	discrete	character	
V17	feeling_sad	feeling_sad	discrete	character	
V18	no_mens	no_mens	discrete	character	
V19	no_pain	no_pain	discrete	character	
V20	no_sex	no_sex	discrete	character	
V21	no_condom	no_condom	discrete	character	
V22	desire	desire	discrete	character	
V23	hiv	hiv	discrete	character	
V24	pregnant	pregnant	discrete	character	
V25	estradiol	estradiol	contin	numeric	

WHICH_daily_diary

Content

Cases	427
Variable(s)	25
Structure	Type: Keys: ()
Version	
Producer	
Missing Data	

Variables

ID	NAME	LABEL	TYPE	FORMAT	QUESTION
V26	ID	ID	contin	numeric	
V27	site	site	discrete	character	
V28	ITT_arm	ITT_arm	discrete	character	
V29	PP_arm	PP_arm	discrete	character	
V30	complete_obs	complete_obs	discrete	numeric	
V31	menstruating_days	menstruating_days	contin	numeric	
V32	no_mens	no_mens	discrete	character	
V33	severe_pain	severe_pain	discrete	character	
V34	sex_days	sex_days	contin	numeric	
V35	steady_days	steady_days	contin	numeric	
V36	casual_days	casual_days	discrete	numeric	
V37	nosex	nosex	discrete	character	
V38	condomless_days	condomless_days	contin	numeric	
V39	condom_casual_total	condom_casual_total	discrete	numeric	
V40	condom_steady_total	condom_steady_total	discrete	numeric	
V41	nocondom	nocondom	discrete	character	
V42	sex_mens_total	sex_mens_total	discrete	numeric	
V43	sex_during_mens_bin	sex_during_mens_bin	discrete	character	
V44	condomless_sex_mens_total	condomless_sex_mens_total	discrete	numeric	
V45	condomless_sex_during_mens_bin	condomless_sex_during_mens_bin	discrete	numeric	
V46	urge_days	urge_days	contin	numeric	
V47	no_affection_days	no_affection_days	contin	numeric	
V48	no_affection_bin	no_affection_bin	discrete	character	
V49	sad_days	sad_days	contin	numeric	
V50	sad_bin	sad_bin	discrete	character	

ID (ID)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 1-520

Valid cases: 972
Invalid: 0
Minimum: 1
Maximum: 520
Mean: 258.7
Standard deviation: 150.8

site (site)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 4

Valid cases: 972
Invalid: 0

ITT_arm (ITT_arm)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 6

Valid cases: 972
Invalid: 0

PP_arm (PP_arm)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 6

Valid cases: 972
Invalid: 0

visit_code (visit_code)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 8

Valid cases: 972
Invalid: 0

age (age)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 18-39

Valid cases: 972
Invalid: 0
Minimum: 18
Maximum: 39
Mean: 24.8
Standard deviation: 4.7

ethnicity (ethnicity)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 19

Valid cases: 972
Invalid: 0

marital (marital)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 972
Invalid: 0

education1 (education1)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 37

Valid cases: 972
Invalid: 0

income (income)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 13

Valid cases: 972
Invalid: 0

dmpa (dmpa)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 972
Invalid: 0

neten (neten)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 972
Invalid: 0

asex_score (asex_score)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 3-22

Valid cases: 970
Invalid: 2

sexual_dysfunction (sexual_dysfunction)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 970
Invalid: 0

bdi_score (bdi_score)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-30

Valid cases: 970
Invalid: 2
Minimum: 0
Maximum: 30
Mean: 1.7
Standard deviation: 2.4

any_depression (any_depression)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 970
Invalid: 0

feeling_sad (feeling_sad)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 966
Invalid: 0

no_mens (no_mens)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 965
Invalid: 0

no_pain (no_pain)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 21

Valid cases: 725
Invalid: 0

no_sex (no_sex)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 966
Invalid: 0

no_condom (no_condom)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 773
Invalid: 0

desire (desire)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 966
Invalid: 0

hiv (hiv)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 13

Valid cases: 972
Invalid: 0

pregnant (pregnant)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 966
Invalid: 0

estradiol (estradiol)

File: WHICH_demo_estradiol_behaviour

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 1-3670

Valid cases: 966
Invalid: 6
Minimum: 1
Maximum: 3670
Mean: 205.7
Standard deviation: 293.7

ID (ID)

File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 1-520

Valid cases: 427
Invalid: 0
Minimum: 1
Maximum: 520
Mean: 251.5
Standard deviation: 150.3

site (site)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 4

Valid cases: 427
Invalid: 0

ITT_arm (ITT_arm)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 6

Valid cases: 427
Invalid: 0

PP_arm (PP_arm)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 6

Valid cases: 427
Invalid: 0

complete_obs (complete_obs)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 27-28

Valid cases: 427
Invalid: 0

menstruating_days (menstruating_days)

File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-28

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 28
Mean: 1.3
Standard deviation: 2.9

no_mens (no_mens)
File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 427
Invalid: 0

severe_pain (severe_pain)
File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 427
Invalid: 0

sex_days (sex_days)
File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-28

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 28
Mean: 5.3
Standard deviation: 5.1

steady_days (steady_days)
File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-28

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 28
Mean: 5
Standard deviation: 5

casual_days (casual_days)
File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 0-8

Valid cases: 427
Invalid: 0

nosex (nosex)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 427
Invalid: 0

condomless_days (condomless_days)

File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-25

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 25
Mean: 3.1
Standard deviation: 4.3

condom_casual_total (condom_casual_total)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 0-7

Valid cases: 427
Invalid: 0

condom_steady_total (condom_steady_total)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 0-19

Valid cases: 427
Invalid: 0

nocondom (nocondom)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 427
Invalid: 0

sex_mens_total (sex_mens_total)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 0-6

Valid cases: 427
Invalid: 0

sex_during_mens_bin (sex_during_mens_bin)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 427
Invalid: 0

condomless_sex_mens_total (condomless_sex_mens_total)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 0-6

Valid cases: 427
Invalid: 0

condomless_sex_during_mens_bin (condomless_sex_during_mens_bin)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: numeric
Decimals: 0
Range: 0-1

Valid cases: 427
Invalid: 0

urge_days (urge_days)

File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-28

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 28
Mean: 6.4
Standard deviation: 7.3

no_affection_days (no_affection_days)

File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-28

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 28
Mean: 2.5
Standard deviation: 6

no_affection_bin (no_affection_bin)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 32

Valid cases: 427
Invalid: 0

sad_days (sad_days)

File: WHICH_daily_diary

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 0-28

Valid cases: 427
Invalid: 0
Minimum: 0
Maximum: 28
Mean: 3.9
Standard deviation: 6

sad_bin (sad_bin)

File: WHICH_daily_diary

Overview

Type: Discrete
Format: character
Width: 45

Valid cases: 427
Invalid: 0

