Pregnancy & reproductive health updates/conundrums

Chair: Dr Rebecca Metcalfe

Co-chairs: Rebecca Mwebe

This educational event is supported by an unrestricted medical education grants from

GILEAD Creating Possible MSD ViiV Healthcare

BHIVA

British HIV Association

2022 **Spring Conference**

Wed 20th - Fri 22nd April

Manchester Central, Manchester

BHIVA
British HIV Association
2022 Spring Conference
Wed 20th - Fri 22nd April
Manchester Central, Manchester

Pregnancy & breastfeeding update

Dr Laura Byrne

St George's University Hospitals NHS Foundation Trust

Conflict of Interest

In relation to this presentation I declare that I have no conflict of interest

Speakers are required by the Federation of the Royal Colleges of Physicians to disclose conflicts of interest at the beginning of their presentation, with sufficient time for the information to be read by the audience. They should disclose financial relationships with manufacturers of any commercial product and/or providers of commercial services used on or produced for patients relating to the 36 months prior to the event. These include speaker fees, research grants, fees for other educational activities such as training of health professionals and consultation fees. Where a speaker owns shares or stocks directly in a company producing products or services for healthcare this should also be declared. Finally, other conflicts of interest including expert functions in health care or healthcare guidance processes should be declared (eg if the professional is a member of a health board). The Federation considers it good practice to also make speakers' disclosures available in digital format(s) relating to the educational event.

Pregnancy & breastfeeding update

- Epidemiology in the UK
- Conceiving on ART
- Other pregnancy outcomes
- Infant feeding

Epidemiology

- Universal antenatal HIV screening was introduced in England/UK in 2000 - 2002
- Uptake has exceeded 97% since 2011
- ISOSS (prev NSHPC) collects data on all diagnosed women who become pregnant, and their children
- Currently around 1000-1200 pregnancies py (85% live births)

Epidemiology

Maternal demographics, early 2000s and now (UK)

		2000-04	2015-19
Country/region of report	London	62.5%	37.5%
	Rest of England	33.8%	56.3%
	Scotland	2.8%	3.4%
	Wales / N. Ireland	1.0%	2.7%

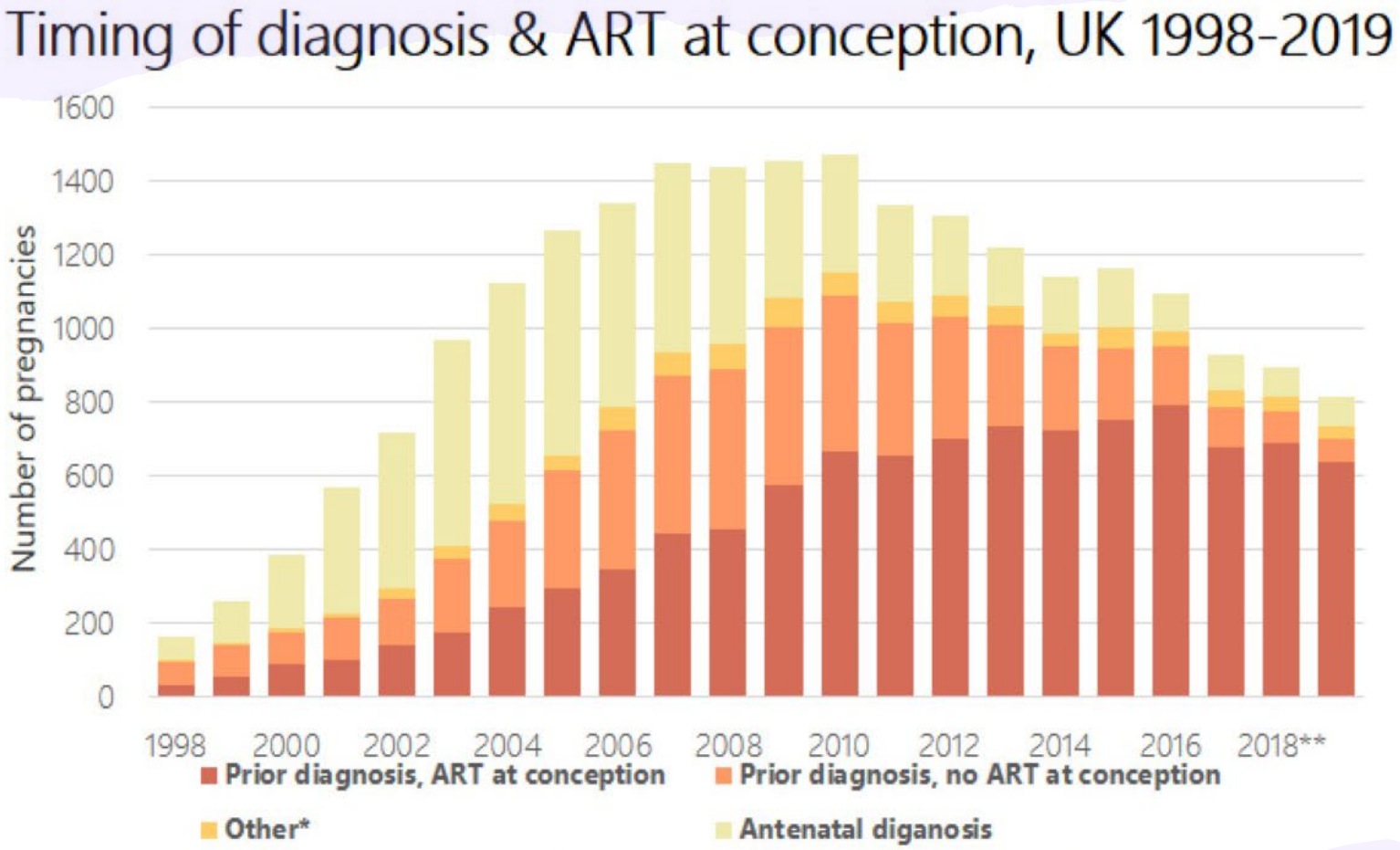
Median age (years)	29	34
IDU-acquired HIV	2.6%	1.1%
Perinatal HIV	0.03%	2.9%
Sub-Saharan Africa-born	77.2%	67.1%
Eastern Europe*-born	0.3%	6.1%

* includes the Baltic states (Estonia, Latvia, Lithuania)

Source: pregnancies reported through ISOSS maternity scheme by June 2021

ISOSS
Integrated Screening Outcomes Surveillance Service

Epidemiology



Conception on ART

20.3% in 2000-2004

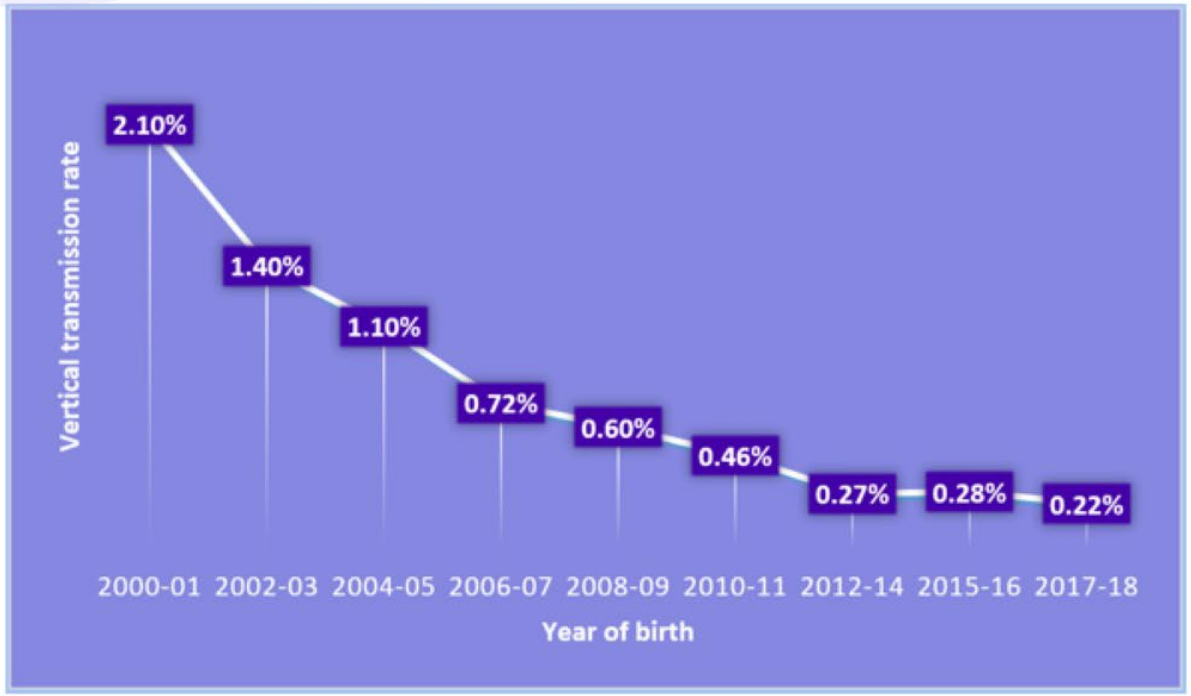
75.5% in 2015-2019

* contains pregnancies lacking information on precise timing of diagnosis and/or ART use

ISOSS

Epidemiology

Vertical transmission in UK, 2000-2018



Data for 2000-11 from Townsend *et al.* AIDS 2014; data for 2012-14 from Peters *et al.* CID 2016; data for 2015-16 from *Peters et al.* HIV Drug Therapy Glasgow 2018; data for 2017-18 from Peters *et al.* CROI 2021

In 2012-14 among the 87% of women delivering with suppressed virus the VT rate was **0.14%**

Data gap

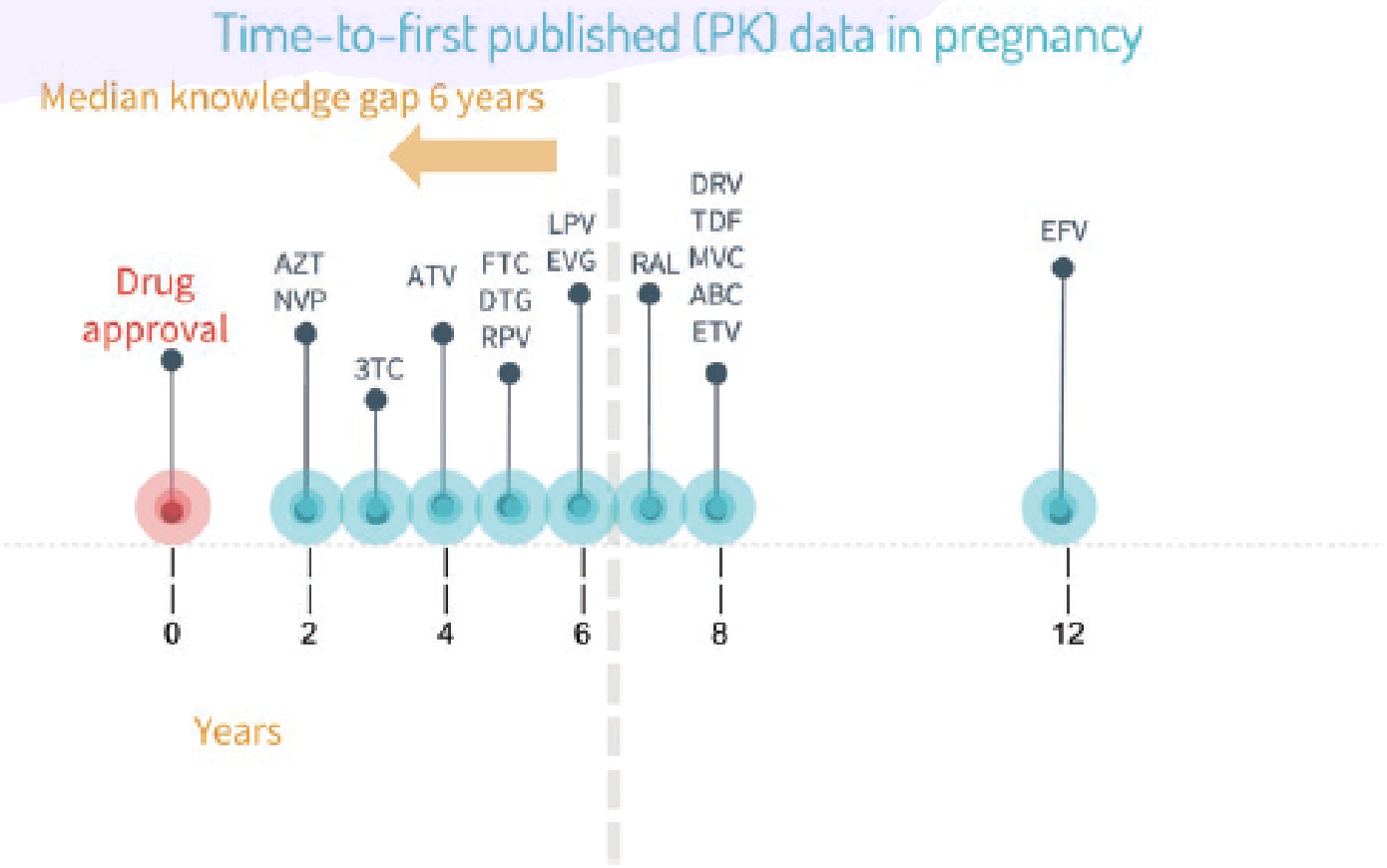


Figure 1. Years between US Food and Drug Administration approval and publication of pregnancy data for different antiretroviral drugs. Abbreviations: 3TC, lamivudine; ABC, abacavir; ATV, atazanavir; AZT, zidovudine; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; ETV, etravirine; EVG, elvitegravir; FTC, emtricitabine; LPV, lopinavir; MVC, maraviroc; NVP, nevirapine; PK, pharmacokinetic; RAL, raltegravir; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate.

Importance of prospective studies in pregnant and breastfeeding women living with HIV. Angela Colbers et al, CID Feb 2019

Tania

→ 27 year old woman with PHIV
→ Longstanding adherence difficulties

→ TAF/FTC + DTG 50mg od
→ VL < 50 c/ml, CD4 201 cells/micL
→ No resistance

→ Period 5 days late
→ PT positive in clinic

→ Older son aged 3, HIV-
→ Difficult relationship with partner, live separately
→ 1 bedroom flat
→ Working part-time

→ Prev severe N&V in pregnancy
→ Prev CS with son at 39/40 (VL 500 c/ml)
→ Formula fed older son

Should I switch my ART?

TAF in pregnancy: pharmacokinetics

IMPAACT 1026s

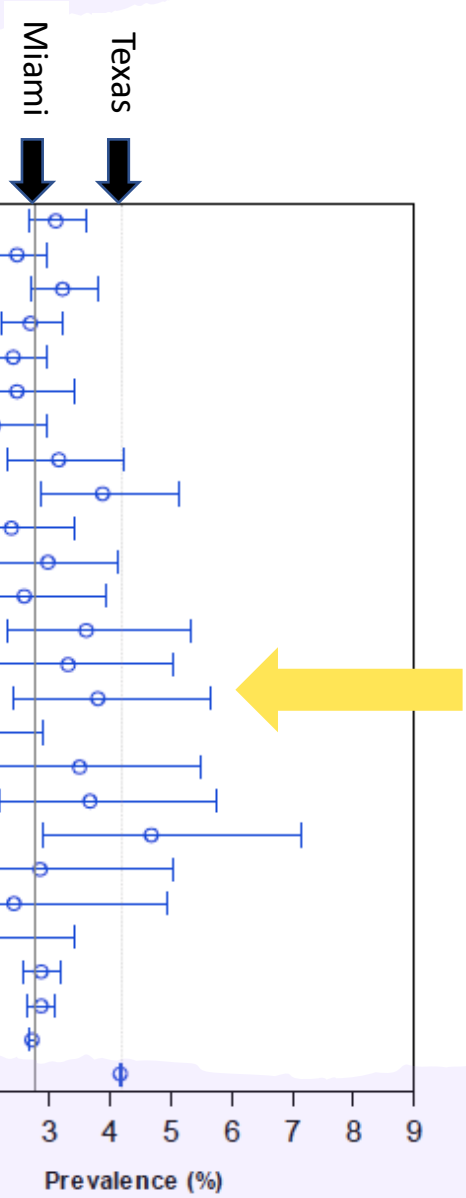
→ boosted TAF (*n*=31) similar levels to postpartum / non-pregnant

→ un-boosted TAF (*n*=27) (25mg) lower AUC antepartum vs. postpartum but similar to non-pregnant

Brooks et al AIDS 2021

TAF in pregnancy: teratogenicity

	Defects/Live Births	Prevalence (%)	Lower 95% CI	Upper 95% CI
Lamivudine	170/5472	3.11	2.66	3.60
Tenofovir DF	113/4576	2.47	2.04	2.96
Zidovudine	136/4229	3.22	2.70	3.79
Emtricitabine	110/4094	2.69	2.21	3.23
Ritonavir	84/3482	2.41	1.93	2.98
Atazanavir	36/1457	2.47	1.74	3.40
Lopinavir	30/1441	2.08	1.41	2.96
Abacavir	44/1391	3.16	2.31	4.22
Nelfinavir	47/1212	3.88	2.86	5.12
Efavirenz	28/1177	2.38	1.59	3.42
Nevirapine	35/1173	2.98	2.09	4.13
Stavudine	21/811	2.59	1.61	3.93
Darunavir	24/665	3.61	2.32	5.32
Dolutegravir	21/634	3.31	2.06	5.02
Tenofovir Alafenamide	23/606	3.80	2.42	5.64
Rilpivirine	9/583	1.54	0.71	2.91
Raltegravir	18/514	3.50	2.09	5.48
Cobicistat	18/490	3.67	2.19	5.74
Didanosine	20/427	4.68	2.88	7.14
Elvitegravir	11/386	2.85	1.43	5.04
Indinavir	7/289	2.42	0.98	4.93
Telbivudine	3/254	1.18	0.24	3.41
First Trimester APR	319/11132	2.87	2.56	3.19
Any Trimester APR	599/20899	2.87	2.64	3.10
MACDP		2.72	2.68	2.76
TBDR		4.17	4.15	4.19



DTG in pregnancy: teratogenicity

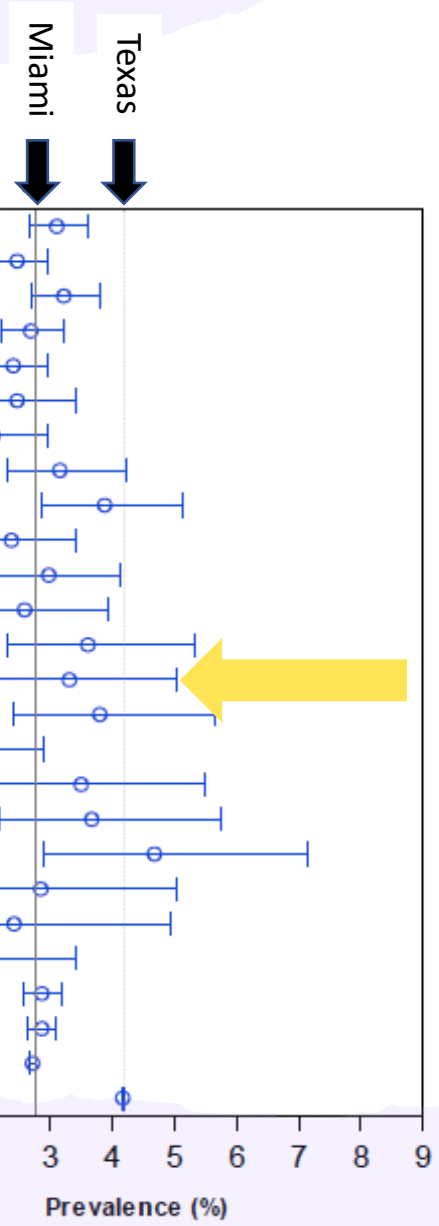
Table 1. Prevalence Difference of NTDs by Antiretroviral and HIV Exposure Categories, 2014-2021

Exposure group vs. Comparison group	Prevalence Difference (%) (95% CI)
DTG at conception vs. Non-DTG at conception	0.06 (-0.03, 0.20)
DTG at conception vs. EFV at conception	0.09 (-0.00, 0.23)
DTG at conception vs. DTG started in pregnancy	0.10 (-0.03, 0.24)
DTG at conception vs. Women without HIV	0.09 (0.01, 0.23)

Zash et al. Update on neural tube defects with antiretoviral exposure in the Tsepamo study, Botswana. IAS 2021 eposter.

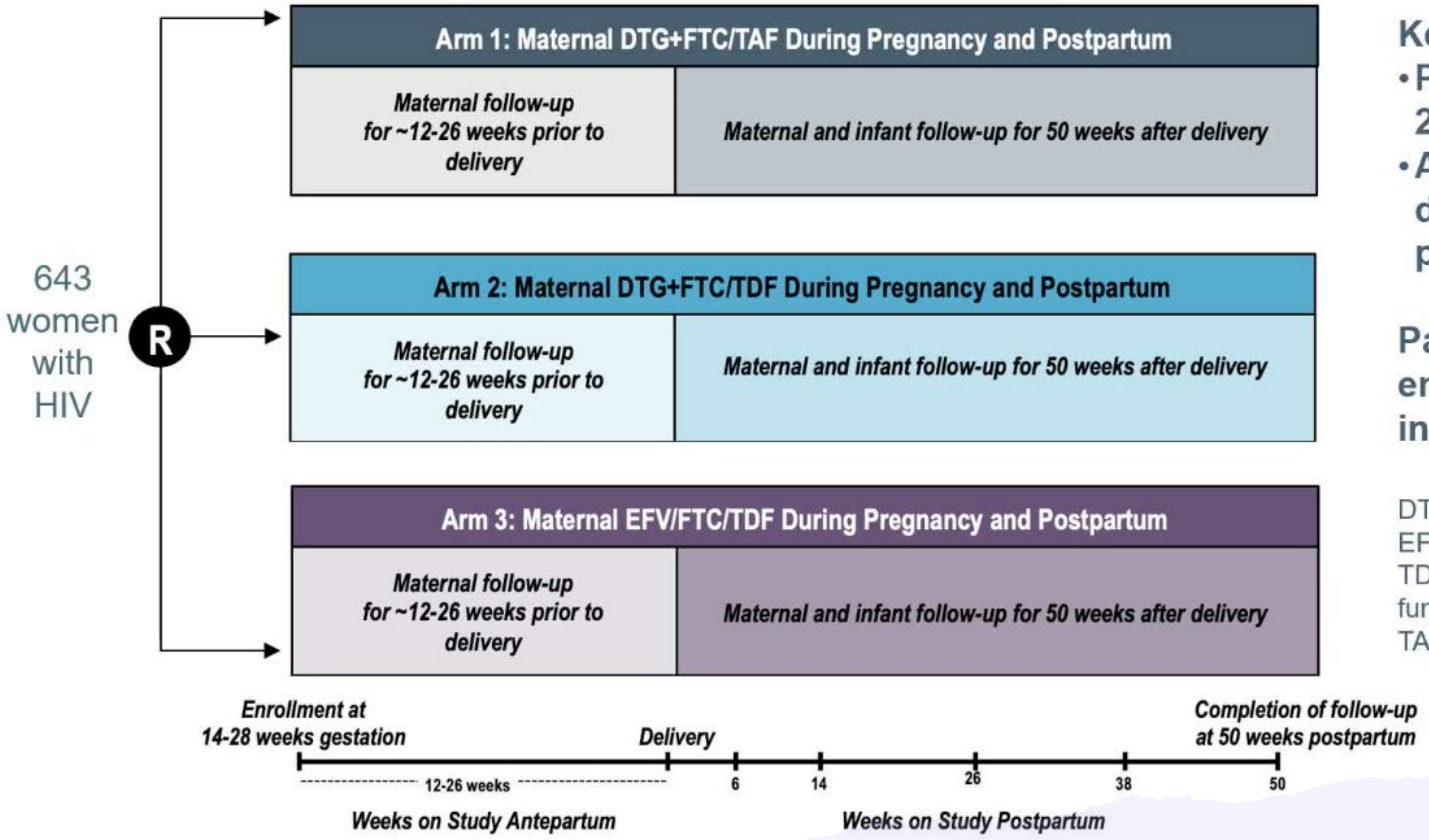
DTG in pregnancy: teratogenicity

	Defects/Live Births	Prevalence (%)	Lower 95% CI	Upper 95% CI
Lamivudine	170/5472	3.11	2.66	3.60
Tenofovir DF	113/4576	2.47	2.04	2.96
Zidovudine	136/4229	3.22	2.70	3.79
Emtricitabine	110/4094	2.69	2.21	3.23
Ritonavir	84/3482	2.41	1.93	2.98
Atazanavir	36/1457	2.47	1.74	3.40
Lopinavir	30/1441	2.08	1.41	2.96
Abacavir	44/1391	3.16	2.31	4.22
Nelfinavir	47/1212	3.88	2.86	5.12
Efavirenz	28/1177	2.38	1.59	3.42
Nevirapine	35/1173	2.98	2.09	4.13
Stavudine	21/811	2.59	1.61	3.93
Darunavir	24/665	3.61	2.32	5.32
Dolutegravir	21/634	3.31	2.06	5.02
Tenofovir Alafenamide	23/606	3.80	2.42	5.64
Rilpivirine	9/583	1.54	0.71	2.91
Raltegravir	18/514	3.50	2.09	5.48
Cobicistat	18/490	3.67	2.19	5.74
Didanosine	20/427	4.68	2.88	7.14
Elvitegravir	11/386	2.85	1.43	5.04
Indinavir	7/289	2.42	0.98	4.93
Telbivudine	3/254	1.18	0.24	3.41
First Trimester APR	319/11132	2.87	2.56	3.19
Any Trimester APR	599/20899	2.87	2.64	3.10
MACDP		2.72	2.68	2.76
TBDR		4.17	4.15	4.19



TAF in pregnancy: other safety outcomes

IMPAACT 2010 'VESTED'



Key Eligibility Criteria

- **Pregnant WLHIV 14-28 weeks gestation**
- **ART-naïve (up to 14 days ART in current pregnancy allowed)**

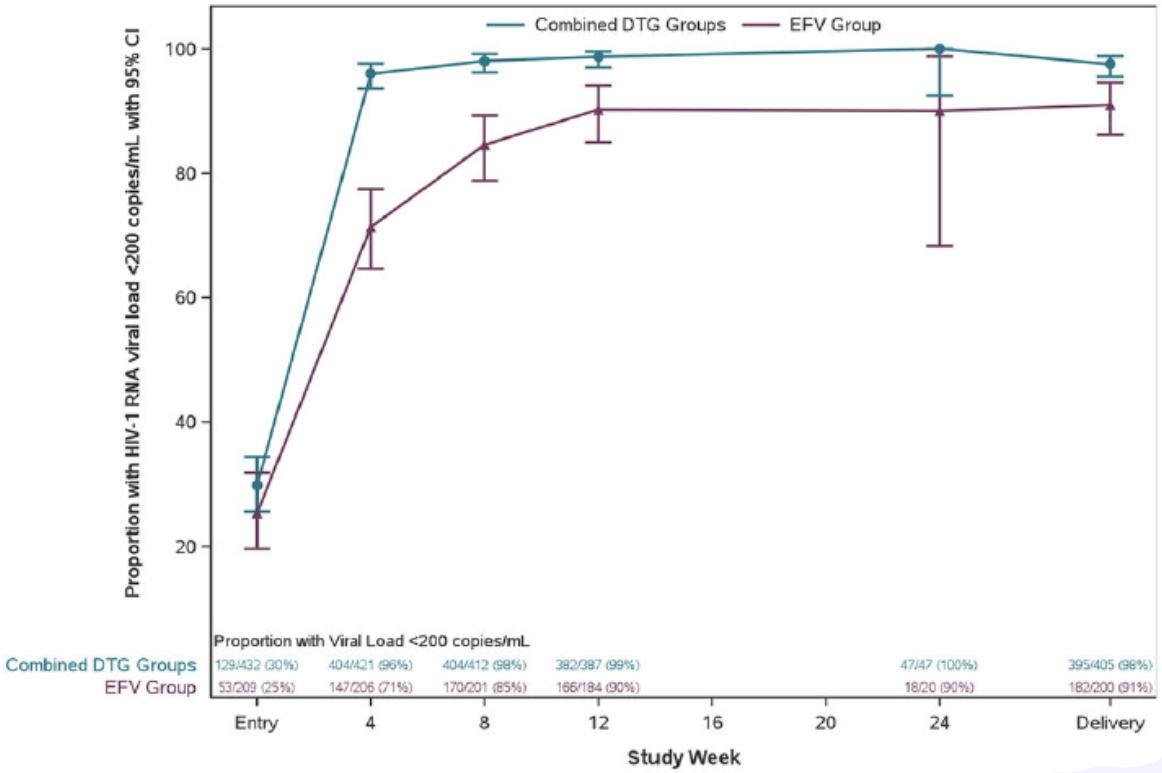
Participants were enrolled at 22 sites in 9 countries

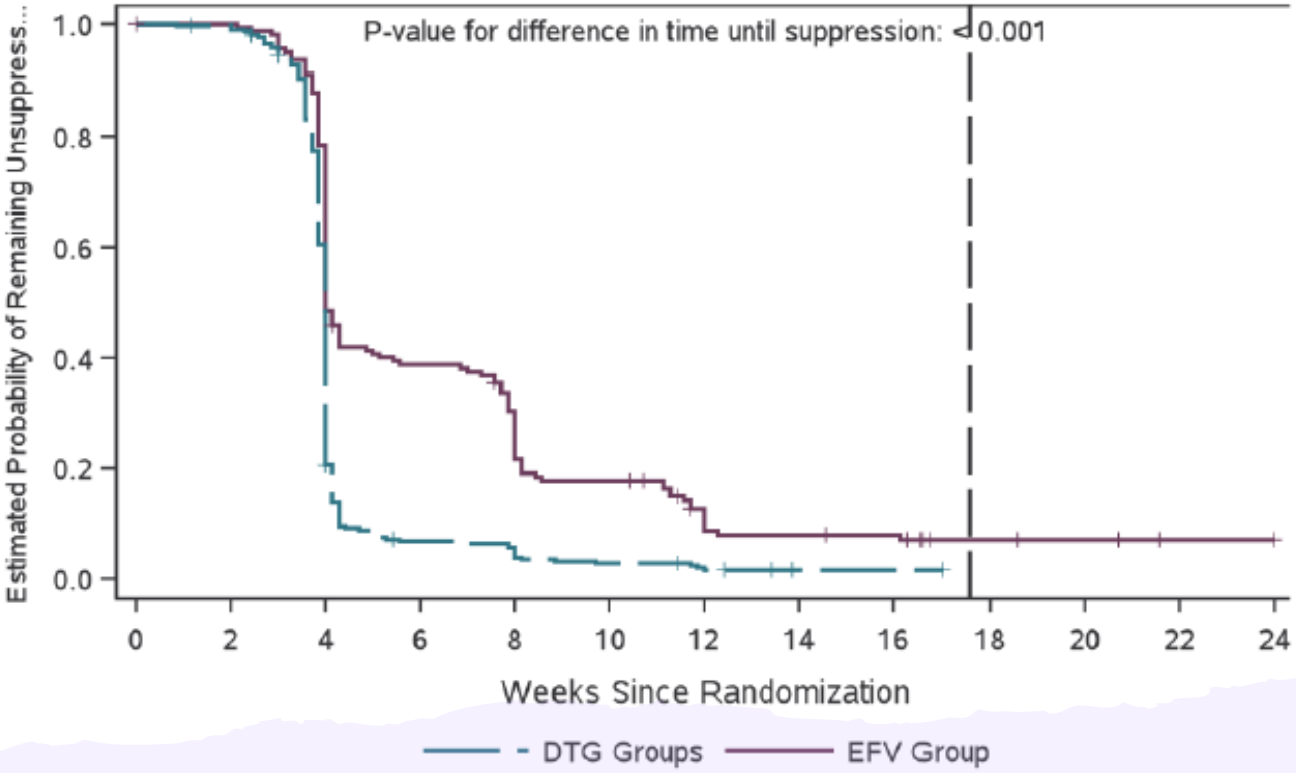
DTG = dolutegravir
EFV = efavirenz
TDF = tenofovir disoproxil fumarate
TAF = tenofovir alafenamide

Lockman & Brummel et al, The Lancet, 2021

TAF in pregnancy: other safety outcomes

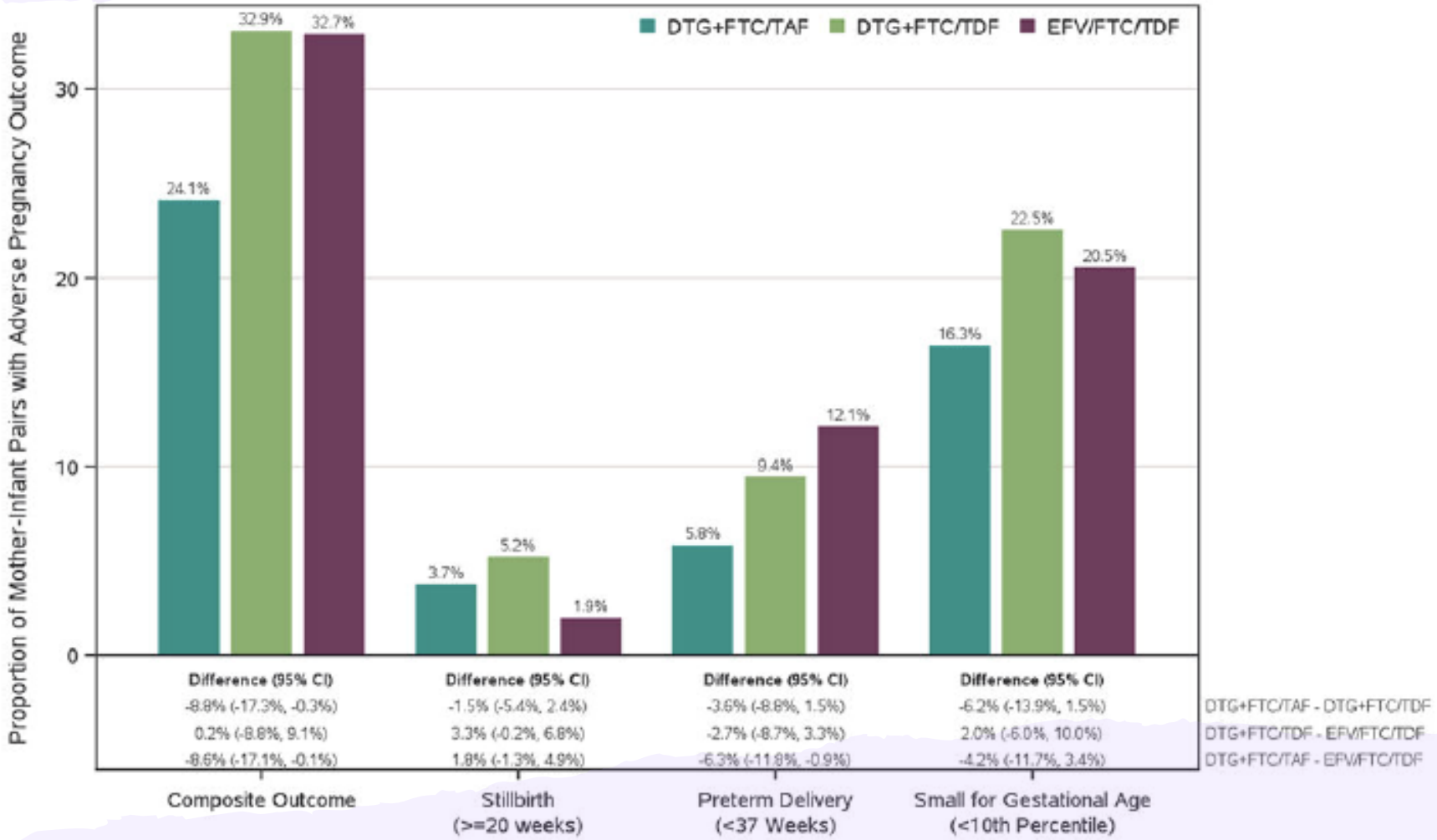
IMPAACT 2010 'VESTED'





TAF in pregnancy: other safety outcomes

IMPAACT 2010 'VESTED'

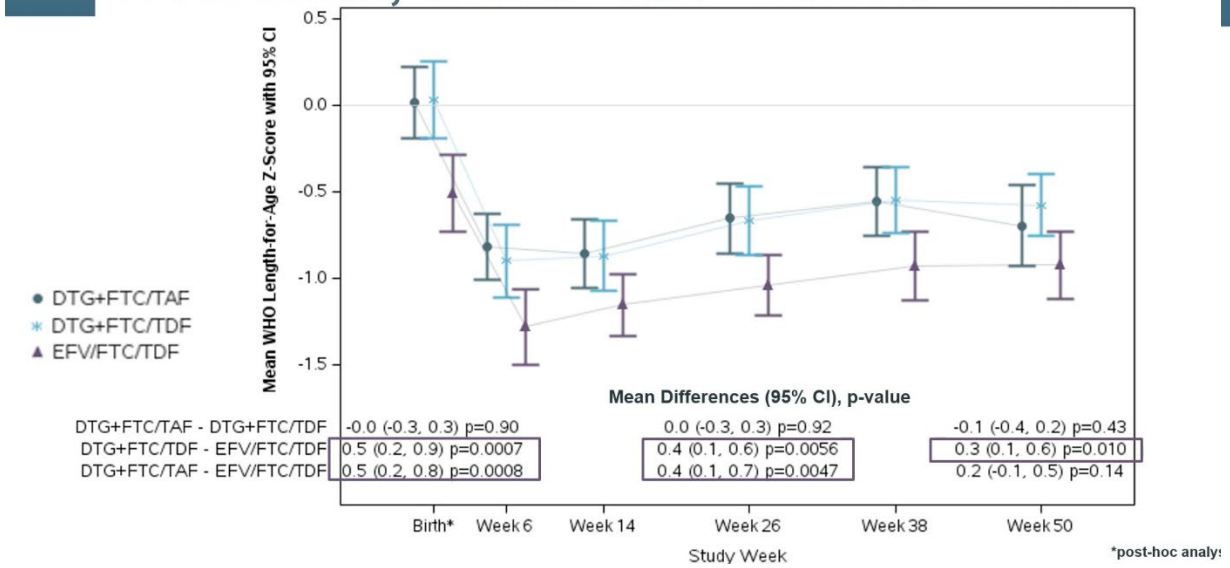


TAF in pregnancy: other safety outcomes

IMPAACT 2010 'VESTED'
Further data presented at CROI 2022

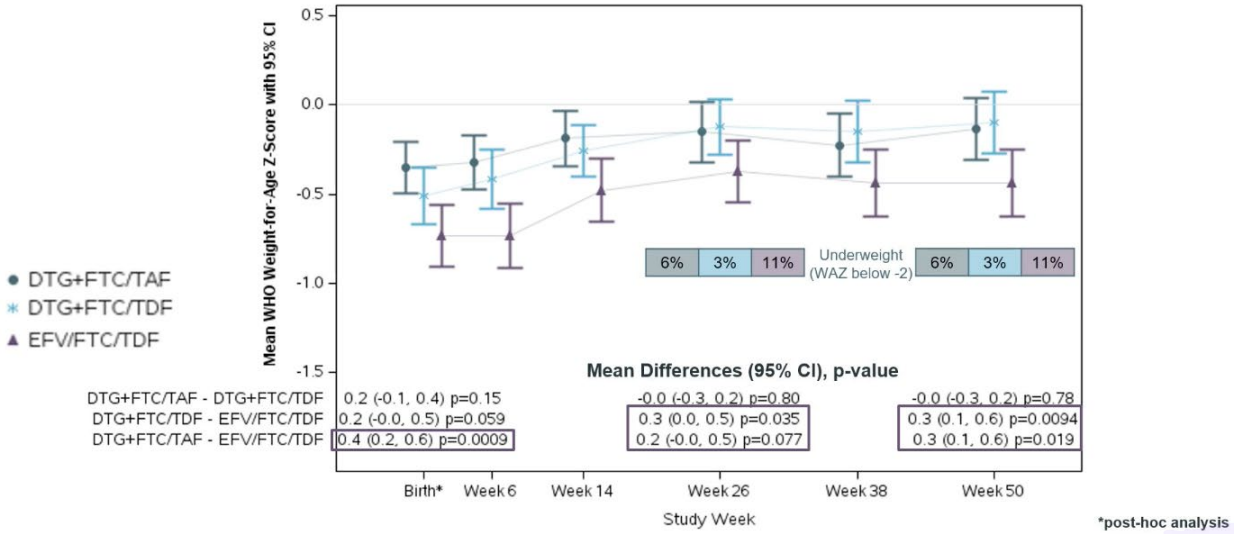
9

Length-for-Age Z-scores lower in EFV vs DTG arms, similar TDF- vs TAF-DTG



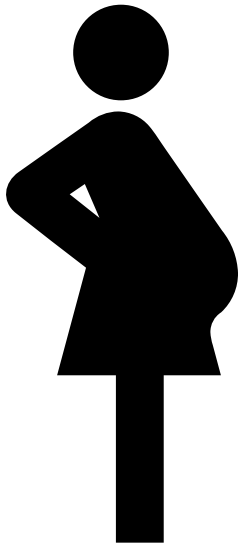
10

Weight-for-Age Z-scores lower in EFV vs DTG arms, similar TDF- vs TAF-DTG



Tania

Would it be safe to breastfeed my baby?



Breastfeeding

Study	Design	Setting	Enrolment	N	cART	VT rate at 6 months (per 1000)
Nduati et al	RCT	Kenya	'92-'98	401	nil	28 (bfeeding) 16 (formula)
Mitra Plus	Cohort	Tanzania	'04 –'06	378	ZDV/3TC/NVP	10
Marazzi et al	Cohort	Mozambique	'05 – '07	313	ZDV/3TC/NVP	6
Amata	Cohort	Rwanda	'05 - 2007	227	D4T/3TC/NVP or ZDV/3TC/EFV	5
Mma Bana	RCT	Botswana	'06 – '08	263	ZDV/3TC/LPV-r	3
BAN	RCT	Malawi	'04 – '08	803	ZDV/3TC + NVP or NFV or LPV-r	26
Kesho Bora	RCT	B. Faso, Kenya, S. Africa	'05 – '08	349	ZDV/3TC/LPV-r	16
PROMISE	RCT	India, SSA (7 countries)	11 - 14	2431	mART vs. iNVP	3 (in both arms)

Breastfeeding: PROMISE

→ Women-infant pairs enrolled 1 week postpartum after negative infant PCR

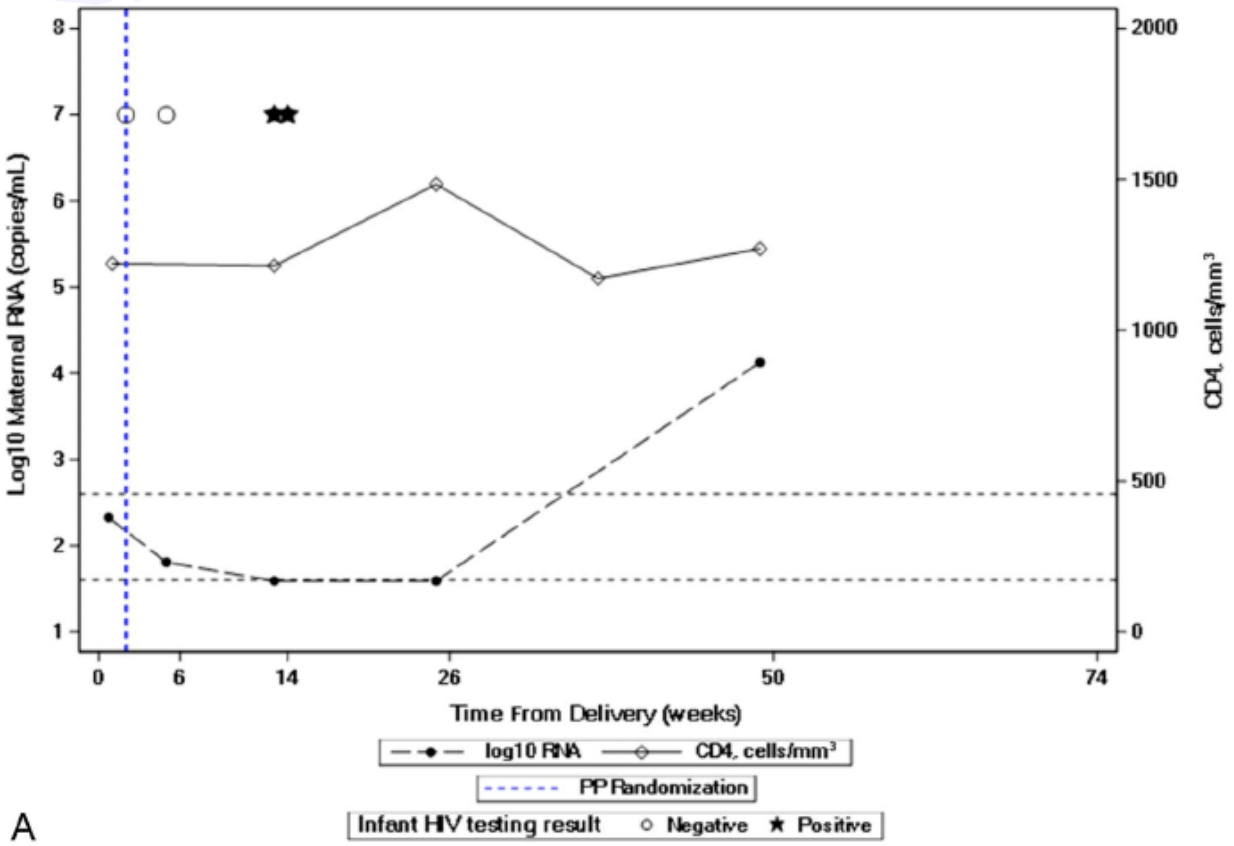
→ Randomised to continuing mART (99% TDF/XTC+ LPV/r) or infant nevirapine

→ Infants in the mART arm received 6/52 NVP then stopped

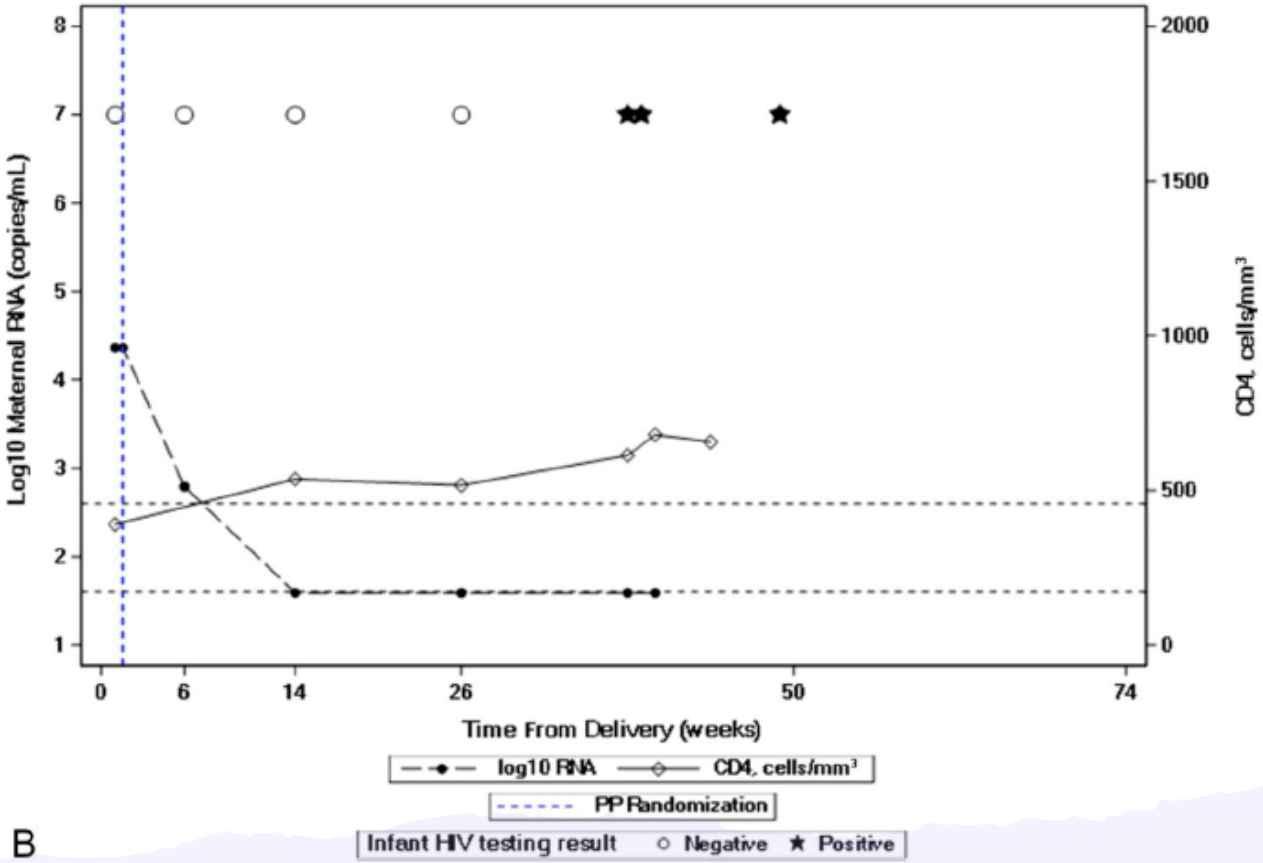
→ 1220 woman-infant pairs were enrolled into the mART arm

→ 75% of these women had VL <1000copies/ml at baseline, this was 85% at week 50.

Breastfeeding: PROMISE



A

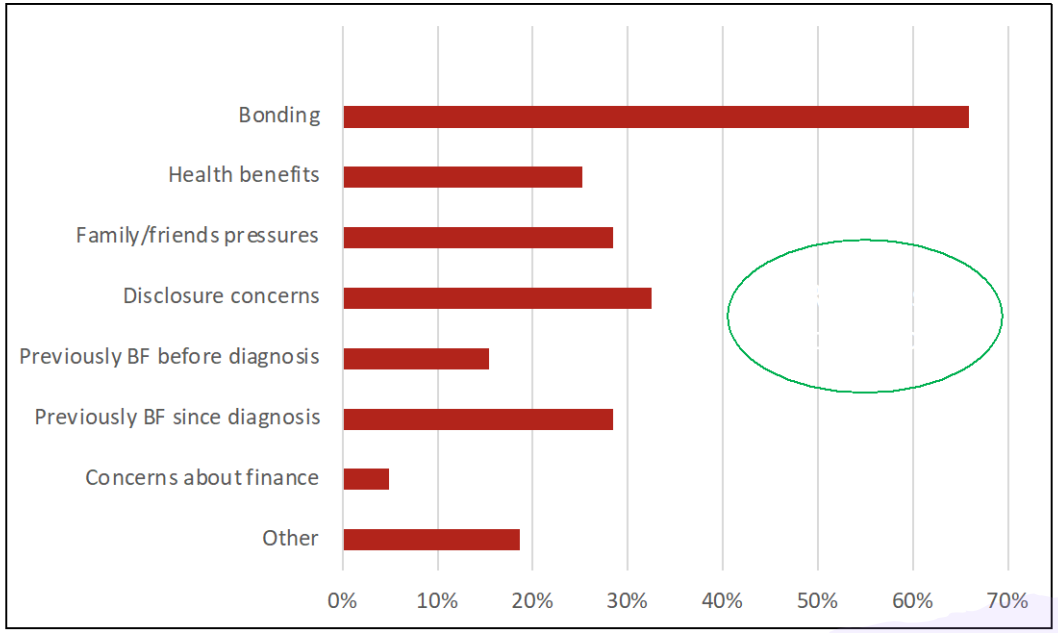


B

Breastfeeding: UK data

Among 9133 livebirth deliveries to HIV diagnosed women 2012-2020:
151/9133 (1.8%) were reported as supported to breastfeed

Reported reasons for breastfeeding (n=123)



Wide range of duration:

→ range 1 day- 2 years
→ median duration: 7wk (IQR: 3, 16)

Variety of reasons for stopping:

→ part of a plan to stop (51)
→ mastitis (3)
→ viral load rebound (7)
→ travel/testing burden (1)

ISOSS
Integrated Screening Outcomes Surveillance Service

Tania

BHIVA

British HIV Association

2022 **Spring Conference**

Wed 20th - Fri 22nd April

Manchester Central, Manchester

Post-reproductive health in women living with HIV

Dr Shema Tariq

University College London/Mortimer Market Centre, UK

This educational event is supported by an unrestricted medical education grants from

GILEAD Creating Possible MSD ViiV Healthcare

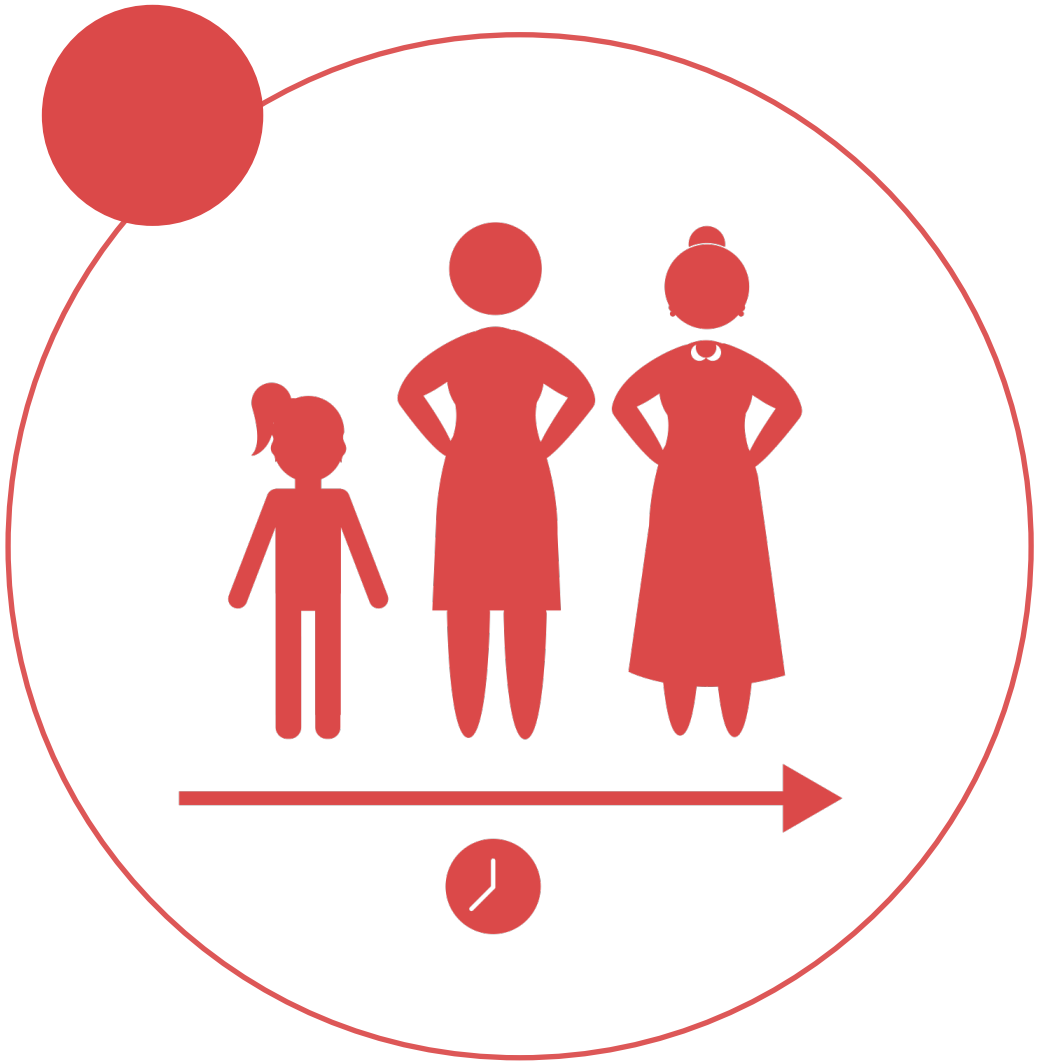
BHIVA
British HIV Association
2022 Spring Conference
Wed 20th - Fri 22nd April
Manchester Central, Manchester

Post-reproductive health in women living with HIV

Shema Tariq, University College London/Mortimer Market Centre

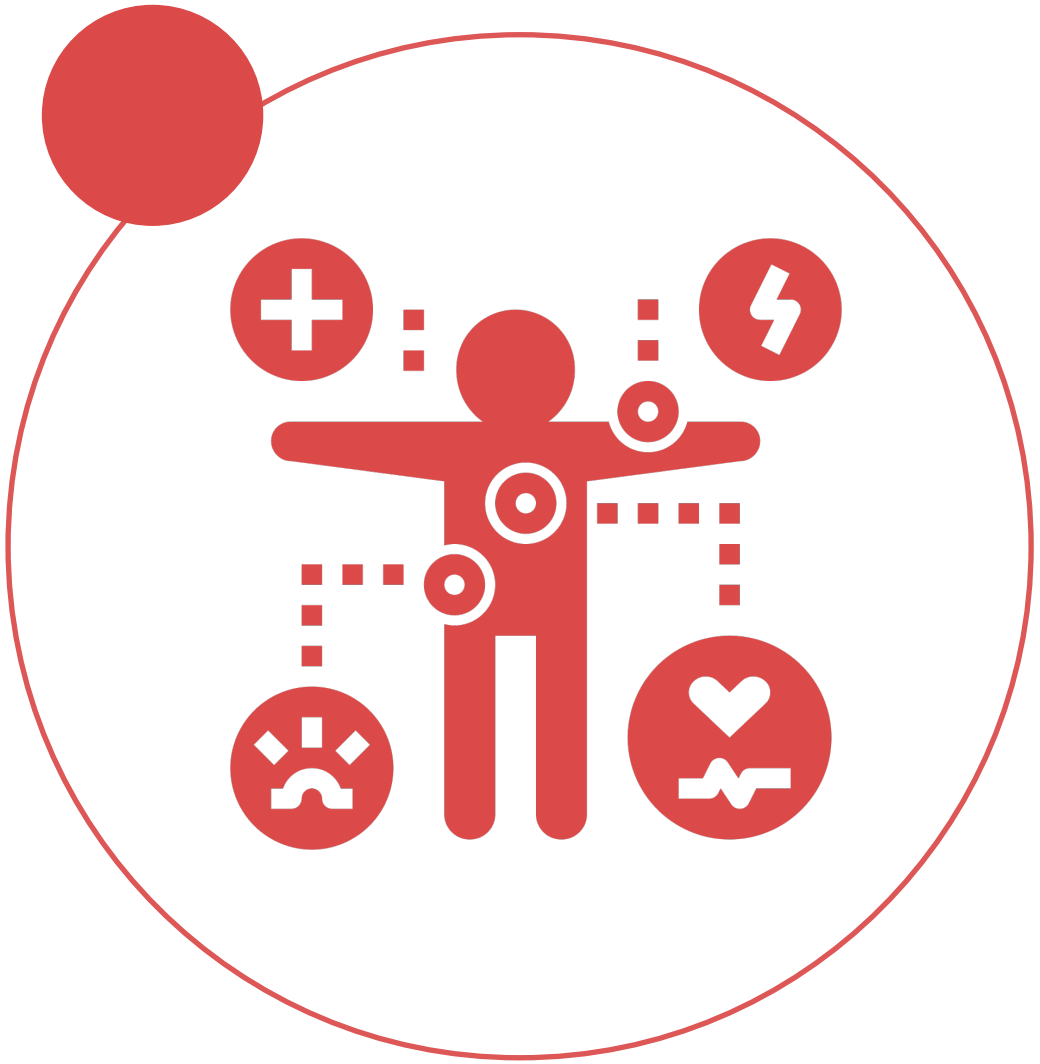
Conflict of Interest

I have received honoraria from Gilead Sciences for preparation of educational material and speaking engagements. The PRIME Study has been funded by the NIHR, the Wellcome Trust and BHIVA.



Maria

- Aged 53
- HIV diagnosed antenatally in 2007
- Disengaged from care post-partum
- Nadir CD4 180
- Re-presented to care in 2011
- TRU/NVP
- Irregular periods aged 45
- LMP aged 50



Maria

- Now has multiple symptoms
- Brain fog, hot flushes, fatigue, vaginal dryness, low mood, poor sleep
- Menopause Rating scale=32 (severe)
- Adherence challenges: VL<40
- Osteopenia on DEXA (also FH)

Maria

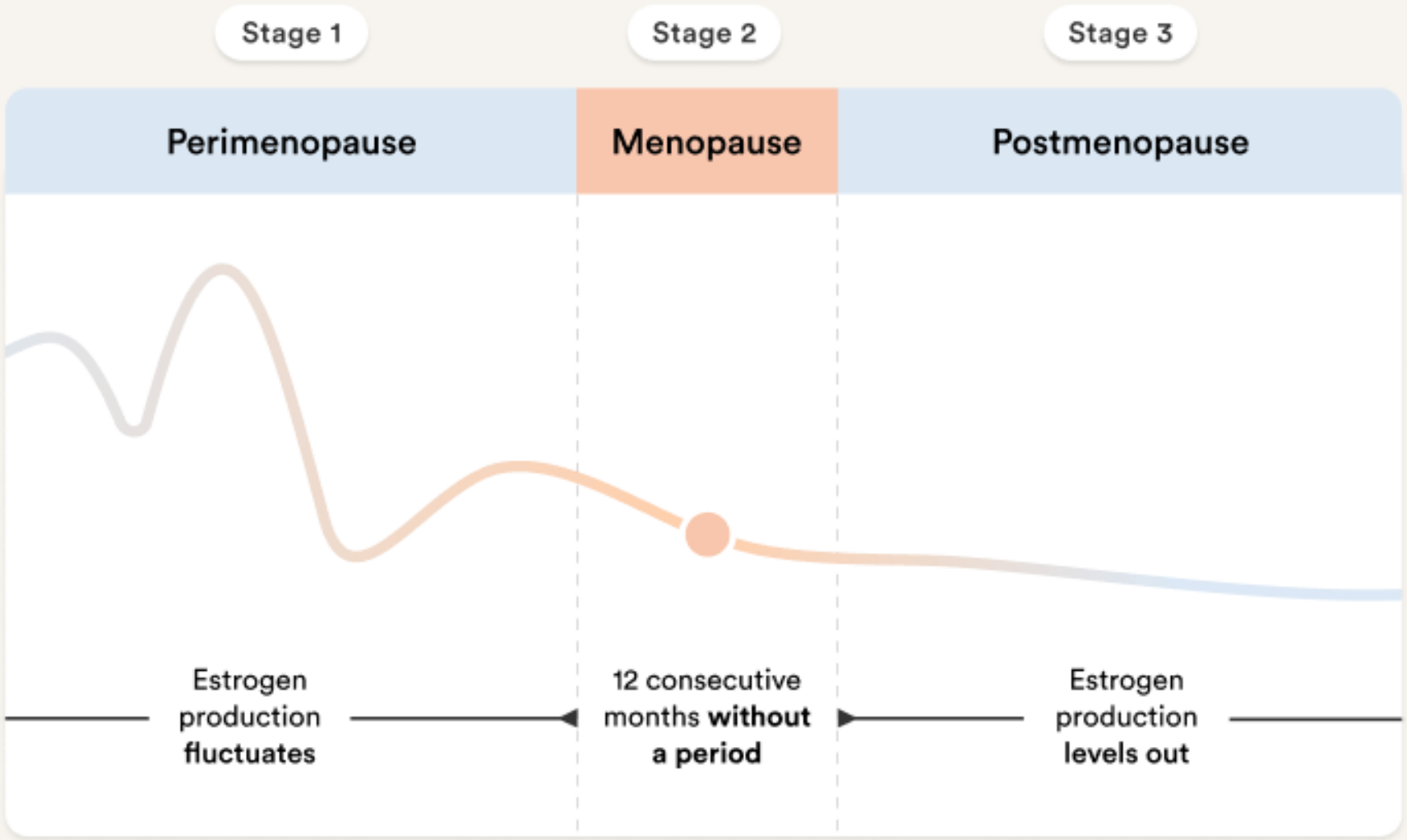
- Transdermal oestrogen + micronised progestogen (dose adjusted)
- Vaginal oestrogen pessary
- Lifestyle optimisation
- No FSH needed
- Qrisk documented, recent DEXA
- Breast and cervical screening
- Does not want to switch ART
- GP management with support

I just feel alive again. I feel like me.

Maria, 3 months after commencing HRT

Stages of Menopause

Understanding the changes in your body during menopause.



Menopause and HIV

Bone disease | CVD | HIV-related | Vasomotor | Psychological

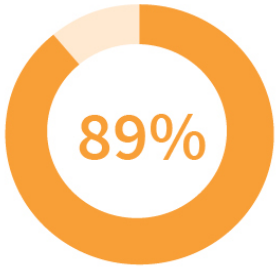
Source: 1. Looby SE *et al.* (2013); 2. Schoenbaum EE *et al.* (2005); 3. Ferreira CE *at al.* (2007); 4. Miller SA *et al.* (2005); 5. Clark RA *et al.* (2000); 6. Looby SE *et al.* (2018); 7. Rubin LH *et al.* (2014); 8. Lui-Filho JF *et al.* (2014) ; 9. Valdares AL *et al.* (2014); 10. Cortes Y *et al.* (2015); 11. Sharma A *et al.* (2015); 12. Blanco JR *et al.* (2019); 13. Solomon D *et al.* (2018); 14. Schnall R *et al.* (2018)

Findings: Menopausal symptoms in women living with HIV

Prevalence of menopausal symptoms

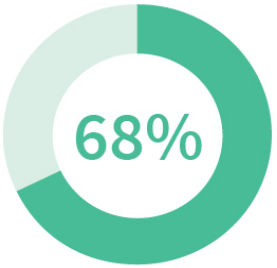
Somatic

hot flushes, palpitations, joint and muscle discomfort, sleep disturbance



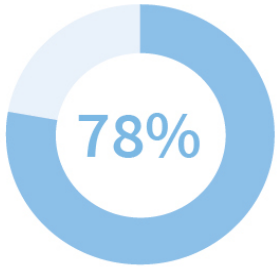
Urogenital

vaginal dryness, urinary tract symptoms, sexual problems



Psychological

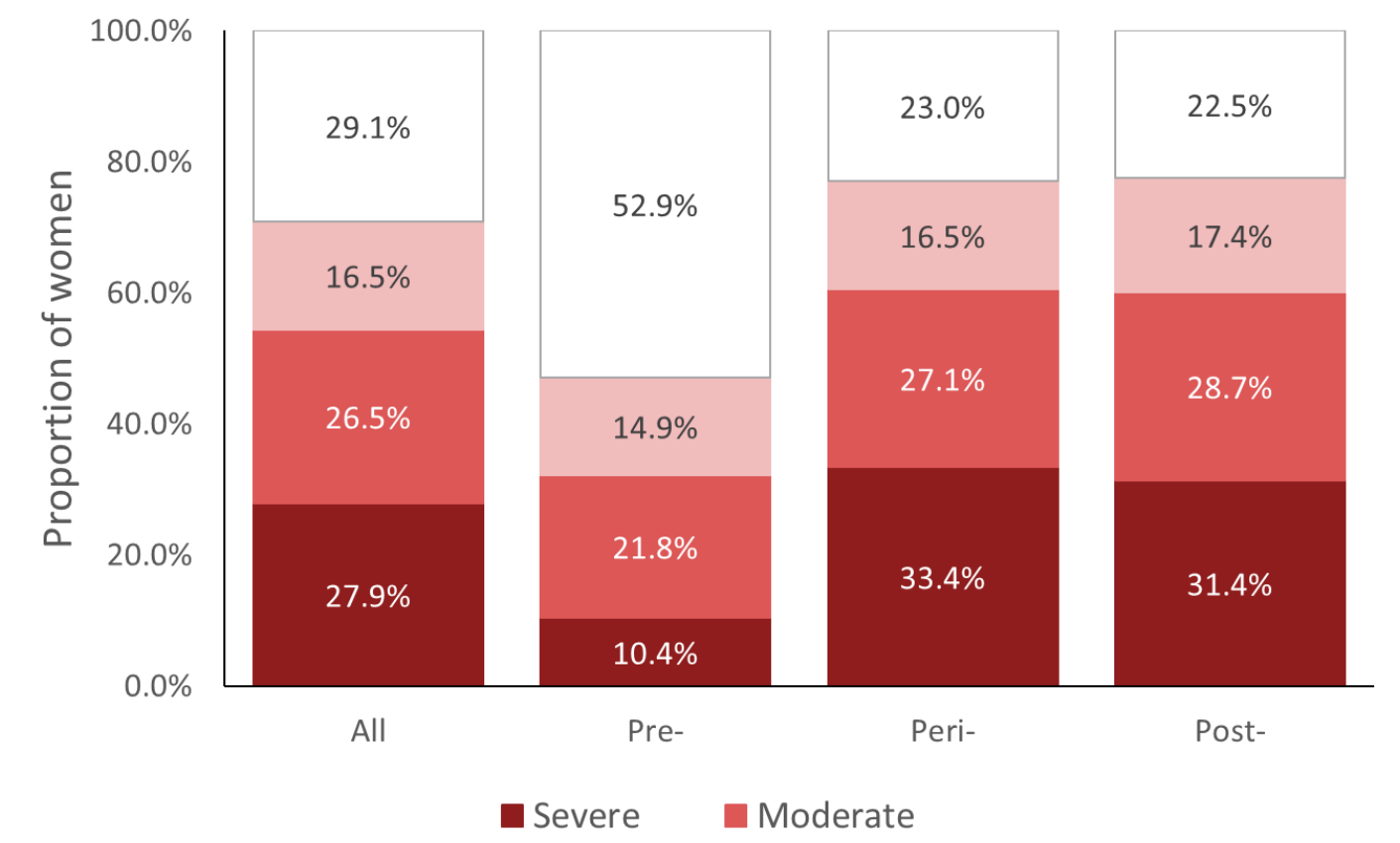
depression, anxiety, irritability, exhaustion



> *It leaves you feeling 'what is going on here'? Is it HIV? Is it the menopause?*

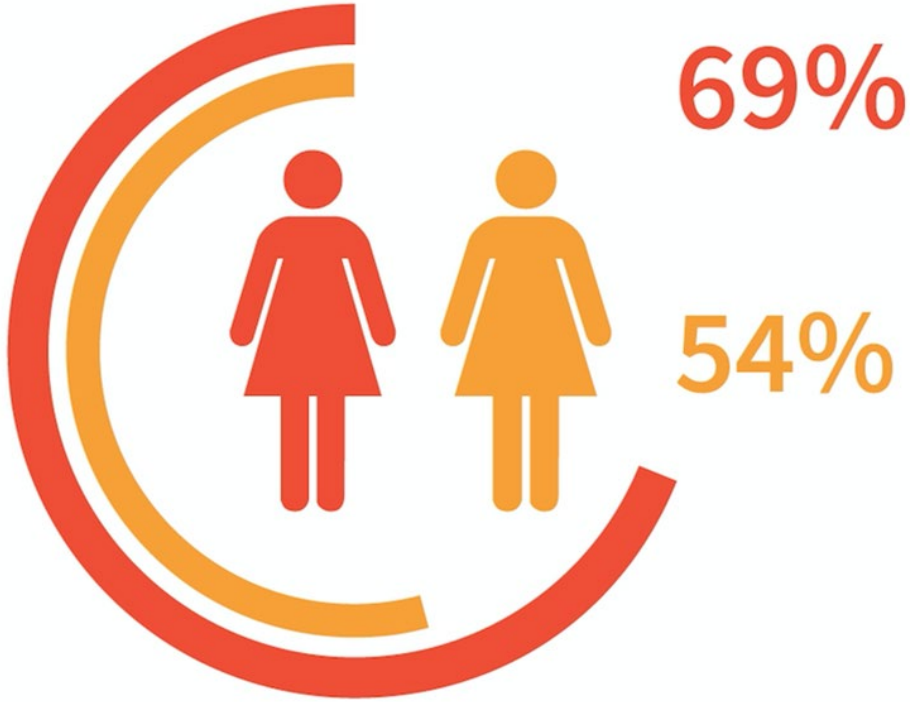
Source: Tariq S *et al.* (2017)

Severity of menopausal symptoms



Source: Okhai et al. (2021)

HIV and sexual function



Women with HIV reporting ≥1 sexual problem in past 1 year

Women without HIV reporting ≥1 sexual problem in past 1 year

Source: Toorabally et al. (2019); Mezones-Holguin et al. (2022)

Menopause Rating Scale

- Standardised scale
- 11 questions, 5-point Likert scale
- Somatic, psychological, urogenital
- Validated in diverse populations (not HIV)
- Can be used to measure response to HRT

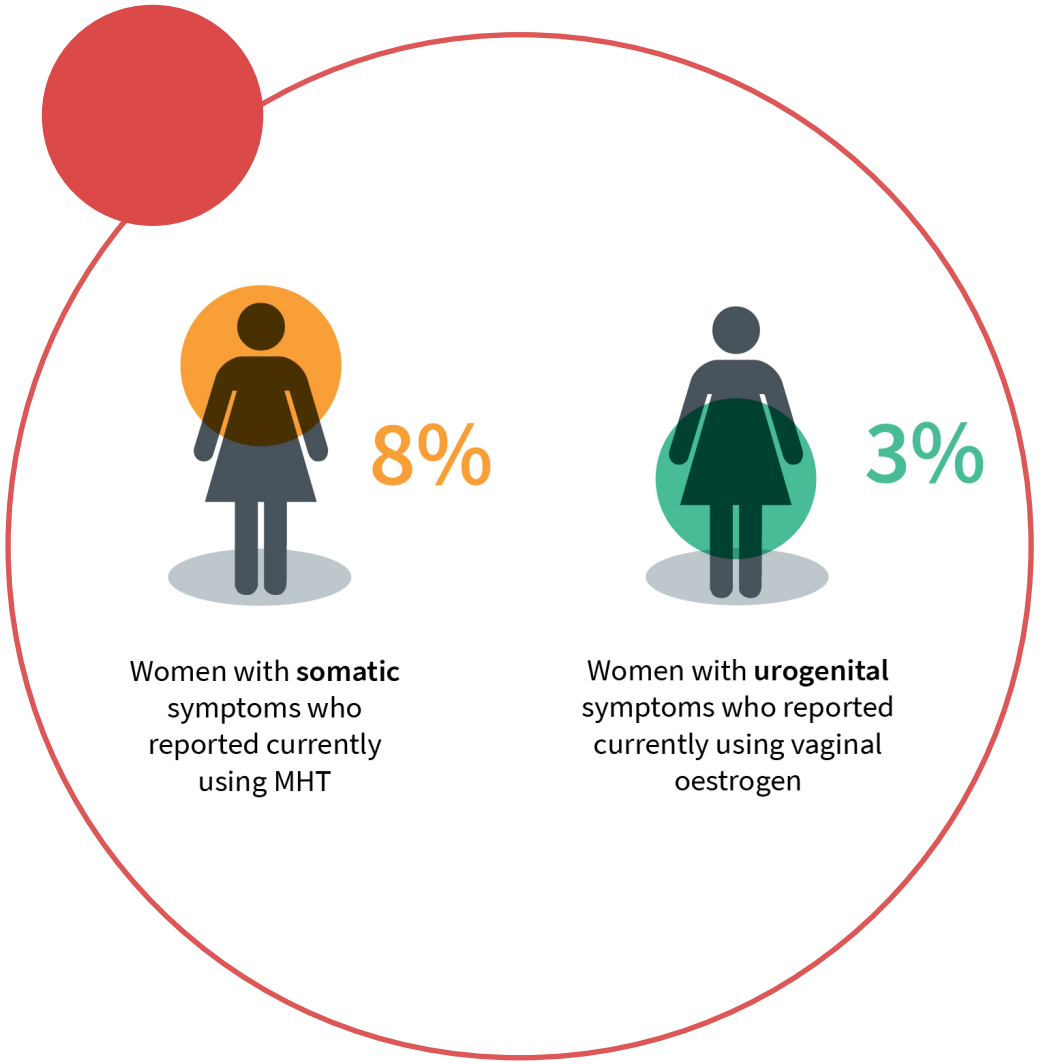
Symptoms:	none	mild	moderate	severe	extremely severe
Score =	0	1	2	3	4
1. Hot flashes, sweating (episodes of sweating)	☐	☐	☐	☐	☐
2. Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness)	☐	☐	☐	☐	☐
3. Sleep problems (difficulty in falling asleep, difficulty in sleeping through the night, waking up early)	☐	☐	☐	☐	☐
4. Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings)	☐	☐	☐	☐	☐
5. Irritability (feeling nervous, inner tension, feeling aggressive)	☐	☐	☐	☐	☐
6. Anxiety (inner restlessness, feeling panicky)	☐	☐	☐	☐	☐
7. Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness)	☐	☐	☐	☐	☐
8. Sexual problems (change in sexual desire, in sexual activity and satisfaction)	☐	☐	☐	☐	☐
9. Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence)	☐	☐	☐	☐	☐
10. Dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse)	☐	☐	☐	☐	☐
11. Joint and muscular discomfort (pain in the joints, rheumatoid complaints)	☐	☐	☐	☐	☐

Source: https://zeg-berlin.de

Impact of menopausal symptoms

- Reduced adherence to ART[1,2]
- Reduced clinic attendance[1,2]
- Increased psychological distress[3]
- Reduced quality of life[4]

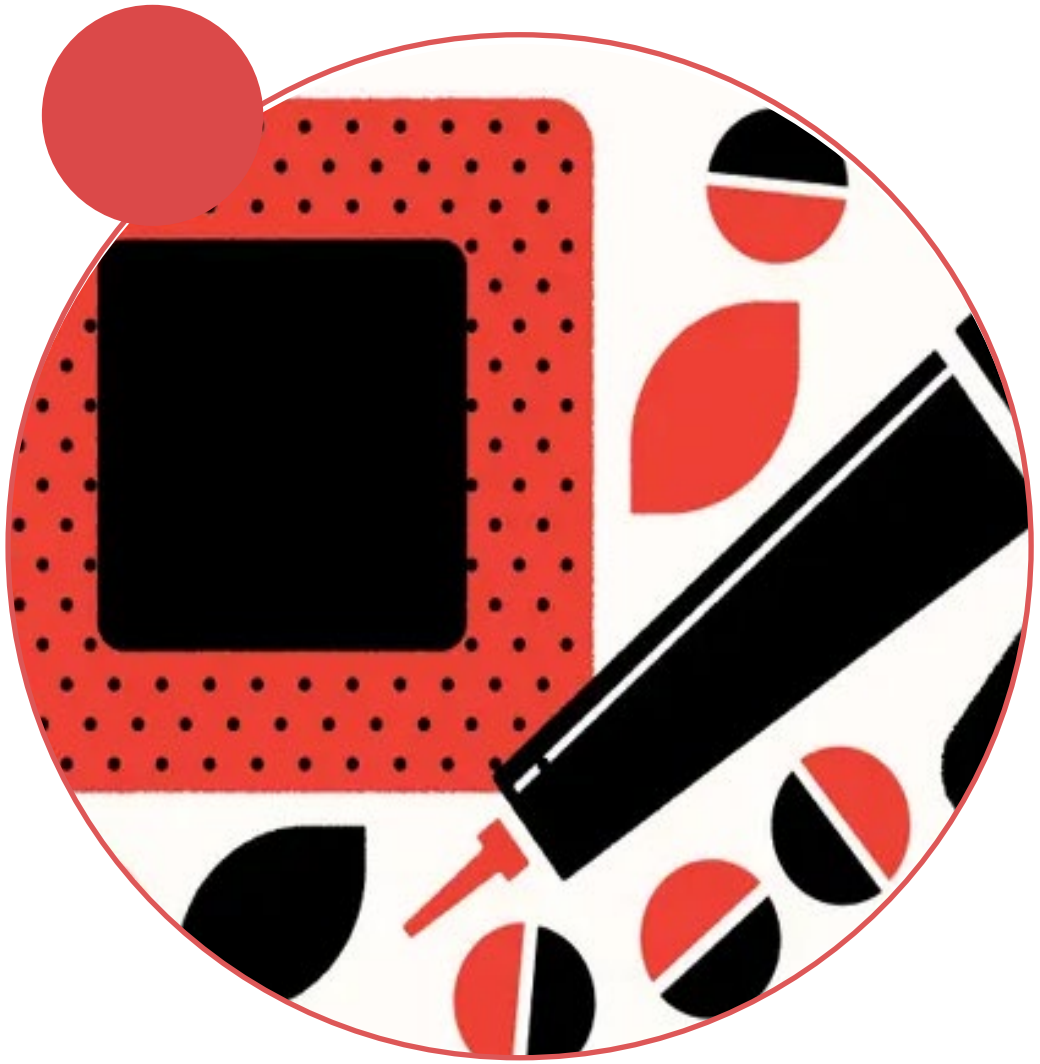
Source: 1. Solomon et al. (2020); 2. Haag et al. (2022); 3. Sabin et al. (2021); 4. Okhai at el. (2022)



Hormone replacement therapy

- Under-used in general and in HIV
- Not contraindicated in HIV
- Improves QoL/CVD/bone health
- For vasomotor/mood symptoms
- No FSH if >45
- DDIs can be managed
- Transdermal oestrogen
- Micronised progestogen

Source: Tariq at el. (2022); Hachfeld et al. (2022)



Avoid bioidentical HRT

- Customised compounded formulations
- Doses based on saliva/serum profiles
- No evidence
- Unregulated
- Very little safety advice
- Expensive

- Increased prevalence of menopause ≤45 in HIV
- ALL women with menopause <40 should be prescribed HRT (or COC) until at least 50

Source: Van Ommen et al. (2021)

Beyond HRT

- Other treatments (SSRIs, CBT, vaginal moisturisers)
- Lifestyle optimisation
- Screening for comorbidities
- Information and support

Sophia

POSITIVELY UK

nam aidsmap

UCL

GROWS

Poster PO91

Key points

- Natural transition with wide ranging health impacts
- Clinical diagnosis in women aged >45
- HRT improves symptoms & reduces comorbidity risk
- Establish clinical pathway
- Support and information are key

Ask about symptoms and periods

Acknowledgements

- NIHR, Wellcome Trust, BHIVA, FTCI
- The PRIME Study Team: Fiona Burns, Richard Gilson, Alexandra Rolland, Caroline Sabin, Abigail Severn, Tuhina Bhattacharyya & Saliha Abbassi
- GROWS Team: Sarah Fraser, Rebecca Mbewe, Juddy Otti, Silvia Petretti, Jacqui Stevenson
- PRIME participating clinics and study participants

Thanks!

You can find me at:

- @Savoy__Truffle or @Prime_UCL
- s.tariq@ucl.ac.uk

BHIVA

British HIV Association

2022 **Spring Conference**

Wed 20th - Fri 22nd April

Manchester Central, Manchester

Panel discussion additional members

Professor Yvonne Gilleece

University Hospitals Sussex NHS Foundation Trust, UK

Bakita Kasadha

University of Oxford, UK

This educational event is supported by an unrestricted medical education grants from

GILEAD Creating Possible MSD ViiV Healthcare

BHIVA

British HIV Association

2022 **Spring Conference**

Wed 20th - Fri 22nd April

Manchester Central, Manchester