L’importanza degli studi sulla popolazione transgender: il punto di vista dell’infettivologo

Marta Boffito, MD, PhD, FRCP

Consultant Physician - HIV Service Director - Clinical Research Facility Lead
Chelsea and Westminster Hospital

Reader, Imperial College London

London, UK

Context 1

- Poor data concerning incidence of HIV-infection in trans and non-binary populations across Europe

- Meta-analysis of a number of small scale studies in USA, six Asia-Pacific, five Latin American, and 3 European countries
  - 49-fold higher likelihood of becoming HIV+ for TW
  - 19% global prevalence of HIV in TW

Baral et al. Lancet Infect Dis. 2013;13:214-22

Context 2

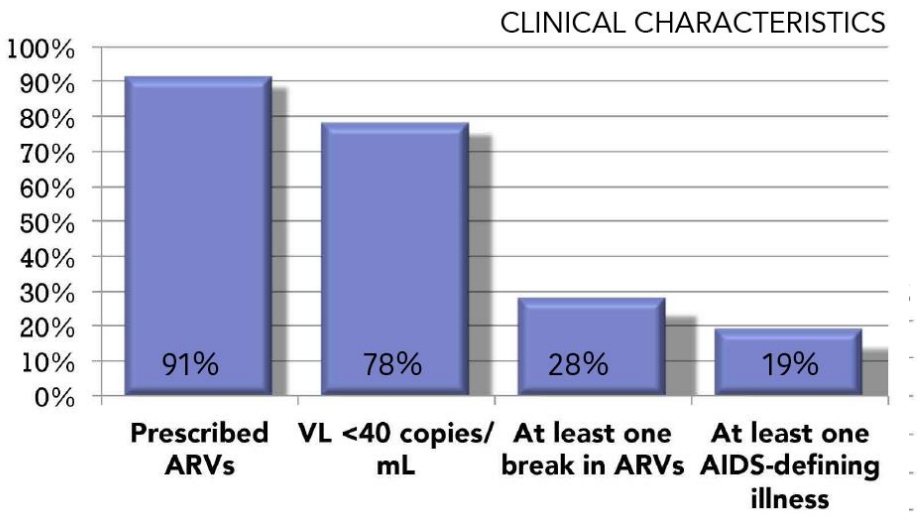
- No reliable estimates for HIV prevalence in transgender men or non-binary people, and very few European data concerning HIV and trans people of any gender identity
- France: single study (N=381) in 2010: prevalence of HIV-infection of 7% in TW, which increased to 17% for sex workers and 36% in those born abroad

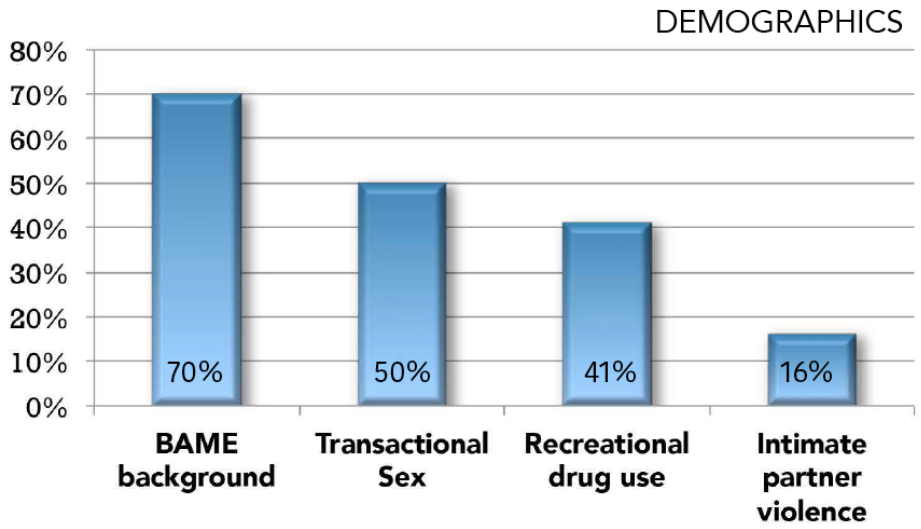
Context 3

- Studies in the USA and Canada indicate that trans people experience multiple barriers to healthcare resulting in late diagnosis of HIV and lower rates of virological suppression than cisgender people
- We are seeing increasing N of TWLWH presenting to our service: affected by the same issues?

Mizuno et al. States. LGBT Health. 2;228-234

Retrospective note review





Wolton et al. BHIVA 2012

THE TIME STUDY: TRANS PEOPLE LIVING WITH HIV THROUGHOUT EUROPE

Primary

- To assess the rate of virological response to antiretroviral therapy in transgender and non-binary (gender diverse) people living with HIV (TPLWH) in Europe

Secondary

- To explore demographics, risk behaviours and community needs
- To explore the barriers and facilitators to adherence to cART
- To report TPLWH experiences with regard to:
  - Stigma
  - Quality of life
  - Prevalence of opportunistic infections
- To record data on:
  - Retention into care
  - Clinical characteristics (e.g. drug toxicity, BMD results, hormone intake, drug interactions between hormones and antiretrovirals, cardiovascular risk, etc.)
- Implement and analyse a trans-inclusive method of gender identity data collection, in order to provide comprehensive demographic information that is acceptable at the community-level and includes a diverse spectrum of trans/non-binary genders across all study sites.

Services for the Trans community

56T is a holistic sexual health and wellbeing service for all trans/non-binary people, their partners and friends. We are a trans-led team, who offer a safe, confidential space for anyone who anyone with sexual health or wellbeing needs. We are open every Wednesday, from 4:30 to 7:00pm on Level 2 at 56 Dean Street.

Our services include:

- Free, confidential sexual health screening
- Liver function tests which are important for monitoring the impact of hormone therapy
- Hepatitis B testing and vaccination
- Cervical smear testing (for anyone over 25 with a cervix)
- PEP (Emergency HIV prevention medication)
- Hormone injections (with ID and proof of prescription)
- Gender identity counselling
- Drug and alcohol counselling
- Housing Advice from Stonewall Housing (first Wednesday of the month)
- Sexual assault and hate crime support and on-going case work (Via Galop)
- Health Adviser support and non-statutory social work
- Social support and community drop-ins
- PrEP (HIV prevention medicine)

56 Dean Street's Trans services are award-winning, and have received acknowledgements for inclusivity & diversity, as well as a Nursing Times Award for 'Enhancing Patient Dignity'.

Implementation and interpretation of studies

Braun et al. LGBT Health. 2017

- Study supported by NIH and Gilead among TW in LA
- >50% concerned that taking cART and feminizing hormone therapy (FHT) may be associated with harmful drug interactions
- Little is clinically understood
- Reason for not taking cART, FHT, or both

Demographics and self-reported treatment regimens of TW (n = 87) LA, CA, USA 2016

		HIV serostatus	
	All (n = 87)	*Not living with HIV (n = 40)*	*Living with HIV (n = 47)*
Age (years)*	45.3 (SD 10.8)	42.6 (SD 11.6)	47.5 (SD 9.7)
Living with HIV	47 (54%)	N/A	N/A
Race/ethnicity			
Hispanic	54 (62%)	26 (65%)	28 (60%)
Black/African American	15 (17%)	5 (13%)	10 (21%)
Multiracial	11 (13%)	3 (8%)	8 (17%)
Asian, Alaskan Native/American Indian, White, other	7 (8%)	6 (15%)	1 (2%)
Health insurance coverage			
Medi-Cal (California's Medicaid Program)	39 (45%)	14 (35%)	25 (53%)
Medicare	5 (6%)	4 (10%)	1 (2%)
Dual Medi-Cal–Medicare coverage or private plan	20 (23%)	9 (23%)	11 (23%)
No healthcare insurance	23 (26%)	13 (33%)	10 (21%)
Feminizing HT use			
Current use	56 (64%)	25 (63%)	31 (66%)
HT acquisition outside of medical system ($n = 55$; $n = 23$ HIV− and $n = 32$ HIV+)	14 (25%)	3 (13%)	11 (34%)
Planning future use	17 (20%)	10 (25%)	7 (15%)
No current or planned use	14 (16%)	5 (13%)	9 (19%)
Substance use (last 90 days)*	32 (37%)	10 (25%)	22 (47%)
Alcohol use (last 90 days)	43 (49%)	19 (48%)	24 (51%)
Current tobacco use	31 (36%)	12 (30%)	19 (40%)
Past tobacco use	14 (16%)	9 (23%)	5 (11%)
Unsupervised injections for body modification ($n = 81$; $n = 38$ HIV− and $n = 43$ HIV+)	11 (14%)	5 (13%)	6 (14%)
Antiretroviral therapy			
NRTI	—	1 (2.5%) [PrEP]	46 (98%)
Tenofovir[a]	—	1 (2.5%)	37 (79%)
Abacavir[a]	—	—	11 (23%)
NNRTI	—	—	13 (28%)
PI	—	—	15 (32%)
INSTI	—	—	19 (40%)
Current $CD4^+$ T lymphocyte count (cells/μL, median [IQR], $n = 44$)	—	—	555 (320–763)
HT and/or ART taken differently than prescribed due to DDI concern ($n = 43$)	—	—	17 (40%)
ART (only) taken differently than prescribed due to DDI concern	—	—	5 (12%)
HT (only) taken differently than prescribed due to DDI concern	—	—	5 (12%)
Both HT and ART taken differently than prescribed due to DDI concern			7 (16%)

Mean (standard deviation) or number (percent), unless specified. Percentages may not total 100 due to rounding.

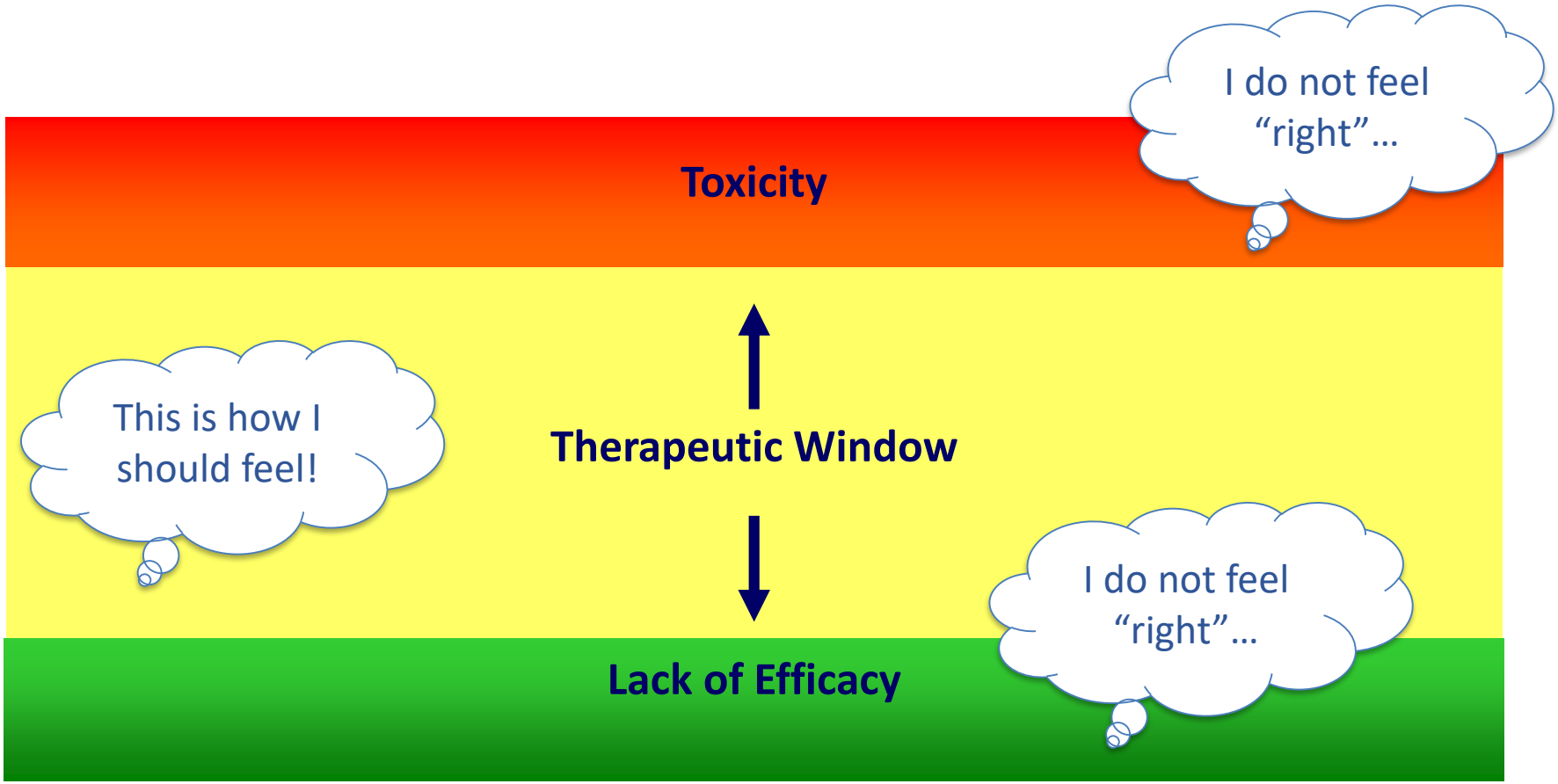
*$P < 0.05$ for transgender women living with HIV compared with transgender women not living with HIV.
[a]Participants were able to report therapy with both tenofovir and abacavir.

ART, antiretroviral therapy; DDI, drug–drug interactions; HT, hormone therapy; INSTI, integrase inhibitor; N/A, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PrEP, preexposure prophylaxis.

Hormones and cART

- Drug interactions between FHT and cART have not been tested
- Data with oral contraceptives (OC)-containing ethinyl estradiol used as a guide
- FHT for TW (tablets, patches, injections) require a much higher dose of estrogen than that used in OC

Clinical significance of DDI



Hormone Therapy for Gender Transitioning

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Estrogen and anti-androgen preparations for use in male to female gender reassignment therapy

		HIV drugs with no predicted effect	HIV drugs predicted to inhibit metabolism	HIV drugs predicted to induce metabolism
Estrogens		RPV, MVC, DTG, RAL, NRTIs (ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV)	ATV/cobi, DRV/cobi, EVG/cobi	ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r, EFV, ETV, NVP
Estradiol oral	*Starting dose*	2 mg/day	1 mg/day	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	4 mg/day	2 mg/day	
	Maximum dose	8 mg/day	4 mg/day	
Estradiol gel (preferred for >40 y and/or smokers)	*Starting dose*	0.75 mg twice daily	0.5 mg twice daily	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	0.75 mg three times daily	0.5 mg three times daily	
	Maximum dose	1.5 mg three times daily	1 mg three times daily	
Estradiol patch (preferred for >40 y and/or smokers)	*Starting dose*	25 µg/day	25 µg/day*	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	50-100 µg/day	37.5-75 µg/day	
	Maximum dose	150 µg/day	100 µg/day	
Conjugated estrogen†	*Starting dose*	1.25-2.5 mg/day	0.625-1.25 mg/day	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	5 mg/day	2.5 mg/day	
	Maximum dose	10 mg/day	5 mg/day	
Ethinylestradiol	*Starting dose*	No interaction expected, but not recommended due to thrombotic risks	Not recommended	Not recommended
	Average dose			
	Maximum dose			
Androgen Blockers		RPV, MVC, DTG, RAL, NRTIs (ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV)	ATV/cobi, ATV/r, DRV/cobi, DRV/r, EVG/cobi, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	EFV, ETV, NVP
Spironolactone	*Starting dose*	50 mg/day	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	150 mg/day		
	Maximum dose	400 mg/day		
Finasteride	*Starting dose*	2.5 mg/day	Finasteride has a large safety margin. No dose adjustment required.	Increase finasteride dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	2.5 mg/day		
	Maximum dose	5 mg day		
Cyproterone acetate	*Starting dose*	50 mg/day	25 mg/day	Increase cyproterone dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	150 mg/day	75 mg/day	
	Maximum dose	150 mg/day	75 mg/day	
Goserelin	*Starting dose*	3.6 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.6 mg/month		
	Maximum dose	3.6 mg/month		
Leuprorelin acetate	*Starting dose*	3.75 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.75 mg/month		
	Maximum dose	3.75 mg/month		
Triptorelin	*Starting dose*	3.75 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.75 mg/month		
	Maximum dose	3.75 mg/month		

† Conjugated estrogen is associated with high thromboembolic risk and therefore should be avoided.

* Matrix type transdermal patch can be cut in order to reduce the amount of hormone delivered/day.

Colour Legend

No clinically significant interaction expected.

Potential interaction which may require dosage adjustment and/or close monitoring.

Coadministration is not recommended.

www.hiv-druginteractions.org

Hormone Therapy for Gender Transitioning

Revised September 2017 *Page 1 of 2*

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Estradiol oral	*Starting dose*	2 mg/day	1 mg/day	Increase estradiol dosage as needed
	Average dose	4 mg/day		
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Estradiol gel (preferred for >40 y and/or smokers)	*Starting dose*	0.75 mg twice daily		
	Average dose	0.75 mg three times daily		
	Maximum dose	1.5 mg three times daily		
Estradiol patch (preferred for >40 y and/or smokers)	*Starting dose*	25 µg/day		
	Average dose	50-100 µg/day		
	Maximum dose	150 µg/day		
Conjugated estrogen†	*Starting dose*	1.25-2.5 mg/day		
	Average dose	5 mg/day		
	Maximum dose	10 mg/day		
Ethinylestradiol	*Starting dose*	No interaction expected, but not recommended due to thrombotic risks		
	Average dose			
	Maximum dose			
Androgen Blockers		RPV, MVC, DTG, RAL, NRTIs (ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV)	EVG	
Spironolactone	*Starting dose*	50 mg/day		
	Average dose	150 mg/day		
	Maximum dose	400 mg/day		
Finasteride	*Starting dose*	2.5 mg/day	Fi	
	Average dose	2.5 mg/day		
	Maximum dose	5 mg day		
Cyproterone acetate	*Starting dose*	50 mg/day		
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Goserelin	*Starting dose*	3.6 mg/month	No dose adjustment required.	No dose adjustment required.
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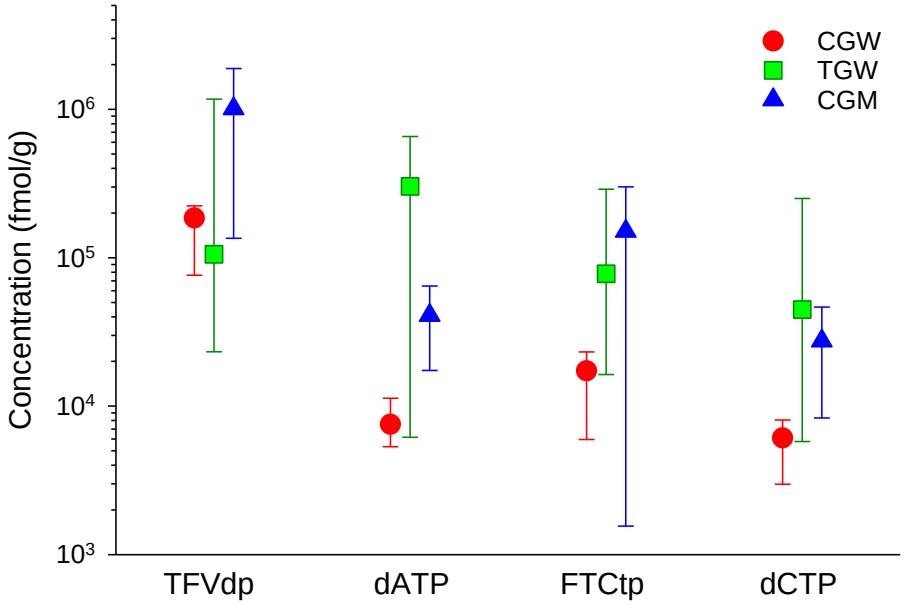
PrEP?

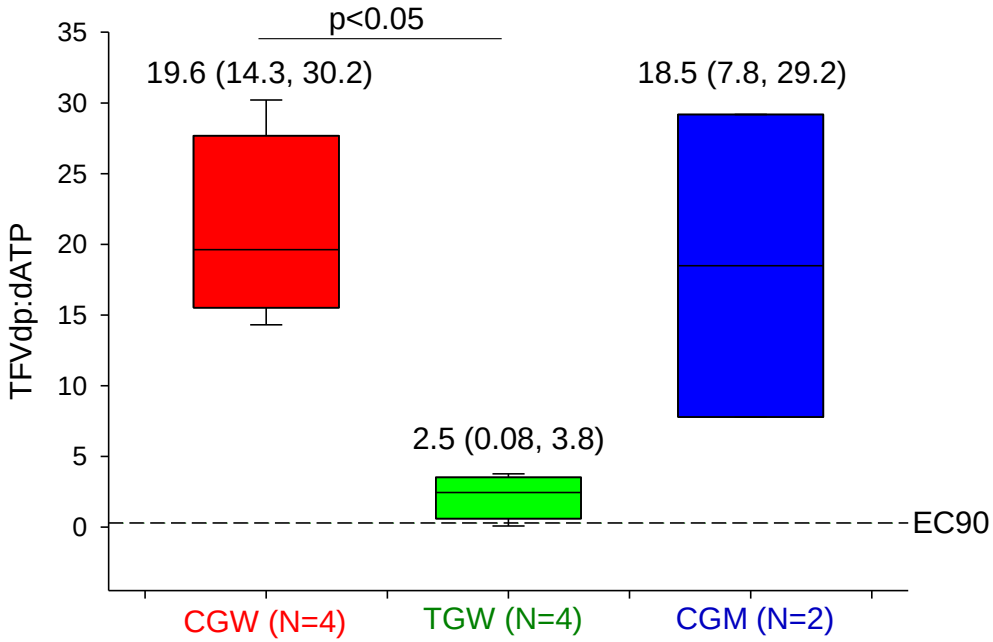
Altered TDF/FTC pharmacology in transgender women: implications for PrEP

Pharmacology Differed in Rectal Tissue of TGW vs CGW and CGM

- All Analytes[1] Median (Min, Max)



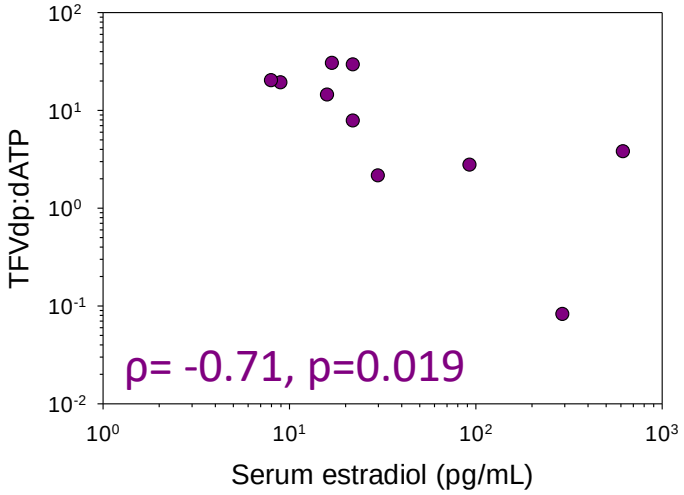
- TFVdp:dATP Median (Min, Max)

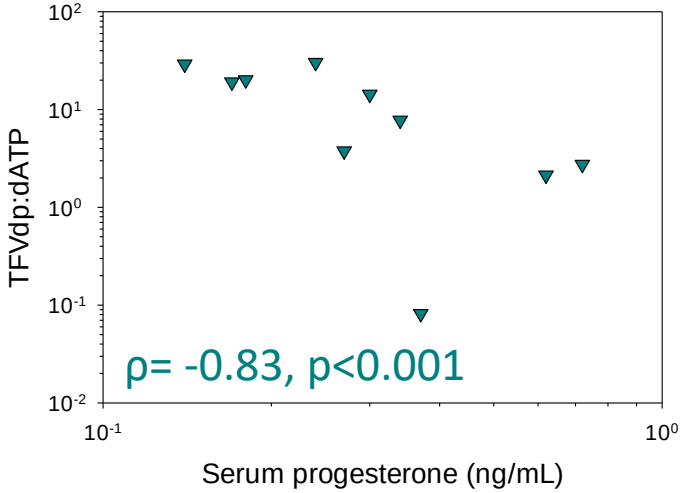


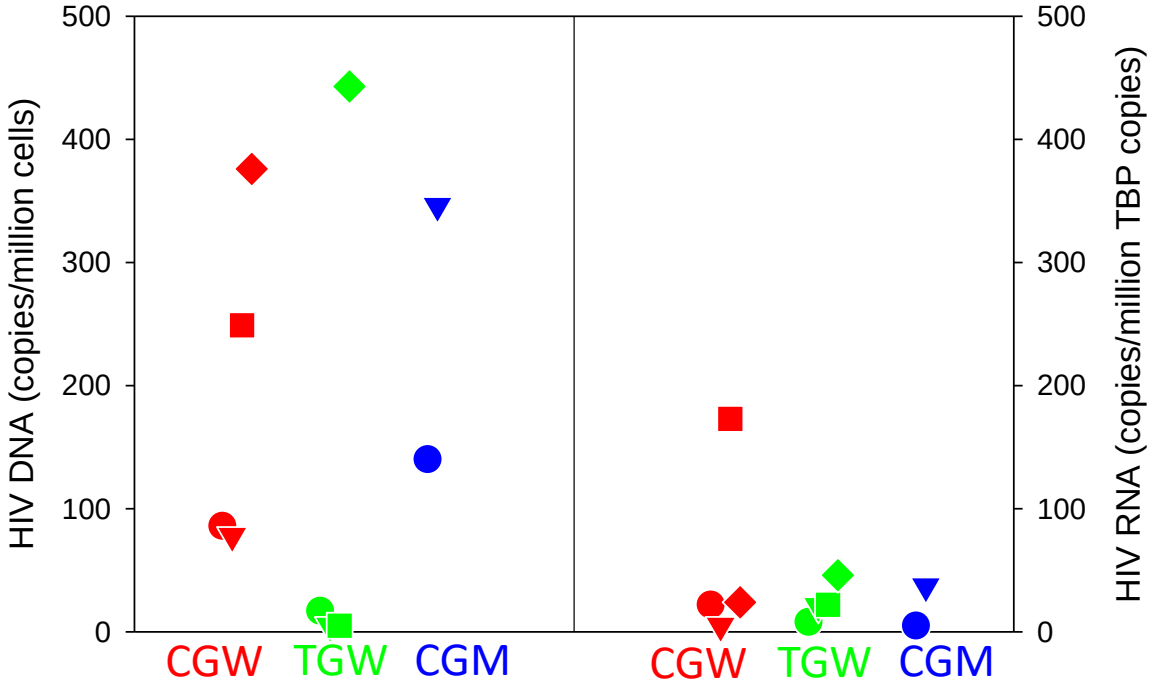
[1]BLQ values imputed at ½ the sample specific lower limit of quantification based on sample mass

Cottrell et al. AIDS2018 TUPDX0106

Female sex hormones correlate with TFVdp:dATP but not HIV DNA and RNA





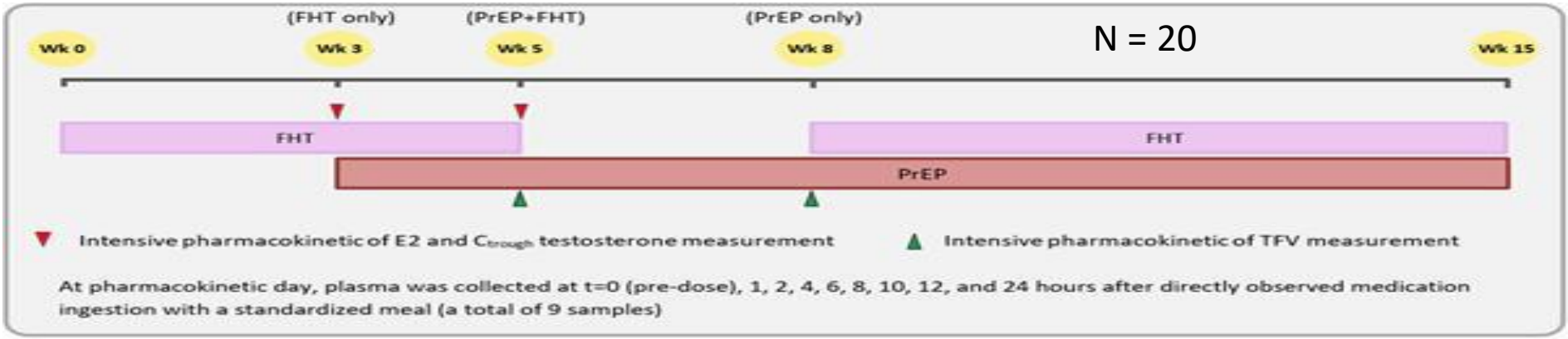


Unlikely to be clinically relevant if TW take daily PrEP as per current recommendations

Cottrell et al. AIDS2018 TUPDX0106

DDIs between FHT and PrEP in transgender women: iFACT study

- Thailand



PLASMA

TFV pharmacokinetic parameter	Week 5 (PrEP+FHT)	Week 8 (PrEP only)	GMR (95%CI)	p-value
AUC0-24 (mg*h/L)	2.28 (26.2)	2.63 (26.9)	0.87 (0.78 - 0.96)	0.009
Cmax (mg/L)	0.36 (34.8)	0.32 (25.3)	1.10 (0.95 - 1.28)	0.2
C24 (mg/L)	0.04 (28.8)	0.05 (28.0)	0.83 (0.76 - 0.90)	<0.001
Half-life (h)	15.19 (15.4)	15.69 (23.0)	0.97 (0.88 - 1.07)	0.53

No effects of PrEP on FHT

FHT = feminizing hormone therapy

Hiransuthikul et al. AIDS2018 TUPDX0107LB

Population data from iPrEx: 339/2499

- PrEP effective in preventing HIV acquisition in transgender women when taken
- Barriers to adherence, particularly among those at the most risk
- Studies should be designed and tailored specifically for this population, rather than adapted from studies of MSM

Deutch et al. Lancet HIV 2015

Conclusions

- Experiences of stigma and discrimination in social and healthcare settings among TWLWH
- Need of data from EU

The TIME study: Trans people living with HIV throughout Europe

- Platform for other research studies
- Lack of knowledge of DDI is not an excuse not to manage DDI: listen to how people feel if you cannot measure drug concentrations
- Individualized care