

HIV-Infected Transgender Women Frequently Take Antiretroviral Therapy and/or Feminizing Hormone Therapy Differently Than Prescribed Due to Drug-Drug Interaction Concerns

HM Braun^{1,2}, J Candelario³, CL Hanlon⁴, ER Segura^{2,5}, JL Clark², JS Currier², JE Lake^{2,6}

Correspondence:
Jordan Lake, MD Msc
Jordan.E.Lake@uth.tmc.edu
6431 Fannin St. | MSB 2.112
Houston, TX 77030

¹ University of California, San Francisco, CA USA ² SAPHIR, University of California, Los Angeles, CA, USA ³ APAIT, Special Service for Groups, Los Angeles, CA, USA ⁴ Dartmouth College, Hanover, NH, USA ⁵ Escuela de Medicina, Universidad Peruana de Ciencias Aplicadas, Lima, Peru ⁶ McGovern Medical School at UTHealth, Houston, TX USA

Background

- Feminizing hormone therapies (HT) are critical to harmonizing gender identity and expression for transgender women (TW), and antiretroviral therapy (ART) is essential for HIV-infected individuals.
- Both HT and ART have potential side effects, and drug-drug interactions (DDI) may exist between some ART and HT.^{1,2}
- Despite a 34-times greater prevalence of HIV infection among TW in the US,³ transgender people have lower healthcare utilization rates⁴ and may seek gender-affirming therapies outside of supervised medical settings.^{5,6}

Study Design

Aim: To assess knowledge of and concern about HT and ART side effects and DDIs, including effects on treatment adherence, among HIV-infected TW in Los Angeles, CA.

Study Design: Cross-sectional survey from a study on contributions of HIV and HT to cardiovascular risk among TW

Eligibility Criteria:

- Self-identified TW
- Age ≥18 years (or 17 years with parental consent)
- HIV-infected TW were required to be on ART and have HIV-1 RNA <50 copies/mL

Study Site: APAIT, a community-based AIDS service organization in Los Angeles, CA

Data Collection: Participants self-reported sociodemographics, medical history, healthcare access and knowledge of ART and HT side effects and ART-HT DDIs.

Data Analysis:

- Primary outcome:** self-reported history of HT or ART use differently than prescribed due to concerns for ART-HT DDI (HIV-infected TW only)
- Descriptive statistics summarized sociodemographics, healthcare access, and knowledge of ART and HT side effects and ART-HT DDIs.
- Generalized linear models identified factors associated with imperfect HT and/or ART use.

Results

Table 1: Demographic and Clinical Characteristics of TW

	HIV Serostatus		
	All (n=87)	HIV-uninfected (HIV-, n=40)	HIV-infected (HIV+, n=47)
Age (in years)*	45.3 ± 10.8	42.6 ± 11.6	47.5 ± 9.7
Living with HIV	47 (54%)	N/A	100%
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%)
Substance Use (last 90 days)*	32 (37%)	10 (25%)	22 (47%)
Alcohol Use (last 90 day)	43 (49%)	19 (48%)	24 (51%)
Current Tobacco Use	31 (36%)	12 (30%)	19 (40%)
History of AIDS diagnosis (HIV+ only)	N/A	N/A	22 (47%)
Current CD4+ T lymphocyte count (cells/μL, HIV+ only)	N/A	N/A	555 ± 271
History of Hypertension	27 (31%)	9 (23%)	18 (38%)
History of High Cholesterol	14 (16%)	9 (23%)	5 (11%)
History of Diabetes	17 (20%)	8 (20%)	9 (19%)
Ever had surgery to feminize body (n=81)	17 (21%)	10 (26%)	7 (16%)

Data presented as number (percent) or mean ± standard deviation. Percentages may not total 100 due to rounding.

*statistically significant (p<0.05) between HIV-infected and HIV-uninfected TW

Table 2: Engagement in Healthcare among TW

	All (n=87)	HIV Serostatus	
		HIV- (n=40)	HIV+ (n=47)
Communication with Healthcare Provider			
Discussed potential HT side effects with their provider (n=73; n=32 HIV- & n=41 HIV+)	50 (69%)	25 (78%)	25 (61%)
Concerned for ART-HT interactions (HIV+ only; n=42)	-	-	24 (57%)
Discussing ART-HT interactions concerns with provider (HIV+ only; n=43)	-	-	21 (49%)
Health Insurance Coverage			
MediCal (California's Medicaid Program)	39 (45%)	14 (35%)	25 (53%)
Medicare	5 (6%)	4 (10%)	1 (2%)
Dual MediCal-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- & 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%)
Unsupervised Injections for Body Modification (n=81; n=38 HIV- & n=43 HIV+)			
	11 (14%)	5 (13%)	6 (14%)

Data presented as number (percent).

Table 3: Treatment Regimen and History of HT-ART Use among HIV-Infected TW

	HIV+ (n=47)
Antiretroviral Therapy	
NRTI	46 (98%)
Tenofovir ^b	37 (79%)
Abacavir ^b	11 (23%)
NNRTI	13 (28%)
PI	15 (32%)
INSTI	19 (40%)
HT and/or ART taken differently than prescribed due to DDI concern (n=43)	
ART use different than prescribed	12 (28%)
HT use different than prescribed	12 (28%)

^bParticipants were able to report therapy with both tenofovir and abacavir.

Data presented as number (percent), unless specified.

NRTI=nucleoside reverse transcriptase inhibitor, PrEP=pre-exposure prophylaxis, NNRTI=non-NRTI, PI=protease inhibitor, INSTI=integrase inhibitor

Table 4: Participant Characteristics Associated with Imperfect Use of HT or ART

Variable	Category label/units	Unadjusted PR (95% CI)	p
Age	Years	0.99 (0.95 – 1.02)	0.54
	Race	Hispanic	1.03 (0.48 – 2.18)
Black		0.81 (0.30 – 2.22)	0.68
Multiracial		1.35 (0.60 – 3.04)	0.48
HT use	Not currently on HT	Ref	Ref
	Currently on HT	0.55 (0.27 – 1.11)	0.10
Substance use (last 90 days)	None	Ref	Ref
	Drug use	1.92 (0.87 – 4.25)	0.10
Alcohol Use (last 90 days)	None	Ref	Ref
	Alcohol use	1.92 (0.87 – 4.25)	0.10

Conclusions

- TW expressed concern about potential ART and HT side effects and DDIs, but often did not discuss these concerns with their healthcare provider(s).
- These concerns contributed to HT and/or ART use differently than prescribed in 40% of HIV-infected TW.
- These results support previous research identifying fear among TW that ART limits the feminizing effects of hormones,⁷ and raise clinical concern as 1) sub-optimal ART adherence increases the risk of developing ART resistance and virologic failure,^{8,9} and 2) intermittent HT use may cause sub-optimal feminization and/or increased risk of HT side effects.¹⁰
- No studies specifically address DDI between ART and the HT doses used for feminizing HT in TW. More data is needed before providing clinical recommendations to providers.
- As higher HT adherence and access to transgender-specific healthcare are associated with higher ART adherence,^{11,12} our data suggests a need for comprehensive care programs for HIV-infected TW, including clinical integration of HT and ART services.
- Future research will address ART-HT DDIs and side effect profile risk for TW, and investigate approaches to mitigate risk.

Acknowledgments

The authors thank the participants who contributed their time and experiences. The authors acknowledge Diane Preciado for her help with participant recruitment as well as Destin Cortez, Tatiana Pavon and the staff at APAIT for their assistance throughout the study. This work was supported in part by the Doris Duke Charitable Foundation through a grant supporting the Doris Duke International Clinical Research Fellows Program at the University of California, San Francisco. HMB is a Doris Duke International Clinical Research Fellow. This research was also supported by the National Institutes of Health grants R25 MH087222 to JLC, K23 AI110532 to JEL and 5P30 AI028697, and by the Gilead Sciences Research Scholars Program in HIV award to JEL.

References

- Fichtenbaum CJ. Clin Pharmacokinet. 2002; 41(14).
- Nanda K. AIDS. 2017; 31.
- Baral SD. Lancet Infect Dis. 2013; 13(3).
- Bradford J. Am J Public Health. 2013; 103.
- Rotondi NK. Am J Public Health. 2013; 103.
- de Haan G. LGBT Health. 2015; 2(4).
- Sevelius JM. Ann Behav Med. 2014; 47(1).
- Sethi AK. Clin Infect Dis. 2013; 37(8).
- Bezabhe WM. Medicine (Baltimore). 2016; 95(15).
- Spack NP. JAMA. 2013; 309(5).
- Sevelius JM. AIDS Care. 2014; 26(8).
- Sevelius JM. J Assoc Nurses AIDS Care 2010; 21(3).