

# Risk for Viral Rebound in the Era of U=U; a CNICS Analysis

## Introduction

- Since 2016, the “Undetectable = Untransmittable (U=U)” campaign has created a paradigm shift in HIV public health messaging and prevention efforts.
- Multiple studies (HPTN 052, PARTNER, PARTNER 2, Opposites Attract) have demonstrated that persons living with HIV (PLWH) with an undetectable HIV viral load (< 200 copies/mL) do not transmit HIV through condomless sex.
- U=U is now endorsed by nearly 400 HIV organizations across 36 countries, including the Centers for Disease Control and Prevention, International AIDS Society, and UNAIDS.
- Despite the campaign’s growing recognition, the implementation of U=U in the clinic setting raises questions for both patients and providers related to counseling, monitoring, and risks of HIV viral rebound among persons eligible for U=U.

## Methods

**Aim:** To inform the implementation and uptake of U=U in the clinic setting, we sought to identify risk factors for viral rebound among persons who started ART and achieved viral suppression.

**Design:** Retrospective study using multi-center data from the Centers for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS), a multisite clinical cohort of PLWH receiving HIV care.

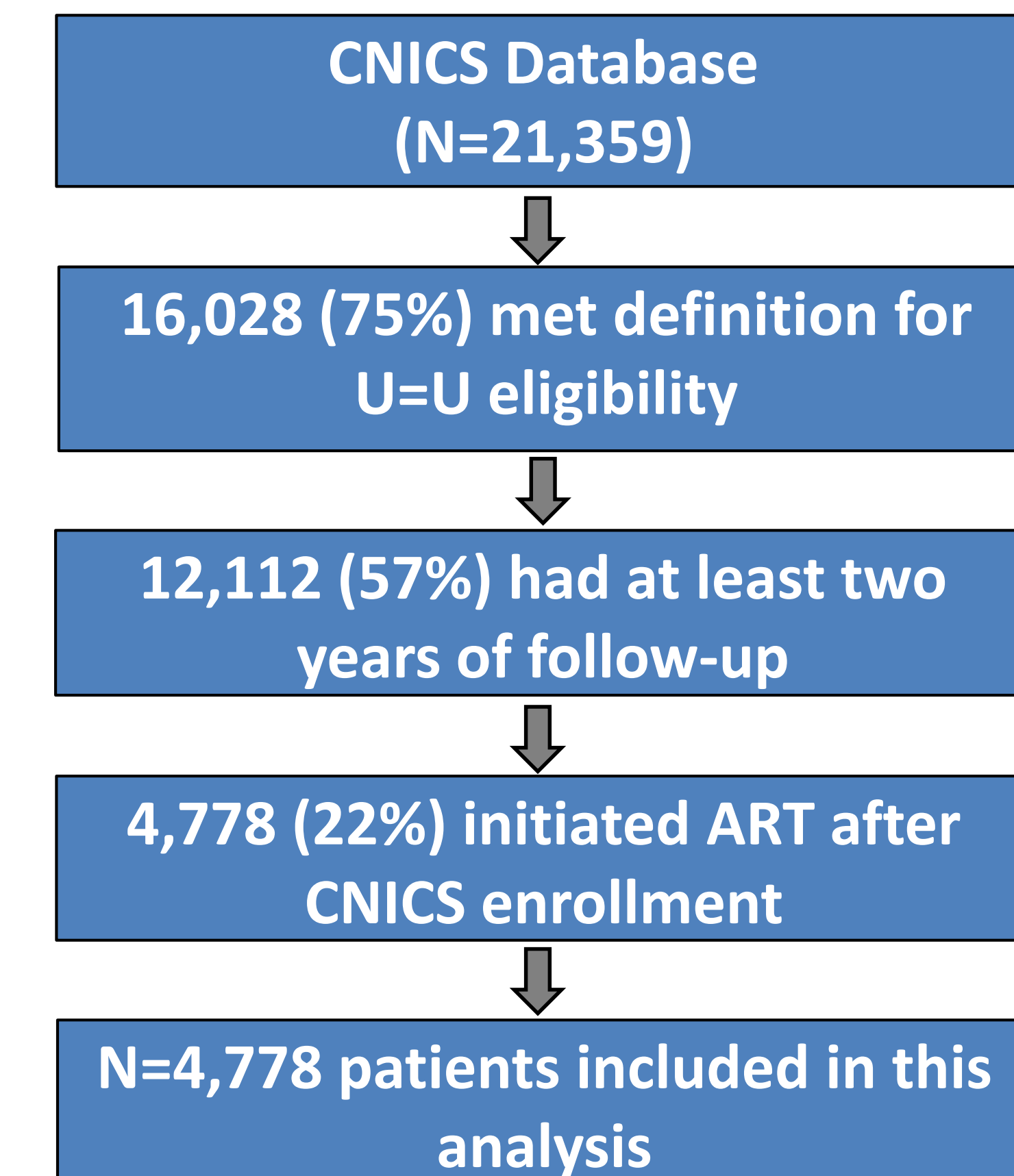
- CNICS Data Repository integrates comprehensive clinical data from outpatient and inpatient encounters including information on demographics, clinical and laboratory data, and medications.
- Study participants included patients who:
  - Started antiretroviral treatment (ART) after CNICS enrollment
  - Considered U=U eligible based upon sustained viral suppression for two consecutive years defined as: 1)  $\geq$  two viral measurements per year for two consecutive years between 2010-2016, and 2) all VL measurements during the two-year period were < 200 copies/ml.
  - Having  $\geq$  two years of follow up after becoming U=U eligible.

**Analysis:** Patients' demographics, patient-reported outcomes, and longitudinal clinical data were analyzed to identify predictors of viral rebound, defined as any VL > 200 copies/mL within two years

- Univariable logistic regression models were conducted and variables with p values < 0.05 were included in a multivariable logistic regression model. The predictive values of individual variables were captured by adjusted odds ratios (aORs).

## Results

**Figure 1. Study Population/Eligibility**



**Table 2. Mental Health/Substance Use**

	Viral Rebound (n = 555)	Viral Suppression (n = 4223)	Total (N = 4778)	P value
	n (%)	n (%)	n (%)	
<b>Health-Related Quality of Life (EQ-5D)</b>				
High	73 (13%)	817 (19%)	890 (19%)	0.016
Medium	98 (18%)	790 (19%)	888 (19%)	
Low	29 (5%)	174 (4%)	203 (4%)	
Missing	355 (64%)	2442 (58%)	2797 (59%)	
<b>Anxiety (PRIME-MD)</b>				
No panic sx	191 (34%)	1675 (40%)	1866 (39%)	0.553
Some panic sx	29 (5%)	234 (6%)	263 (6%)	
Panic disorder	33 (6%)	234 (6%)	267 (6%)	
Missing	302 (54%)	2080 (49%)	2382 (50%)	
<b>Depression (PRIME-MD)</b>				
None	132 (24%)	1424 (34%)	1556 (33%)	<0.001
Mod to sev	57 (10%)	324 (8%)	381 (8%)	
Missing	366 (66%)	2475 (59%)	2841 (59%)	
<b>Alcohol Use – Binge Use (AUDIT-C)</b>				
Never	174 (31%)	1419 (34%)	1593 (33%)	0.193
Infrequent binge	57 (10%)	614 (15%)	671 (14%)	
Frequent binge	16 (3%)	122 (3%)	138 (3%)	
Missing	308 (55%)	2068 (49%)	2376 (50%)	
<b>Cigarette Use</b>				
Never smoked	77 (14%)	915 (22%)	992 (21%)	<0.001
Past smoker	55 (10%)	540 (13%)	595 (12%)	
Current smoker	122 (22%)	733 (17%)	855 (18%)	
Missing	301 (54%)	2035 (48%)	2336 (49%)	
<b>Methamphetamine Use (ASSIST)</b>				
No use	128 (23%)	1249 (30%)	1377 (29%)	0.001
Past use	57 (10%)	492 (12%)	549 (11%)	
Current use	33 (6%)	164 (4%)	197 (4%)	
Missing	337 (61%)	2318 (55%)	2655 (56%)	
<b>Cocaine Use (ASSIST)</b>				
No use	105 (19%)	1108 (26%)	1213 (25%)	<0.001
Past use	82 (15%)	681 (16%)	763 (16%)	
Current use	33 (6%)	122 (3%)	155 (3%)	
Missing	335 (60%)	2312 (55%)	2647 (55%)	
<b>Opiate Use (ASSIST)</b>				
No use	163 (29%)	1594 (38%)	1757 (37%)	0.146
Past or current use	33 (6%)	235 (6%)	268 (6%)	
Missing	359 (65%)	2394 (57%)	2753 (58%)	

**Table 1. Demographics**

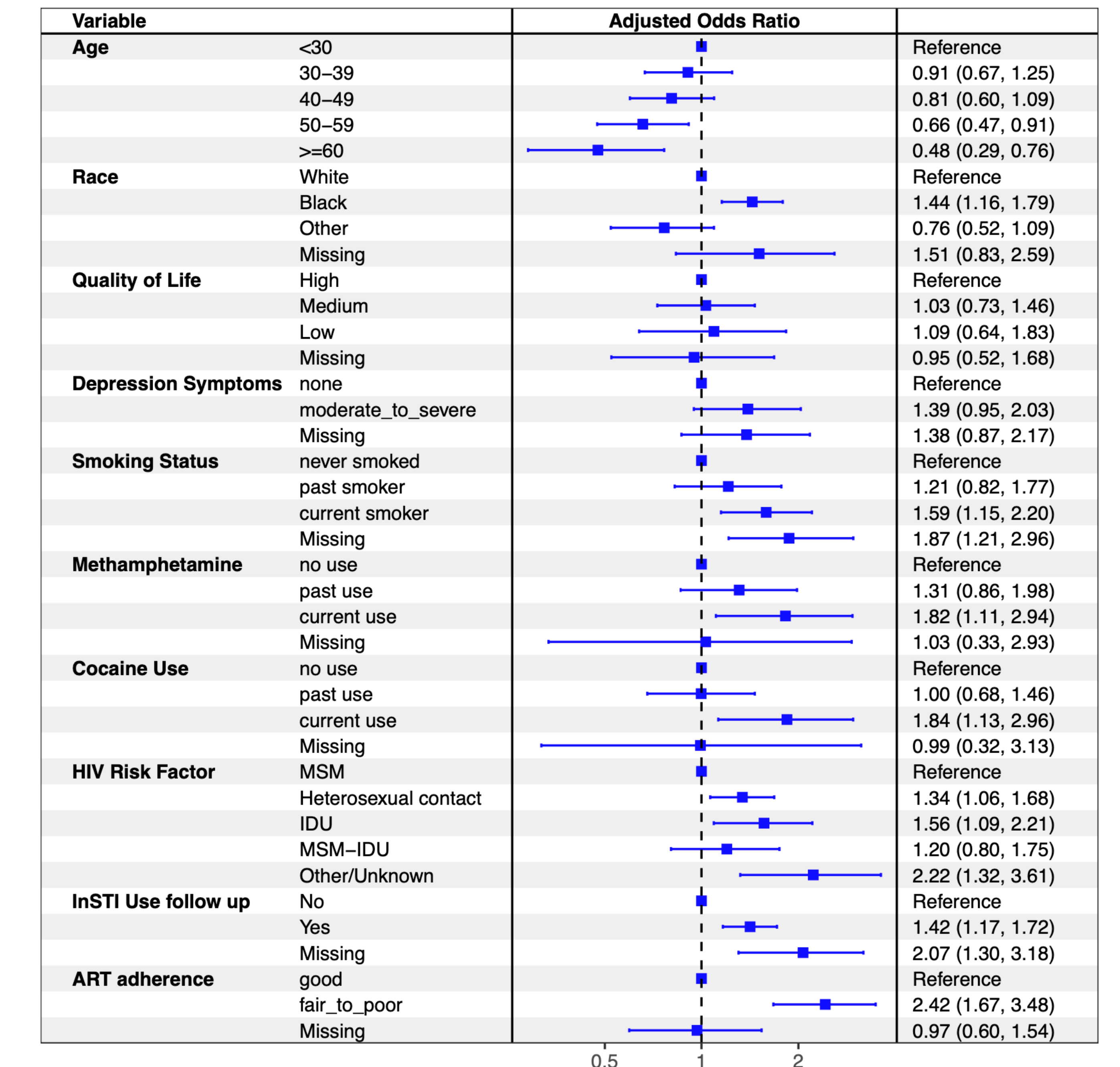
	Viral Rebound (n = 555)	Viral Suppression (n = 4223)	Total (N = 4778)	P value
	n (%)	n (%)	n (%)	
<b>Age</b>				
<30	75 (14%)	469 (11%)	544 (11%)	0.124
30-39	138 (25%)	979 (23%)	1117 (23%)	
40-49	192 (35%)	1448 (34%)	1640 (34%)	
50-59	123 (22%)	1037 (25%)	1160 (24%)	
>=60	27 (5%)	290 (7%)	317 (7%)	
<b>Sex (current)</b>				
Male	383 (69%)	2816 (67%)	3199 (67%)	0.098
Female	112 (20%)	680 (16%)	792 (17%)	
Missing	60 (11%)	727 (17%)	787 (16%)	
<b>Race</b>				
White	238 (43%)	2188 (52%)	2426 (51%)	<0.001
Black	263 (47%)	1550 (37%)	1813 (38%)	
Other	38 (7%)	394 (9%)	432 (9%)	
Missing	16 (3%)	91 (2%)	107 (2%)	
<b>Ethnicity</b>				
Non-Hispanic	400 (72%)	3211 (76%)	3611 (76%)	0.906
Hispanic	75 (14%)	617 (15%)	692 (14%)	
Missing	80 (14%)	395 (9%)	475 (10%)	

**Table 3. HIV-Related Characteristics & Care**

	Viral Rebound (n = 555)	Viral Suppression (n = 4223)	Total (N = 4778)	P value
	n (%)	n (%)	n (%)	
<b>Primary HIV Risk Factor</b>				
MSM	274 (49%)	2483 (59%)	2757 (58%)	<0.001
Heterosexual	170 (31%)	1107 (26%)	1277 (27%)	
IDU	53 (10%)	285 (7%)	338 (7%)	
MSM-IDU	36 (6%)	255 (6%)	291 (6%)	
Other/Unknown	22 (4%)	93 (2%)	115 (2%)	
<b>Duration of Care at CNICS Site</b>				
<2 years	146 (26%)	1202 (28%)	1348 (28%)	0.728
2-4 years	143 (26%)	1084 (26%)	1227 (26%)	
5-9 years	154 (28%)	1109 (26%)	1263 (26%)	
$\geq$ 10 years	112 (20%)	828 (20%)	940 (20%)	
Missing	0 (0%)	0 (0%)	0 (0%)	
<b>Duration of Antiretroviral Therapy (ARV)</b>				
<2 years	160 (29%)	1482 (35%)	1642 (34%)	0.242
2-4 years	121 (22%)	949 (22%)	1070 (22%)	
5-9 years	111 (20%)	820 (19%)	931 (19%)	
$\geq$ 10 years	77 (14%)	566 (13%)	643 (13%)	
Missing	86 (15%)	406 (10%)	492 (10%)	
<b>Integrase Strand Transfer Inhibitor (InSTI) Use at Baseline</b>				
No	359 (65%)	3064 (73%)	3423 (72%)	0.066
Yes	110 (20%)	753 (18%)	863 (18%)	
Missing	86 (15%)	406 (10%)	492 (10%)	
<b>InSTI Use at Follow-up</b>				
No	326 (59%)	2869 (68%)	3195 (67%)	<0.001
Yes	201 (36%)	1248 (30%)	1449 (30%)	
Missing	28 (5%)	106 (3%)	134 (3%)	
<b>Self-reported ARV Adherence</b>				
Good	144 (26%)	1551 (37%)	1695 (35%)	<0.001
Fair to poor	54 (10%)	189 (4%)	243 (5%)	
Missing	357 (64%)	2483 (59%)	2840 (59%)	

## Results Cont'd

**Figure 2. Multivariable Logistic Regression Model**



## Discussion

- 4778 patients met eligibility for U=U with two years of sustained viral suppression.
- 555 (12%) experienced viral rebound during subsequent two-year follow-up period.
- Multivariate analysis: the odds of viral rebound were significantly greater among: 1) Black race; 2) current smoker; 3) current use of amphetamines; 4) current use of cocaine; 5) those with heterosexual, IDU, or other/unknown risk compared to MSM; 6) InSTI use during follow-up; and 7) fair to poor ART adherence
- Older age (> 50) was protective against viral rebound
- Majority (88%) of persons eligible for U=U maintain suppression over time; however treatment is dynamic and affected by many factors (e.g. substance use) which has implications for counseling, VL monitoring, & assuring retention in care.
- Further research is needed to identify synergistic risk factors that increase probability of viral rebound to inform optimal implementation of U=U.

## Acknowledgements

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