

# Less is More:

## The Impact of Lower Pill Burden on Adherence to Antiretroviral Therapy among Treatment-Naive Patients with HIV Infection in the United States

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# Background

- Non-adherence to antiretroviral therapy (ART) regimens result in
  - Lack of sustained virological suppression, increased risk of onwards transmission, development of drug resistance, poorer overall health, quality of life and survival
- Second line and third line therapy are costly\*
  - Over 20% of newly treated patients switch their initial treatment regimen within 2 years

\* Solem CT, Snedecor SJ, Khachatryan A, Nedrow K, Tawadrous M, Chambers R, et al. (2014) Cost of Treatment in a US Commercially Insured, HIV-1–Infected Population. PLoS ONE 9(5): e98152.



# Rationale

- Optimum adherence during the early months after initiation of ART is crucial to ensure long term immuno-virological success<sup>1,2</sup>
- If viral replication is not drastically reduced early in treatment, resistant strains may emerge<sup>3</sup>
- High pill burden is associated with
  - Lower adherence to ART
  - Discontinuation of ART
- Limited real world evidence on impact of single-tablet regimen (STR) on adherence among treatment-naive patients
  - Often from single payer type (Medicare Part D, Medicaid, Third party)
  - No nationally representative study
  - Lack of recent data in the literature

1. Carrieri MP, Raffi F, Lewden C, et al. Impact of early versus late adherence to highly active antiretroviral therapy on immuno-virological response: A 3-year follow-up study. *Antivir Ther (Lond)*. 2003;8(6):585-594.

2. Kitchen CM, Kitchen SG, Dubin JA, Gottlieb MS. Initial virological and immunologic response to highly active antiretroviral therapy predicts long-term clinical outcome. *Clinical infectious diseases*. 2001;33(4):466-472.

3. Moyle GJ. Use of viral resistance patterns to antiretroviral drugs in optimizing selection of drug combinations and sequences. *Drugs*. 1996;52(2):168-185.



# Research Question

- Does adherence differ between treatment-naive HIV infected patients who are prescribed a single-tablet regimen compared to those prescribed a multiple-tablet regimen during the first year?



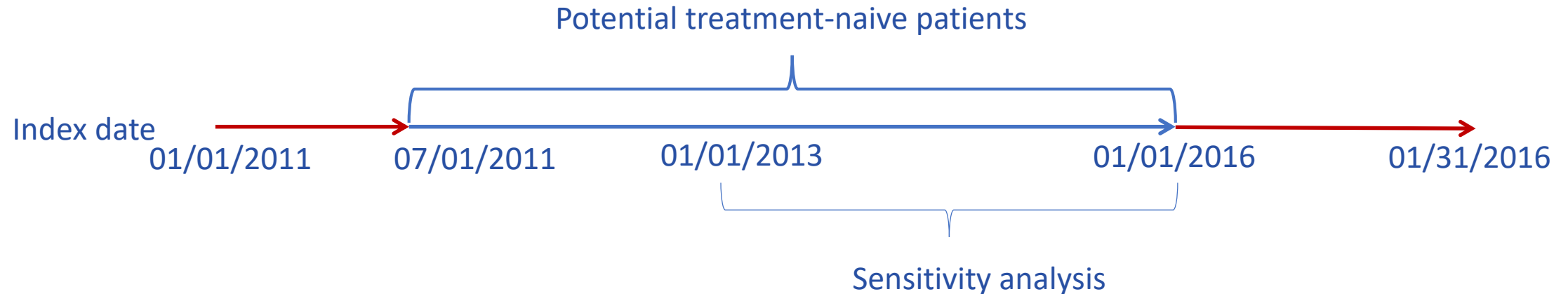
# IQVIA LRx<sup>®</sup> Database

- De-identified patient-level longitudinal prescription database
  - Prescription fill information of a random sample of 69 million patients during 2011-2016
- Nationally representative by sex, age and insurance coverage
- IQVIA receives these data on a weekly basis from ~90% pharmacies throughout the US



# Study Population

- Treatment-naive patients filling at least 1 ART prescription at a participating retail pharmacy
- Index date: First date of ART prescription fill during the study period



# Inclusion and Exclusion Criteria

## Inclusion criteria

- 18 years or older on index date
- HHS recommended regimen for treatment-naïve patients
- Refilled at least once during the follow up period

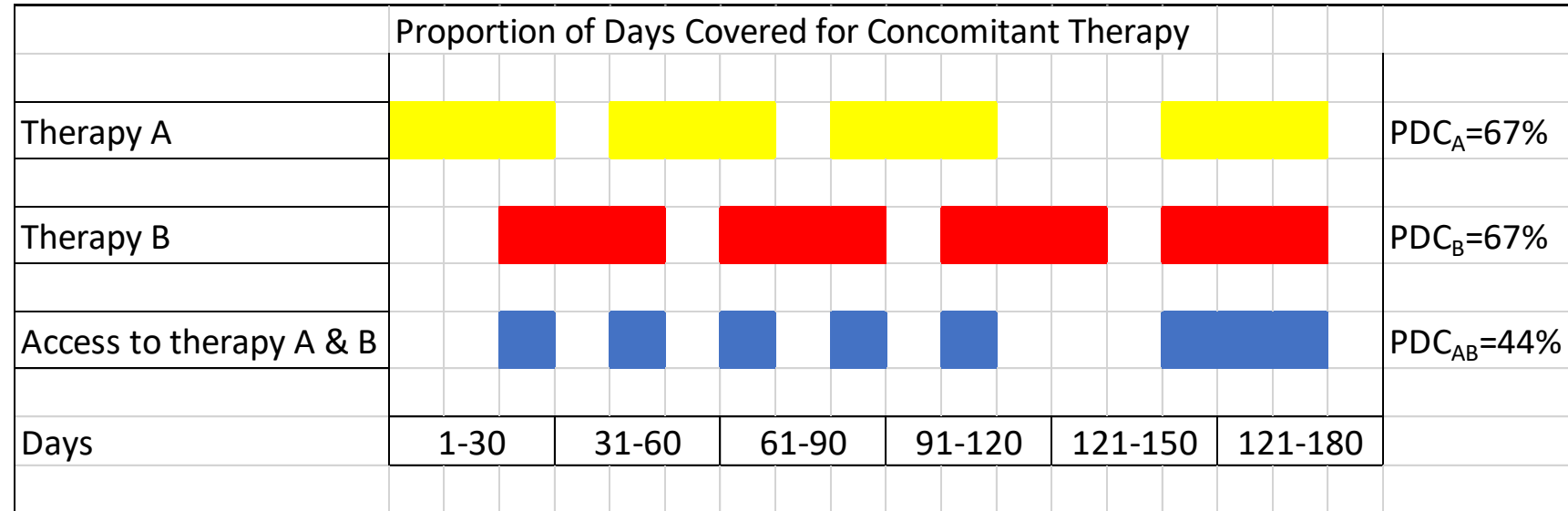
## Exclusion criteria

- Switched regimens during the follow-up period
- On a salvage regimen
- PrEP/incomplete regimen
- Index pharmacy not retail
- Missing covariate data



# Outcome Variable

- Adherence measured using proportion of days covered (PDC)
  - PDC measures the number of days “covered” by a prescription and divides by the number of days in the measurement period (365 days)
  - Patients with >90% PDC considered optimally adherent



Source: Leslie, S.R., Gwadry-Sridhar, F., Thiebaud, P. and Patel, B.V., 2008. Calculating medication compliance, adherence and persistence in administrative pharmacy claims databases. *Pharmaceutical programming*, 1(1), pp.13-19.





# Independent Variables

- Single tablet regimen (vs Multiple tablet regimen)
- Patient characteristics
  - Age,
  - Gender
  - Chronic disease score
  - Opioid use
  - Polypharmacy ( $\geq$ Medications)
- Prescription fill characteristics
  - Index pharmacy type
  - Regimen type (INSTI-, NNRTI-, PI-based)
  - Payment method (Medicare Part D, Medicaid, Third party, Cash)
  - Copay per fill date (0\$, 1-10\$, >10\$)
  - Mail order pharmacy use
- US Census Bureau American Community Survey 2015
  - Predominant race/ethnicity
  - Low income community
  - Pharmacy access
- Linked by zip code of index pharmacy

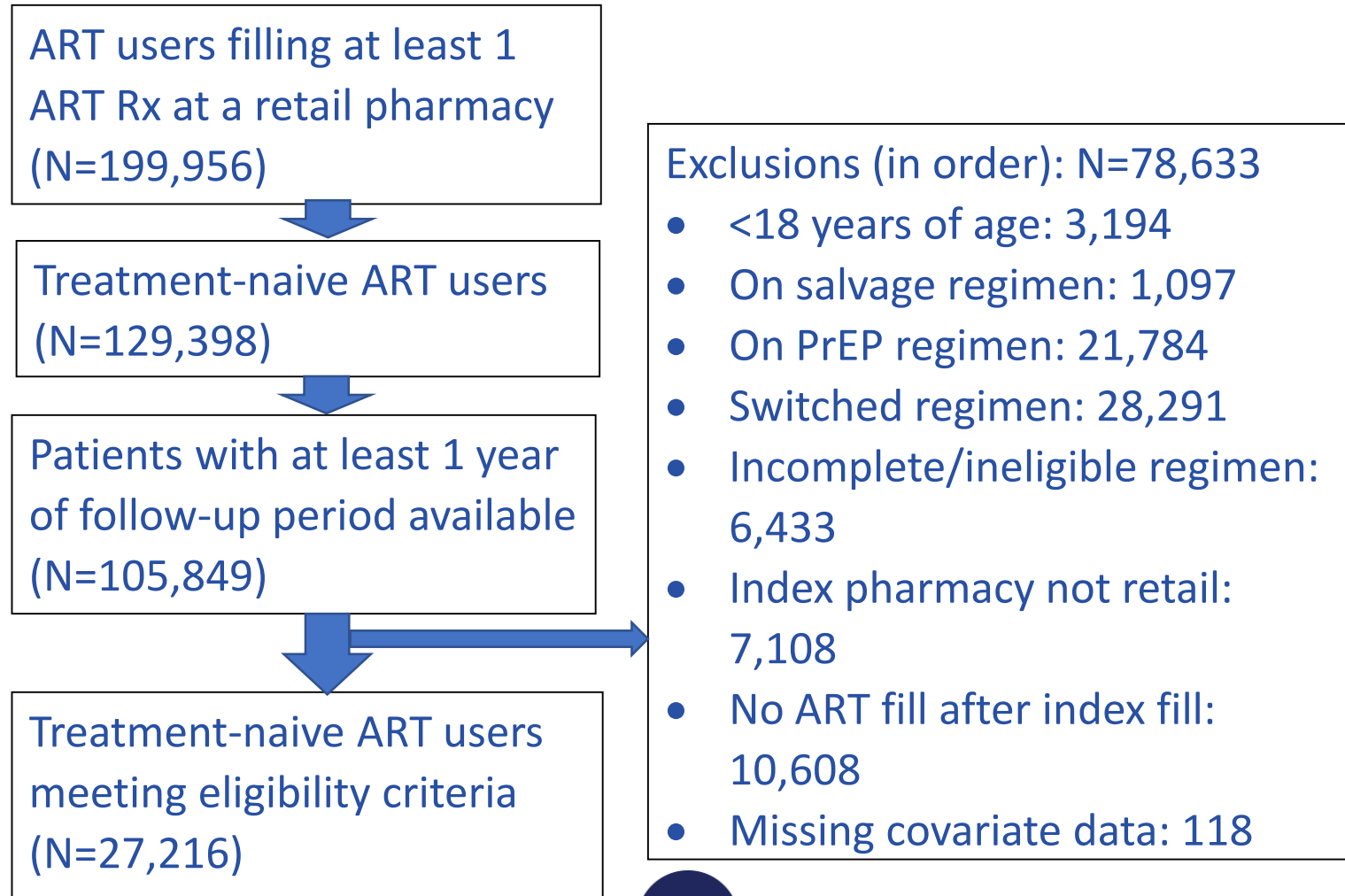


# Statistical Analyses

- Compared distribution of categorical variables between cohorts using chi-square test
- Compared distribution of continuous variables between cohorts using t test
- Poisson regression model with robust variance. Generalized estimating equations to account for clustering at index pharmacy level



# Cohort Derivation



# Cohort Characteristics

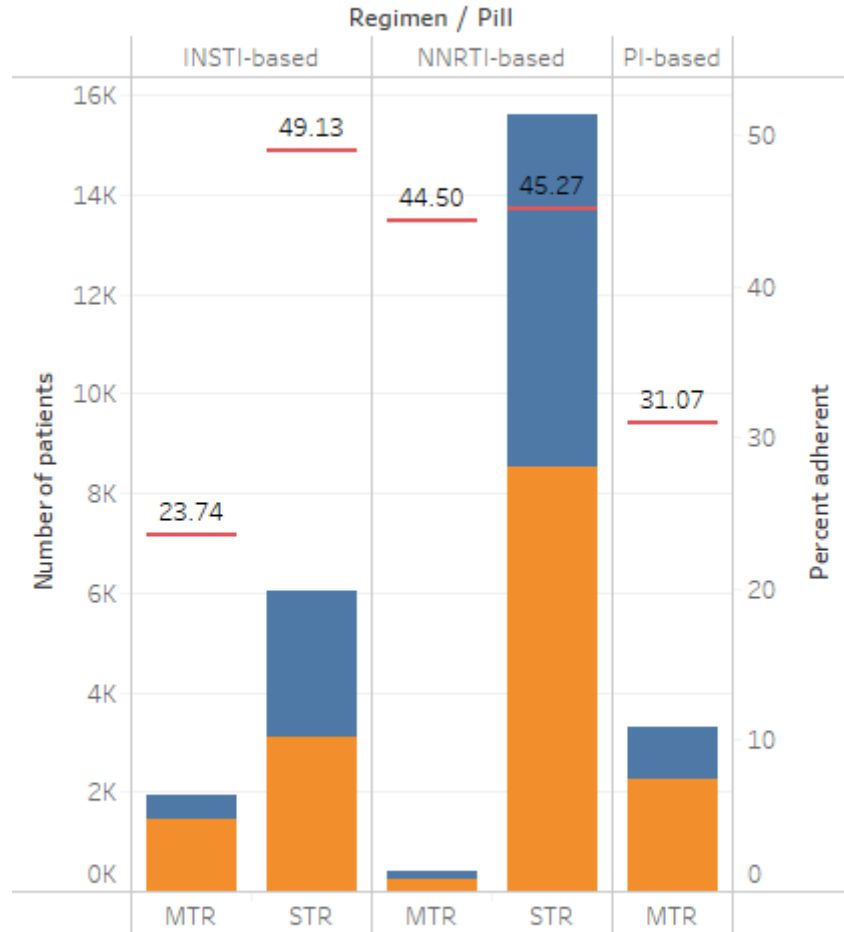
Variable	Overall	STR	MTR
	%	%	%
Age categories (years)			
18-30	24.6	26.2	18.5
31-40	23.5	23.8	22.2
41-50	28.2	27.5	30.8
51-64	20.8	19.7	25.2
64+ years	2.9	2.8	3.3
Gender			
Female	25.8	23.1	36.2
Male	74.1	76.8	63.6
Index pharmacy type			
Chain	59.5	62.9	46.3
Mass merchandizer	6.8	7.9	2.5
Food store	6.0	6.5	3.9
Independent	27.8	22.7	47.3
Used mail order			
Yes	17.5	19.0	11.4
No	82.6	81.0	88.6
Polypharmacy			
Yes	59.5	56.8	69.8
No	40.6	43.2	30.2
Used opioid			
Yes	30.8	30.7	31.1
No	69.2	69.3	68.9

Variable	Overall	STR	MTR
	%	%	%
Index payment type			
Cash	5.3	5.5	4.9
Medicaid	13.7	13.2	15.8
Medicare Part D	9.8	8.7	14.1
Third party	71.2	72.7	65.3
Copay per fill day			
0\$	51.9	51.4	53.8
1-10\$	18.6	17.6	22.5
>10\$	29.6	31.1	23.7
Predominant race/ethnicity			
White	54.4	54.5	54.2
Black	13.0	13.3	11.9
Hispanic	11.9	11.3	14.5
Diverse	20.1	20.5	18.7
Other	0.5	0.5	0.8
Low income community			
Yes	42.9	42.2	45.6
No	57.1	57.8	54.4
Pharmacy access (per 10,000 population)			
<1.75 pharmacies	33.1	33.9	30.2
1.75-2.95 pharmacies	34.1	35.1	30.3
>2.95 pharmacies	32.8	31.0	39.5



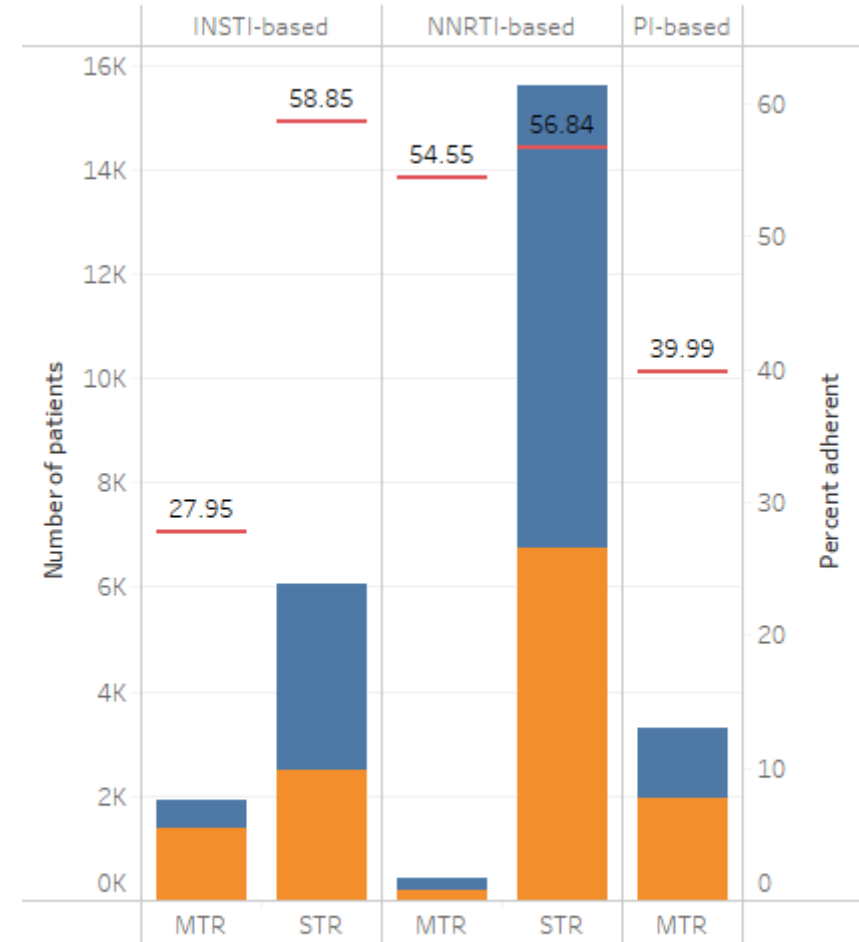
# Adherence by Regimen Type: STR vs MTR

Adherence (>90% PDC) by regimen type



**Measure Names**  
 ■ Number adherent  
 ■ Number not adherent  
 ■ Percent adherent

Adherence (>80% PDC) by regimen type

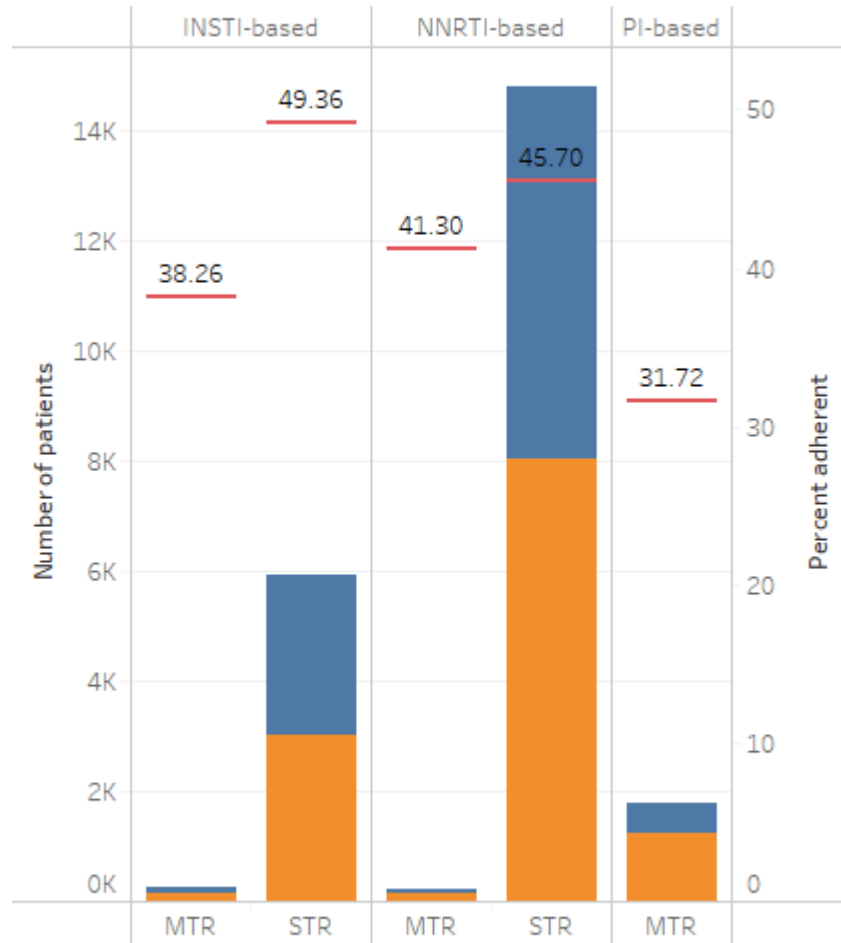


**Measure Names**  
 ■ Number adherent  
 ■ Number not adherent  
 ■ Percent adherent



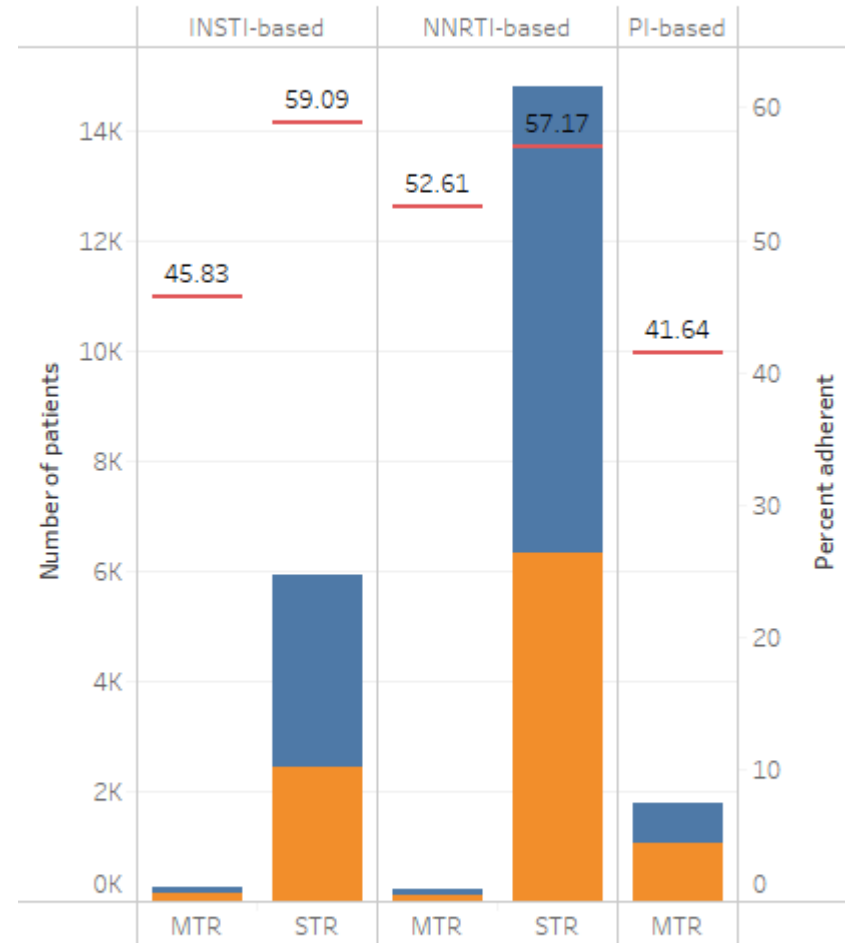
# Adherence by Regimen Type: STR vs MTR (Once Daily)

Adherence (>90% PDC) by regimen type (once daily)



**Measure Names**  
 ■ Number adherent  
 ■ Number not adherent  
 ■ Percent adherent

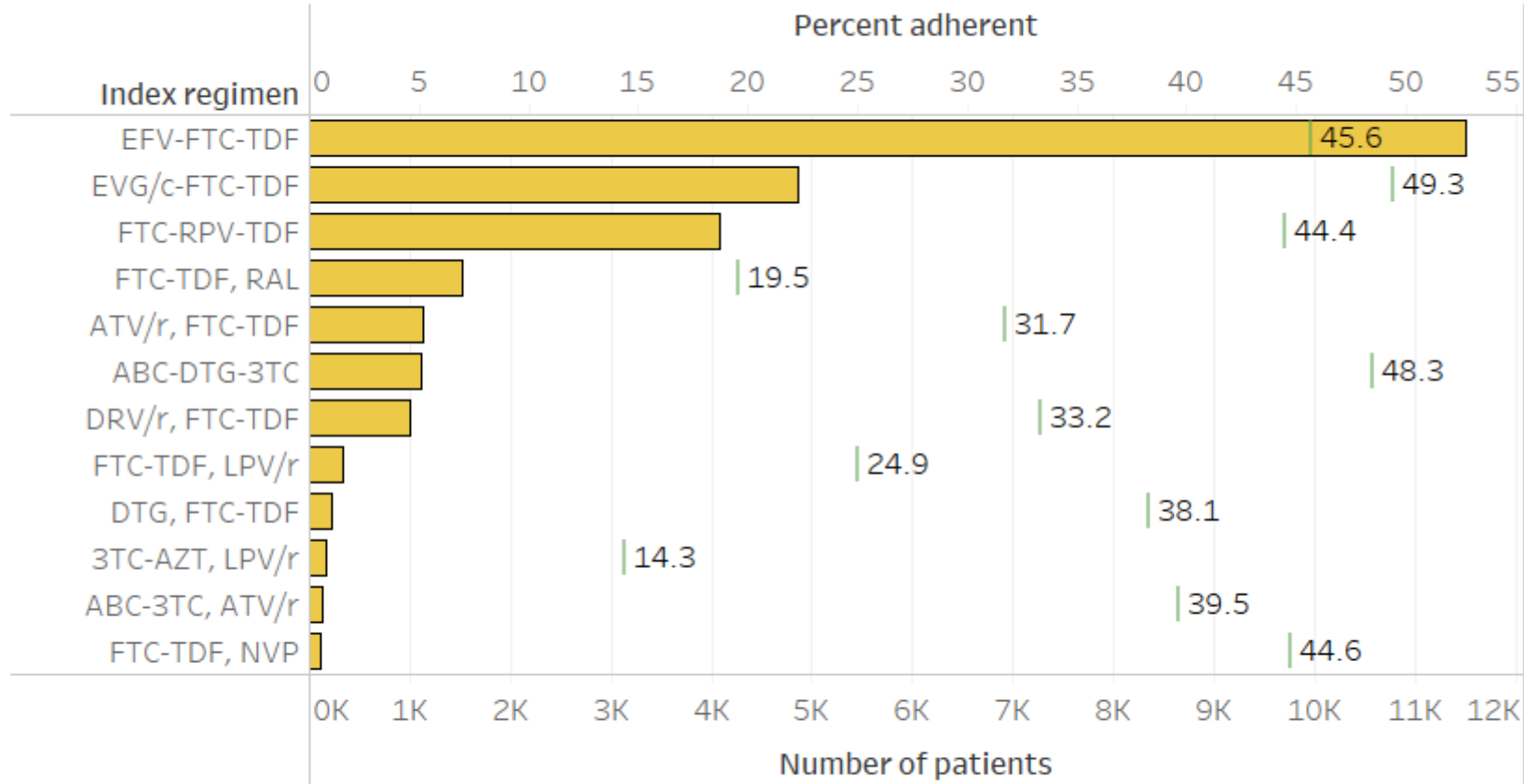
Adherence (>80% PDC) by regimen type (once daily)



**Measure Names**  
 ■ Number adherent  
 ■ Number not adherent  
 ■ Percent adherent



# Adherence by Index Regimen



## Measure Names

- Percent adherent
- Total



# Association between Number of Pills (STR vs MTR) and Adherence, Overall and by Regimen Type

	STR (n=21,603)	MTR (n=5,613)	Unadjusted RR (95% CI)	Adjusted RR* (95% CI)
<b>&gt;90% Adherence</b>	% Adherent	% Adherent		
Overall	46.4	29.6	1.57 (1.50-1.64)	1.76 (1.63-1.90)
INSTI-based	49.1	23.7	2.07 (1.91-2.26)	2.01 (1.76-2.30)
NNRTI-based	45.3	44.6	1.02 (0.91-1.13)	1.06 (0.93-1.21)
<b>&gt;80% Adherence</b>				
Overall	57.4	37.0	1.82 (1.69-1.96)	1.76 (1.63-1.90)
INSTI-based	58.8	27.9	2.11 (1.96-2.27)	2.16 (1.92-2.42)
NNRTI-based	56.9	54.7	1.04 (0.95-1.14)	1.15 (1.03-1.28)

\*Adjusted for age, gender, index pharmacy type, use of mail order, polypharmacy, opioid use, chronic disease score, payment type, copay, predominant race/ethnicity in the community, low income community, pharmacy access





# Sensitivity Analysis – Alternative Definition for Treatment-naive Patient ( $\geq 2$ years of no ART fill)

Association between number of pills (STR vs MTR) and adherence ( $>90\%$  PDC) to ART, overall and by regimen type (n=17,526)

	STR (N=13,904) % Adherent	MTR (N=3,622) % Adherent	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
<b>Overall</b>	47.4	28.8	1.65 (1.56-1.74)	2.07 (1.85-2.30)
<b>Regimen type</b>				
INSTI based regimen	49.1	20.0	2.46 (2.21-2.73)	2.38 (2.04-2.77)
NNRTI based regimen	46.2	49.6	0.93 (0.82-1.06)	0.94 (0.80-1.10)

\*Adjusted for age, gender, index pharmacy type, use of mail order, polypharmacy, opioid use, chronic disease score, payment type, copay, predominant race/ethnicity in the community, low income community, pharmacy access



# Discussion

- Adherence is low overall (STR: 46.4%, MTR: 29.6%)
  - This national data are consistent with the study among 2,174 on Medicaid in South Carolina (STR: 35%, MTR: 22%)\*
- Treatment-naive patients on single tablet regimen had higher adherence compared to those on multiple tablet regimens
- Effect of single tablet regimen on adherence was greater among patients on INSTI-based regimen
- Effect of single tablet regimen on adherence was reduced when analyses were restricted among once daily regimens
- More research/interventions should target treatment-naive patients
- Additional analyses are planned to examine the role of pill size on adherence

\*Scott Sutton, S., Joseph Magagnoli, and James W. Hardin. "Impact of pill burden on adherence, risk of hospitalization, and viral suppression in patients with HIV infection and AIDS receiving antiretroviral therapy." *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 36, no. 4 (2016): 385-401.



# Limitations

- Residual confounding – not adjusted for clinical data, substance abuse, self-efficacy, depression
- No data on side effects/tolerability
- Prescription fill does not guarantee medication intake
- Definition of treatment-naive based on available prescription fill record
  - Results persisted in sensitivity analyses



# QUESTIONS

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