

Objectives

- To evaluate presence of InSTI-associated weight gain in a diverse, urban HIV population using a retrospective cohort design
- To identify risk factors and metabolic implications associated with InSTI-associated weight gain

Introduction

- Integrase strand transfer inhibitors (InSTI) are guideline recommended first line antiretroviral therapy.
- Accumulating data associates excessive weight gain with InSTIs use.
- Identified risk factors include female sex and black race.
- Metabolic implications of InSTI-associated weight gain have yet to be described.
- Such insights are critical to understand the consequences and mechanisms of InSTI-associated weight gain and inform guideline recommendations on ART switch

Methods

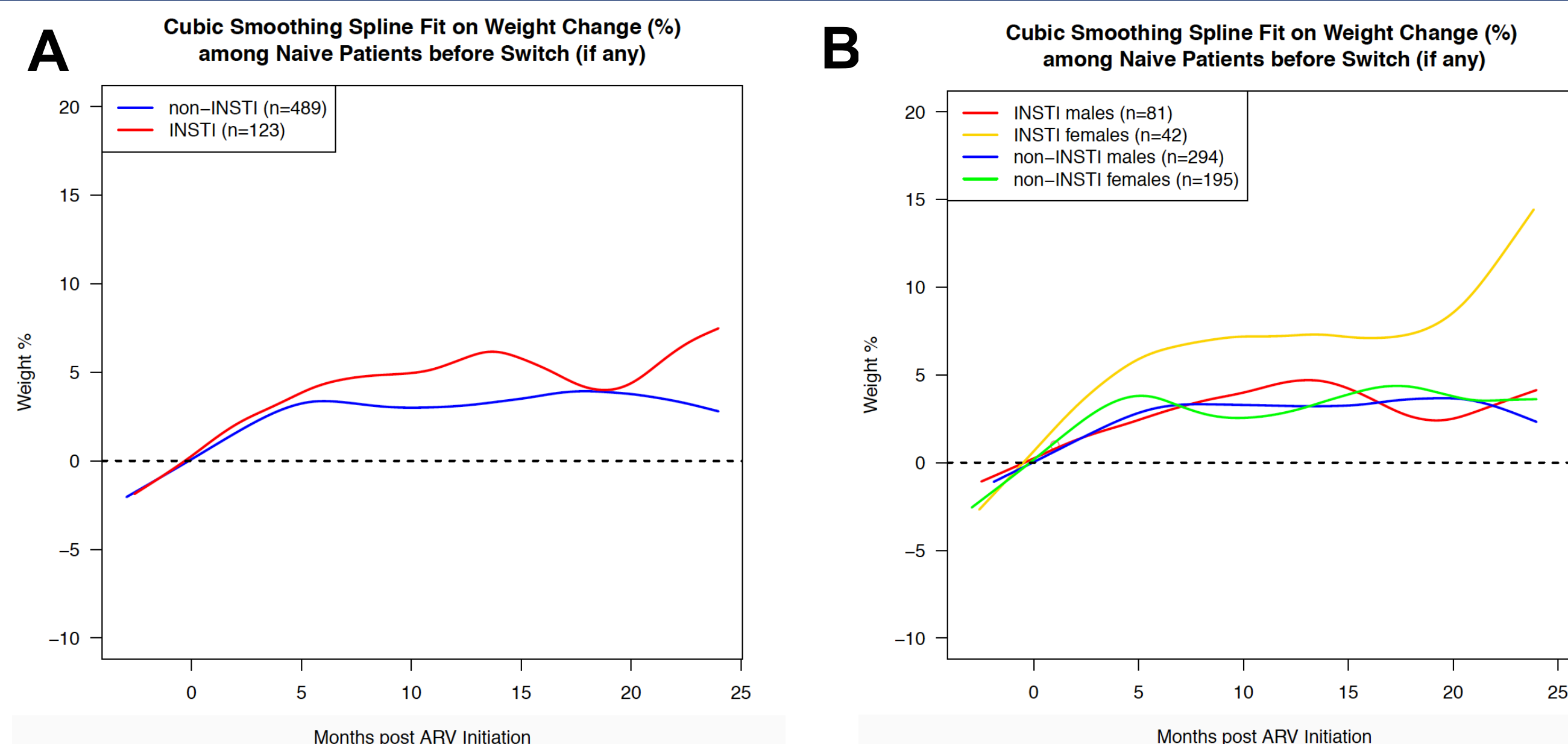
- Demographic, pharmacy, billing and laboratory data from hospital clinical data warehouse was obtained for ART-naïve HIV patients seen at Boston Medical Center between FY 2007-2017.
- Patients initiated and remained on an InSTI for at least 18 months were compared to those on an alternate regimen
- The primary outcome was percentage weight change from baseline in the first 24 months of ART estimated by linear mixed effects model fit by restricted maximum likelihood
- The secondary outcome was incident diabetes mellitus diagnosis in the first 18 months post-ART initiation using progression free-survival (PFS)
- For secondary outcome, PFS rates were estimated by the Kaplan-Meier method and difference between groups was determined using the log-rank test, and Cox proportional hazards model all using R v.3.6.2.

1. Cohort baseline characteristics of ART-naïve patients

	Total (N=612)	Median (IQR / %)		P-value ¹
		non-INSTIs (N=489)	INSTIs (N=123)	
Age	41.56 (32.8-49.7)	41.79 (33.0-49.5)	39.23 (32.3-51.1)	0.7
Sex: Female	237 (38.7%)	195 (39.9%)	42 (34.1%)	0.3
Race: White	119 (19.4%)	90 (18.4%)	29 (23.6%)	
Race: Black/African American	339 (55.4%)	276 (56.4%)	63 (51.2%)	0.6
Race: Asian	10 (1.6%)	8 (1.6%)	2 (1.6%)	
Ethnicity: Hispanic or Latino	121 (19.7%)	99 (20.1%)	22 (17.9%)	0.7
Year of ARV initiation	2011 (2009-2013)	2010 (2009-2012)	2015 (2014-2016)	<0.001
INSTI agent at ARV initiation				
Raltegravir			30 (24.4%)	
Dolutegravir			78 (63.4%)	
Elvitegravir			15 (12.2%)	
Weight (lbs)	164.95 (143.7-186)	165 (145-185.8)	164.02 (141-187.4)	0.7
BMI	25.55 (22.9-28.9)	25.57 (23.0-29.0)	25.54 (22.7-28.6)	0.8
HbA1C (%)	5.65 (5.5-6.1)	5.8 (5.5-6.2)	5.35 (5.1-5.6)	0.1
HIV Viral Load (copies/mL)	0 (0-4300.8)	0 (0-1629)	185 (0-19771)	0.4
CD4 Count (cells/mL)	352 (179-523)	354 (210-516.5)	337 (33-580)	0.7

¹P-value for continuous variables were obtained using two-sample Student t-test; p-value for categorical variable obtained using two-sided Fisher's exact test

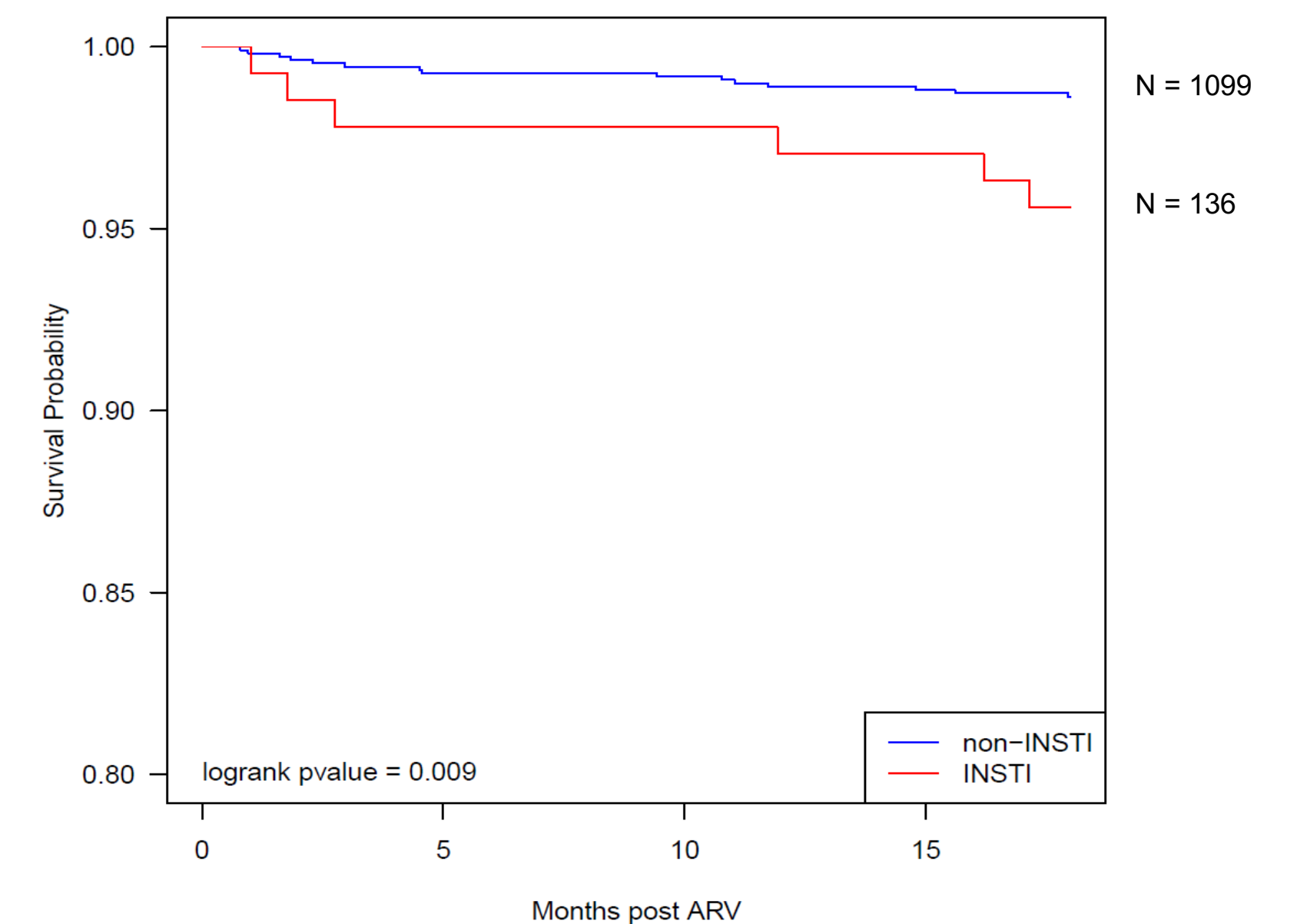
2. Percent weight gain in first 24-months post-ART initiation by ART type alone (A) and by gender (B)



3. Adjusted multivariable analysis of 24-month weight gain due to InSTIs

Cohort Characteristic	Weight Gain (%)	95% Confidence Interval	*INSTI effect after adjusting ARV initiation year, age at baseline, ethnicity, NRTI, CD4 and viral load at baseline.
Males			
White	1.68	-3.88, 7.24	
Non-white	2.08	-2.52, 6.68	
Females			
White	10.62	2.83, 18.41	
Non-white	11.02	5.17, 16.88	

4. Incidence of Diabetes Diagnosis (ICD code) by type of ART in first 18 months post-initiation



HR = 3.29, p=0.014

Conclusions

- Females demonstrate higher InSTI-associated weight gain, suggesting gender differences in susceptibility to weight effects
- InSTI use is also associated with greater incident diabetes diagnoses following initiation in ART-naïve patients
- Further studies are needed to explore the risk of other metabolic comorbidities associated with InSTI weight gain, as well as risk mitigation and management strategies