

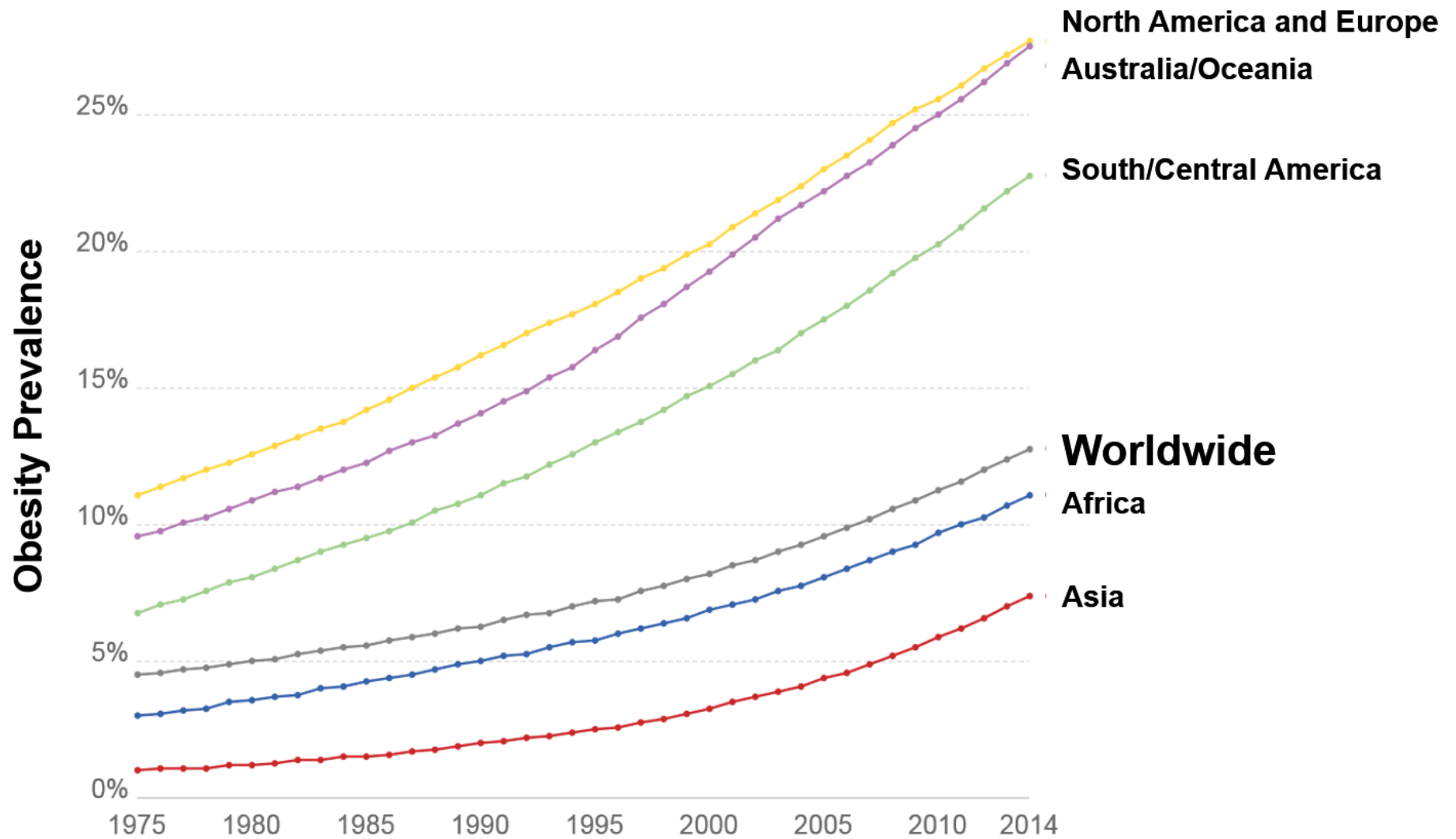


Weight Gain with Antiretroviral Therapy

Kassem Bourgi, MD

Assistant Professor of Medicine

Indiana University, Indianapolis

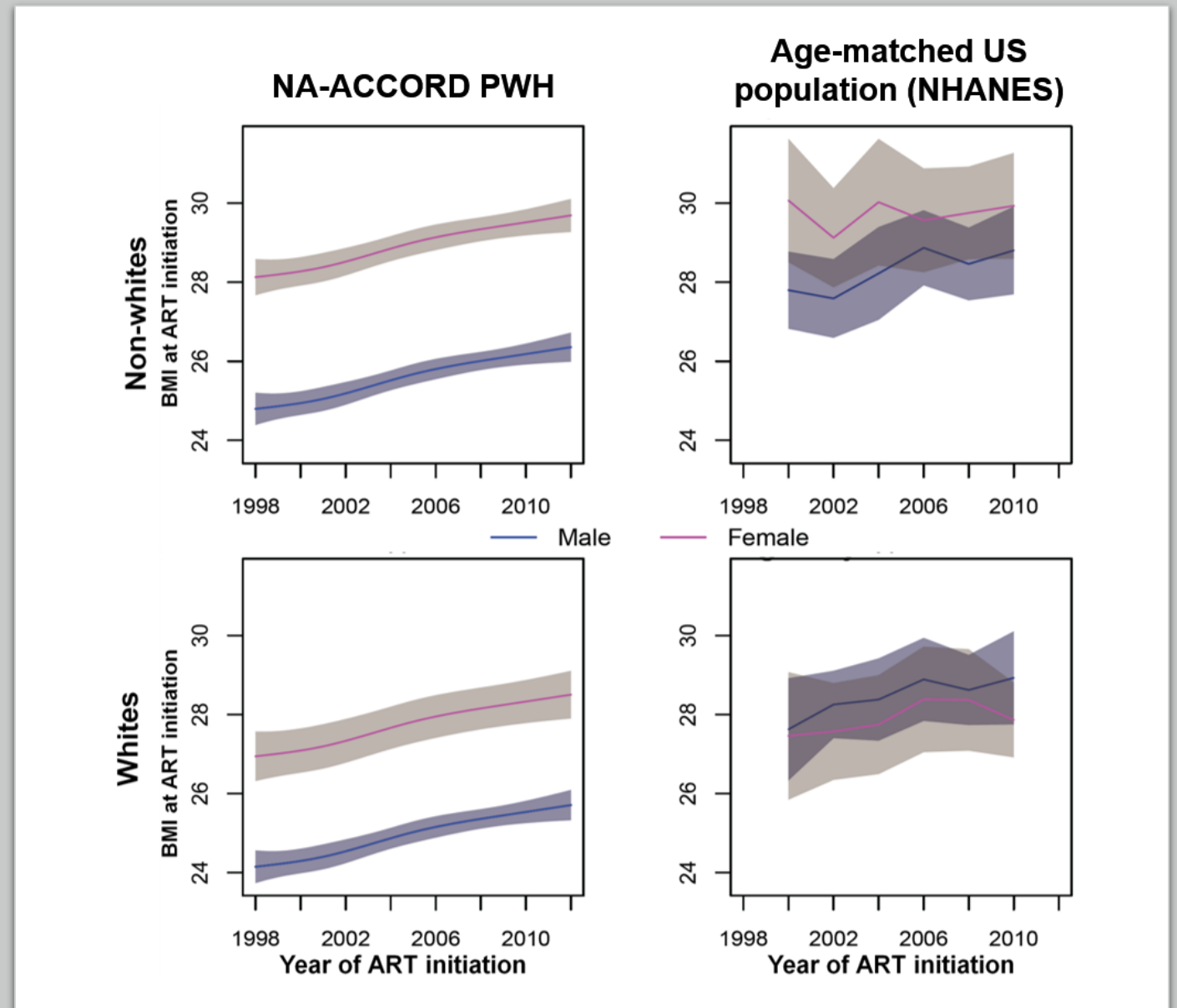


Worldwide Prevalence of Obesity

Source: WHO Fact Sheets 2018 & UN Food and Agricultural Organization

Rising Obesity Among Persons with HIV (PWH)

- BMI at ART initiation in 14,000 patients from 1998-2010
- **NA-ACCORD:** North American AIDS Cohort Collaboration on Research and Design
- **NHANES:** National Health and Nutrition Education Survey



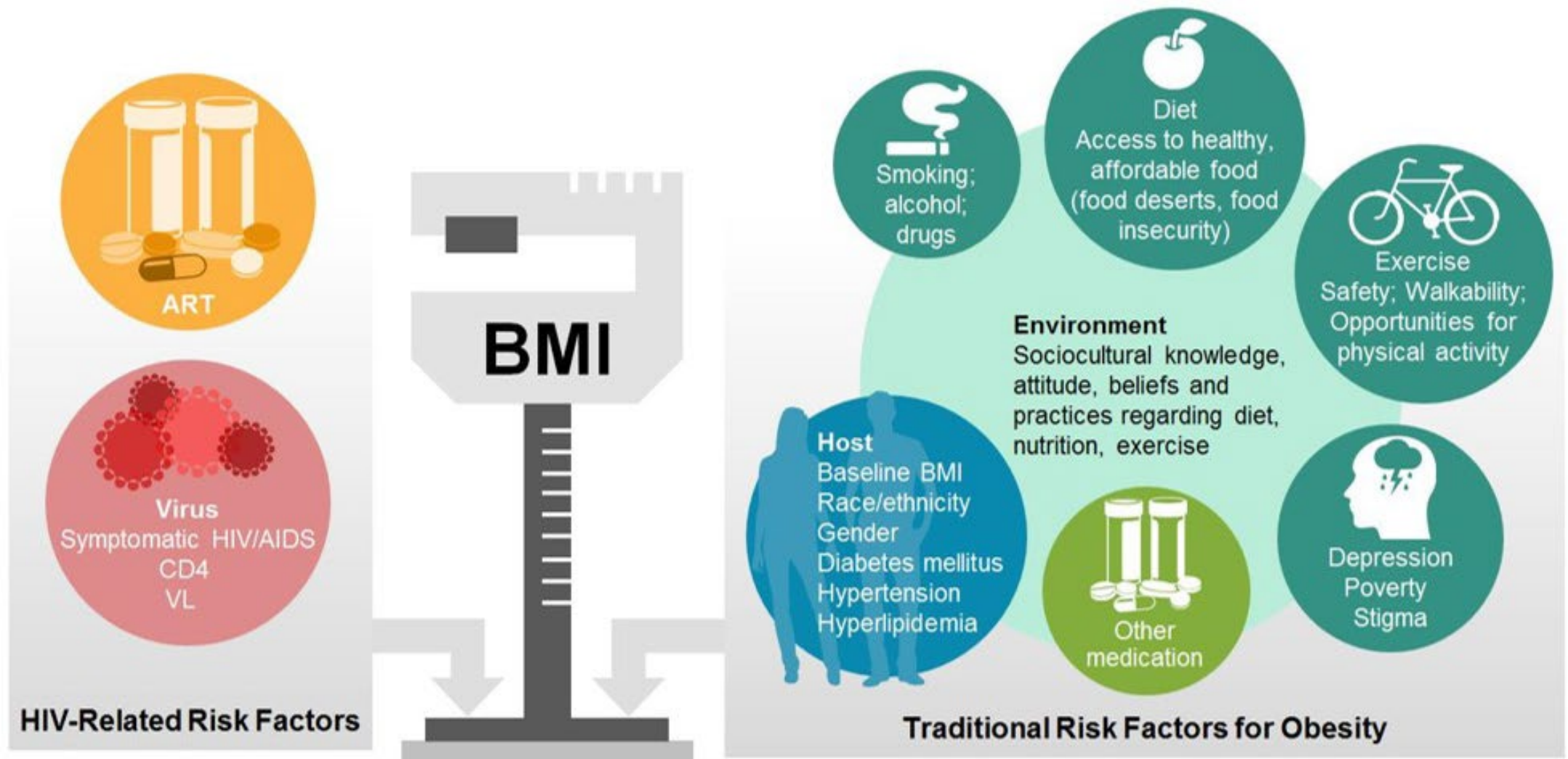
Weight Gain after Starting ART

>80% of total 3-year weight gain occurred in first 12 months

Greatest among white men and non-white women

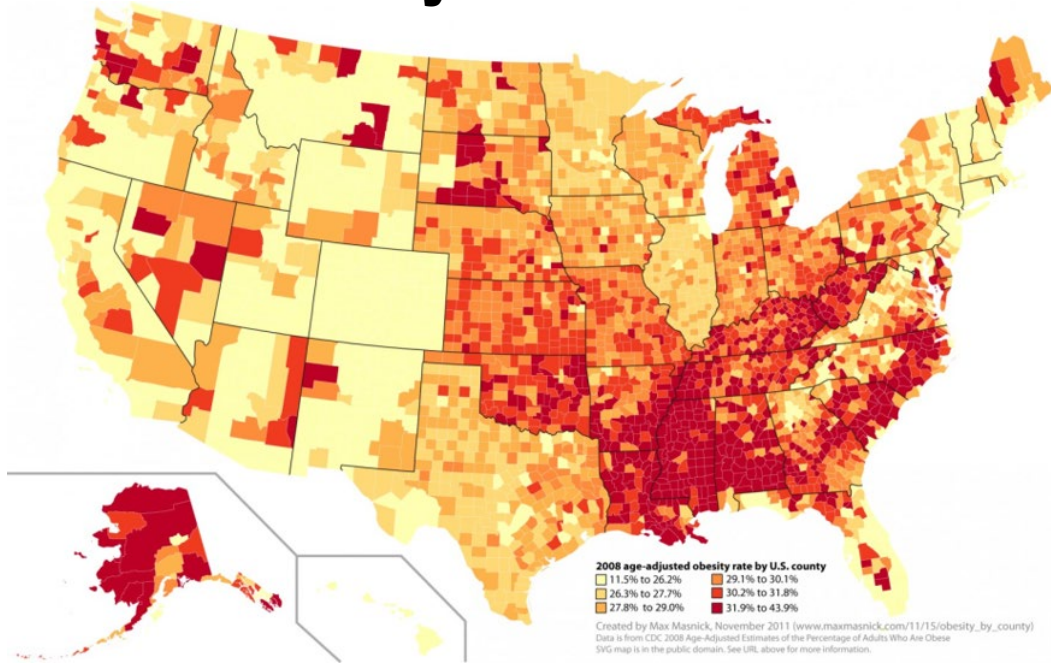
In the first 3 years of ART:

- One-quarter of patients with a normal BMI became overweight
- One-fifth of those previously overweight became obese

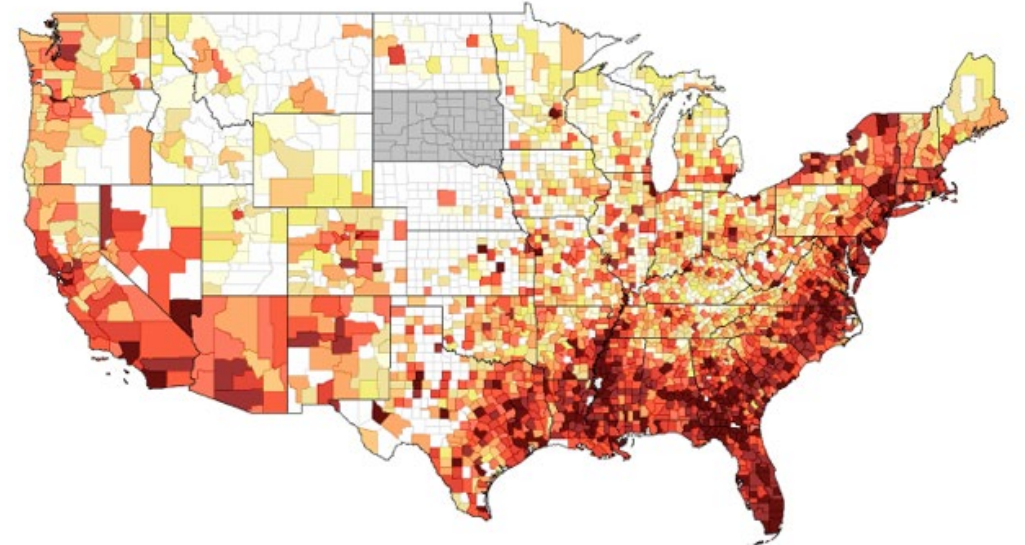


Risk Factors for Weight Gain Among PWH

Obesity Prevalence



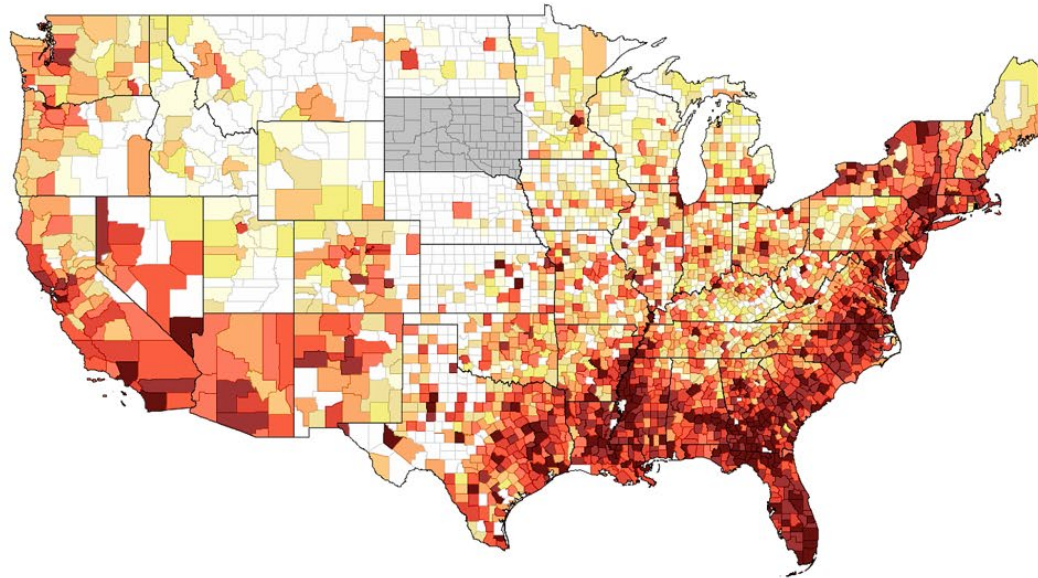
HIV Prevalence



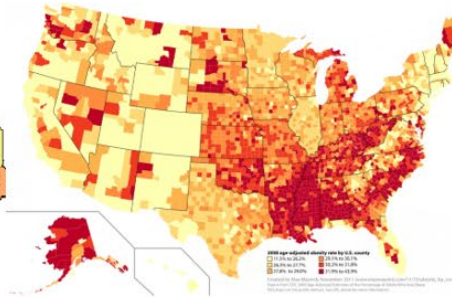
Overlapping HIV and Obesity Epidemics

Overlapping Epidemics

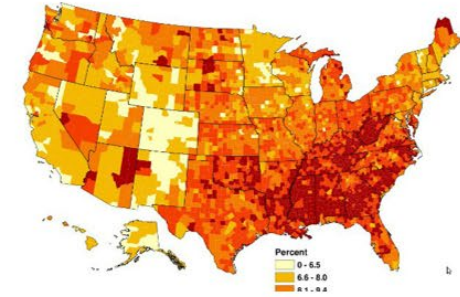
HIV prevalence



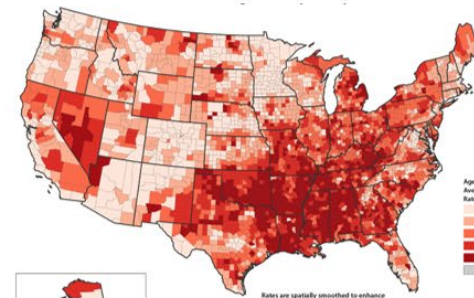
Obesity prevalence



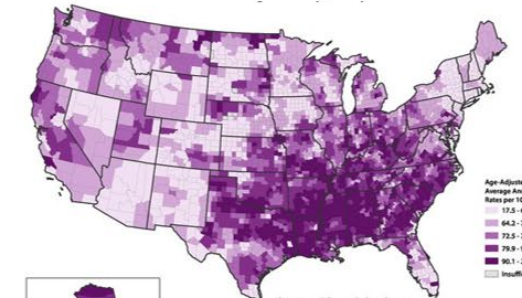
Diabetes prevalence



Heart Disease Deaths



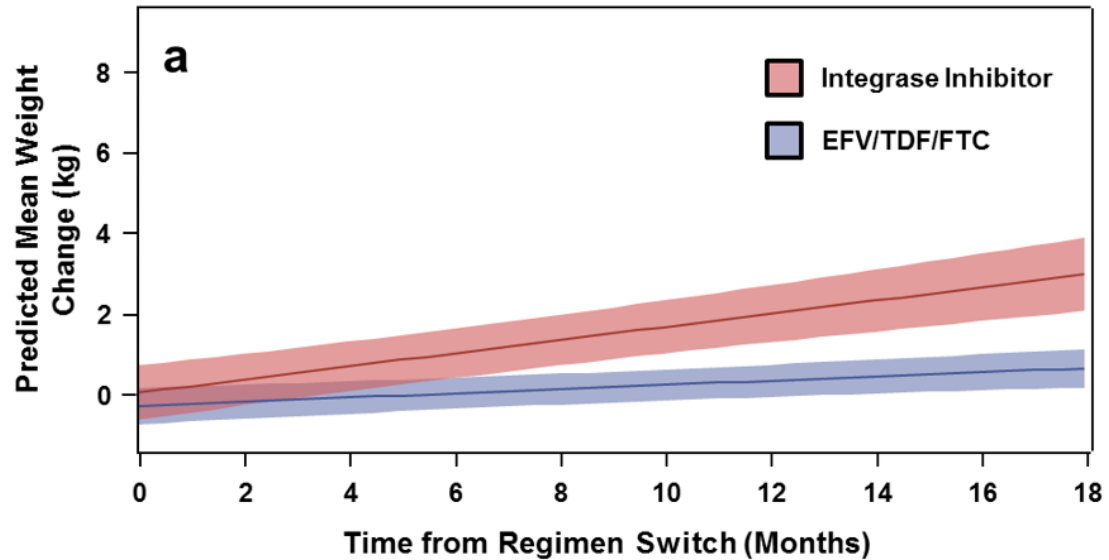
Stroke Deaths



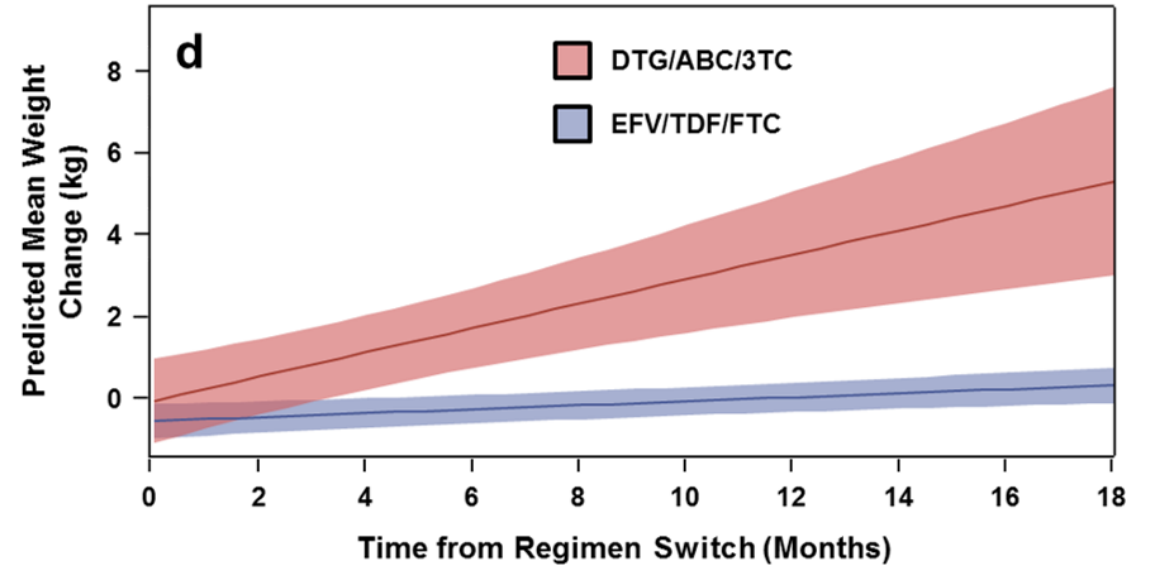
2

**Early Reports of
Increased Weight Gain
with INSTI**

Integrase inhibitor regimens versus EFV/TDF/FTC



DTG/ABC/3TC versus EFV/TDF/FTC



Weight gain in PWH switched from Efavirenz to INSTI-based regimens

- Retrospective, single-site study (n=495)
- Adults on EFV/TDF/FTC with viral suppression for 2 years switched to an INSTI vs. continued on EFV/TDF/FTC
- Weight gain highest among those switching to Dolutegravir with ABC/3TC

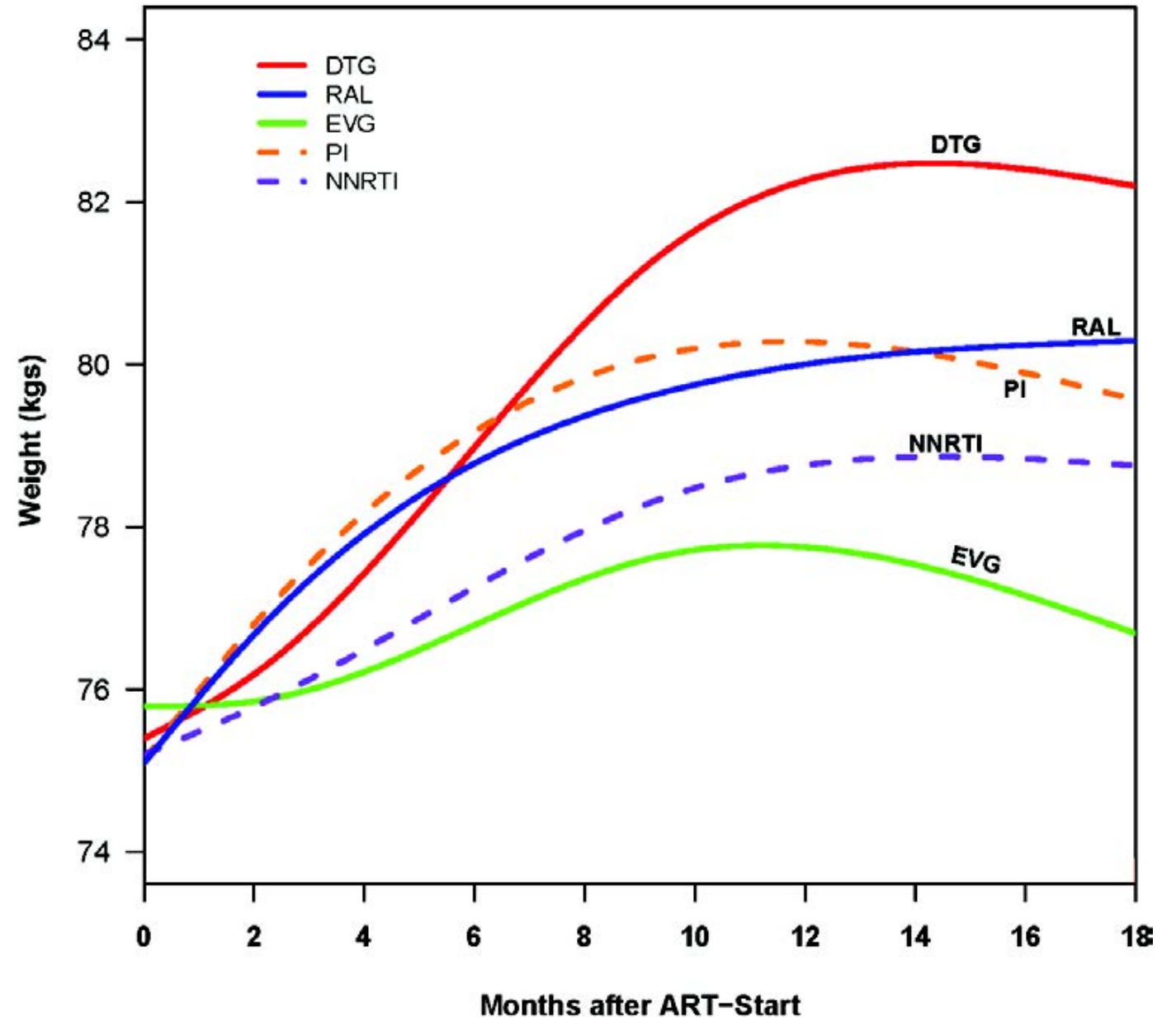
3

**Weight Gain by ART
Regimen**

VUMC Cohort

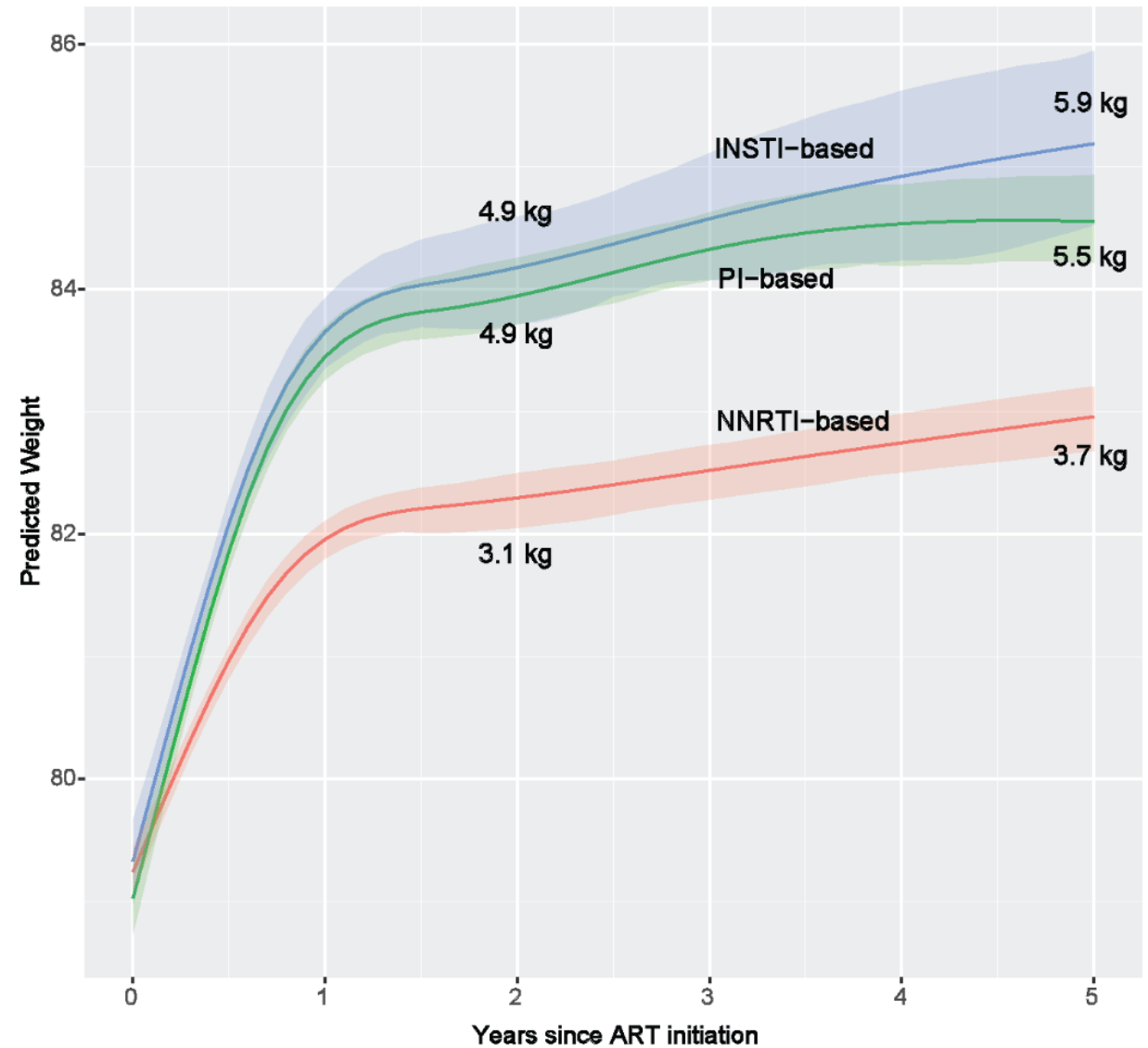
*1,152 ART-naive
PWH*

DTG +6.0 kg
PI +4.1 kg
RAL +3.4 kg
NNRTI +2.6 kg
EVG +0.5 kg



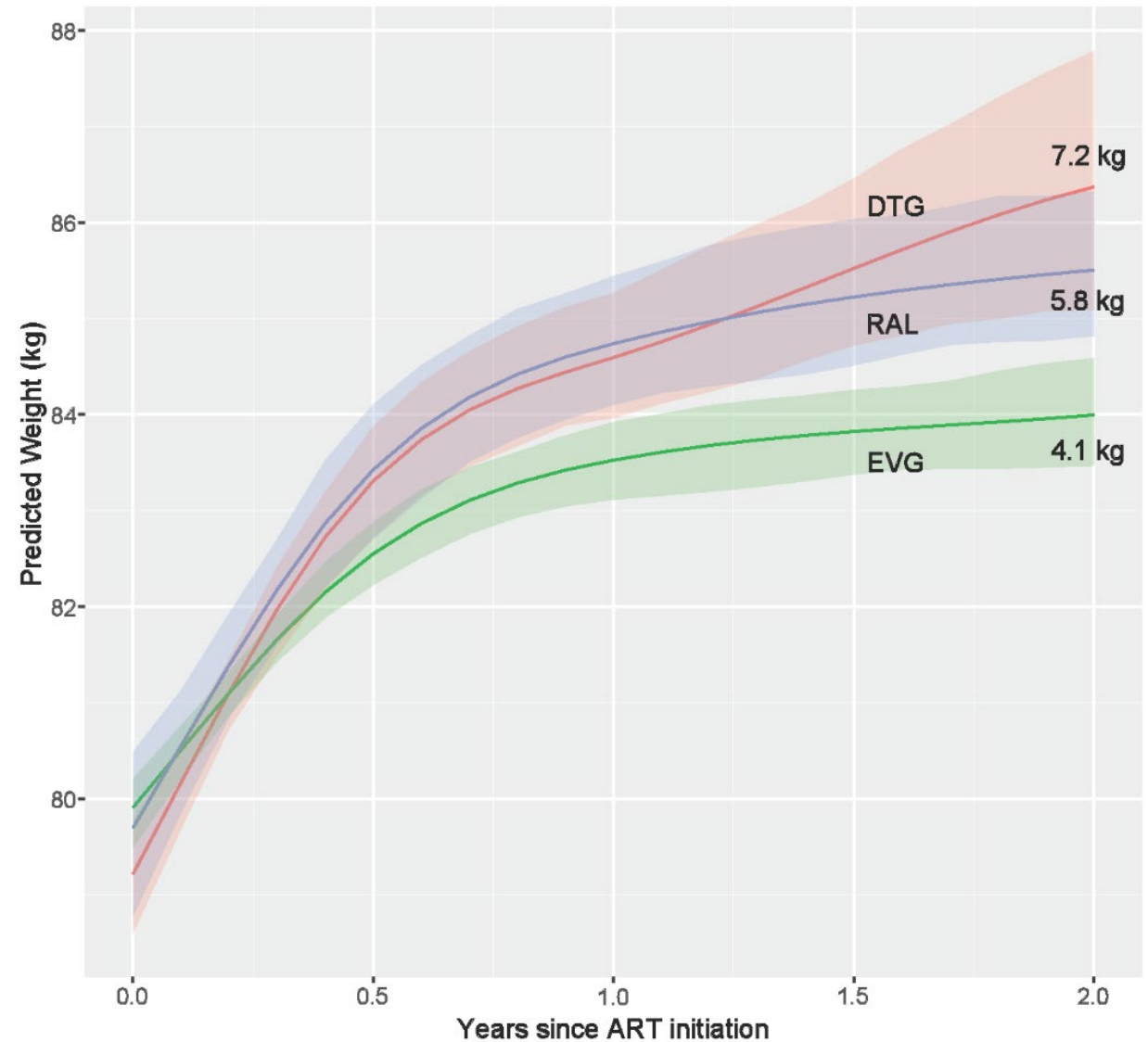
NA-ACCORD Cohort

22,972 patients starting ART from 2007-2016 in the US and Canada

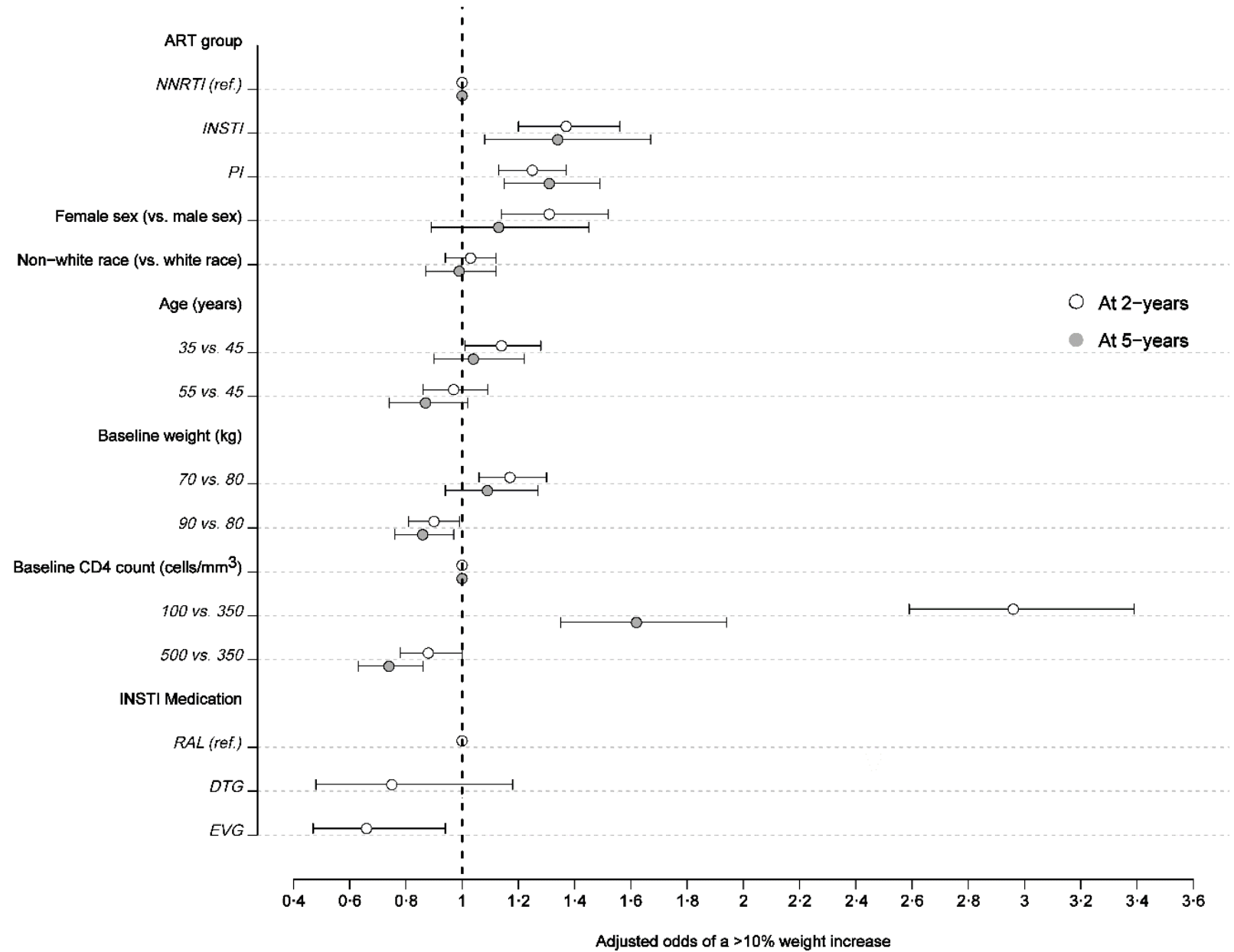


NA-ACCORD Cohort

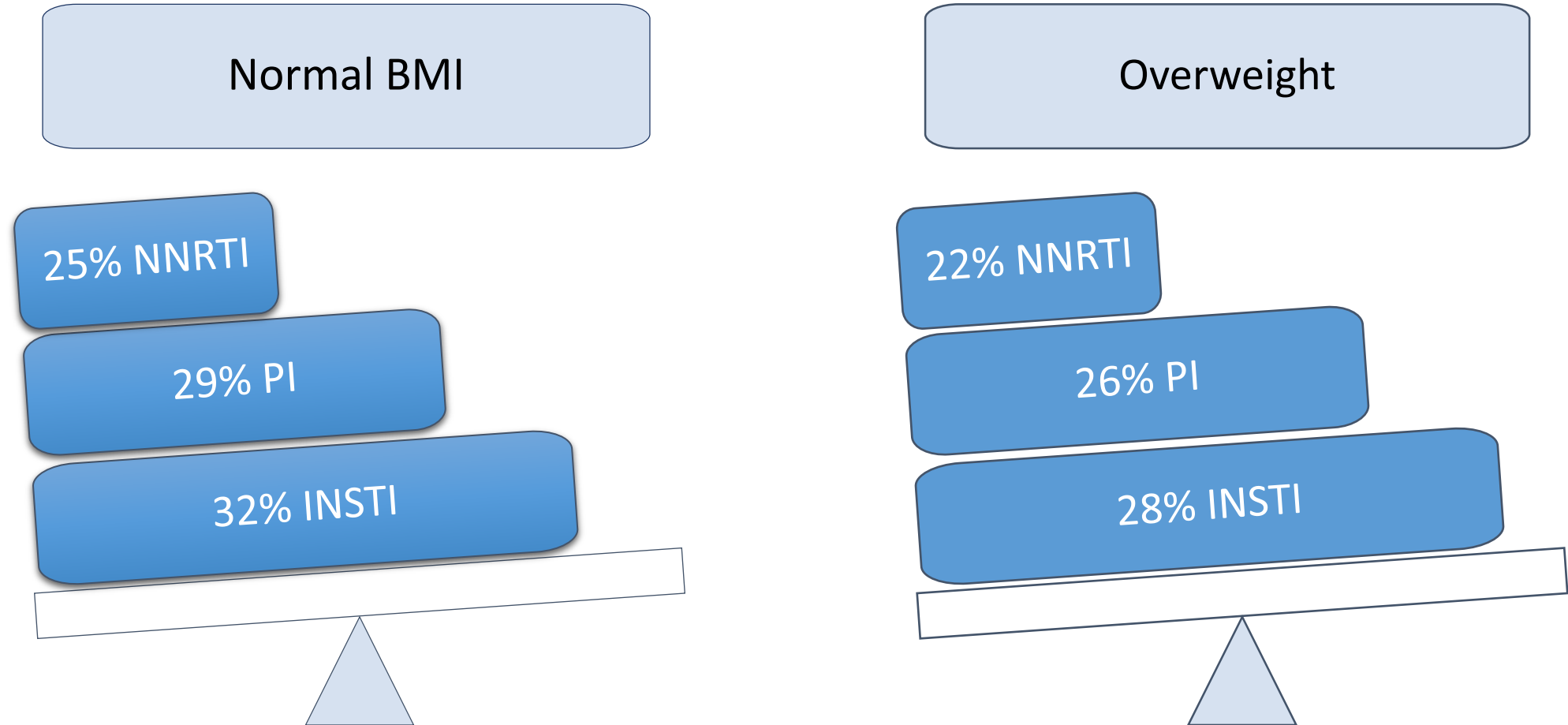
*4,190 patients
starting INSTI drugs
from 2007-2016 in
the US and Canada*



Odds of excessive Weight Gain



Progression to Obesity



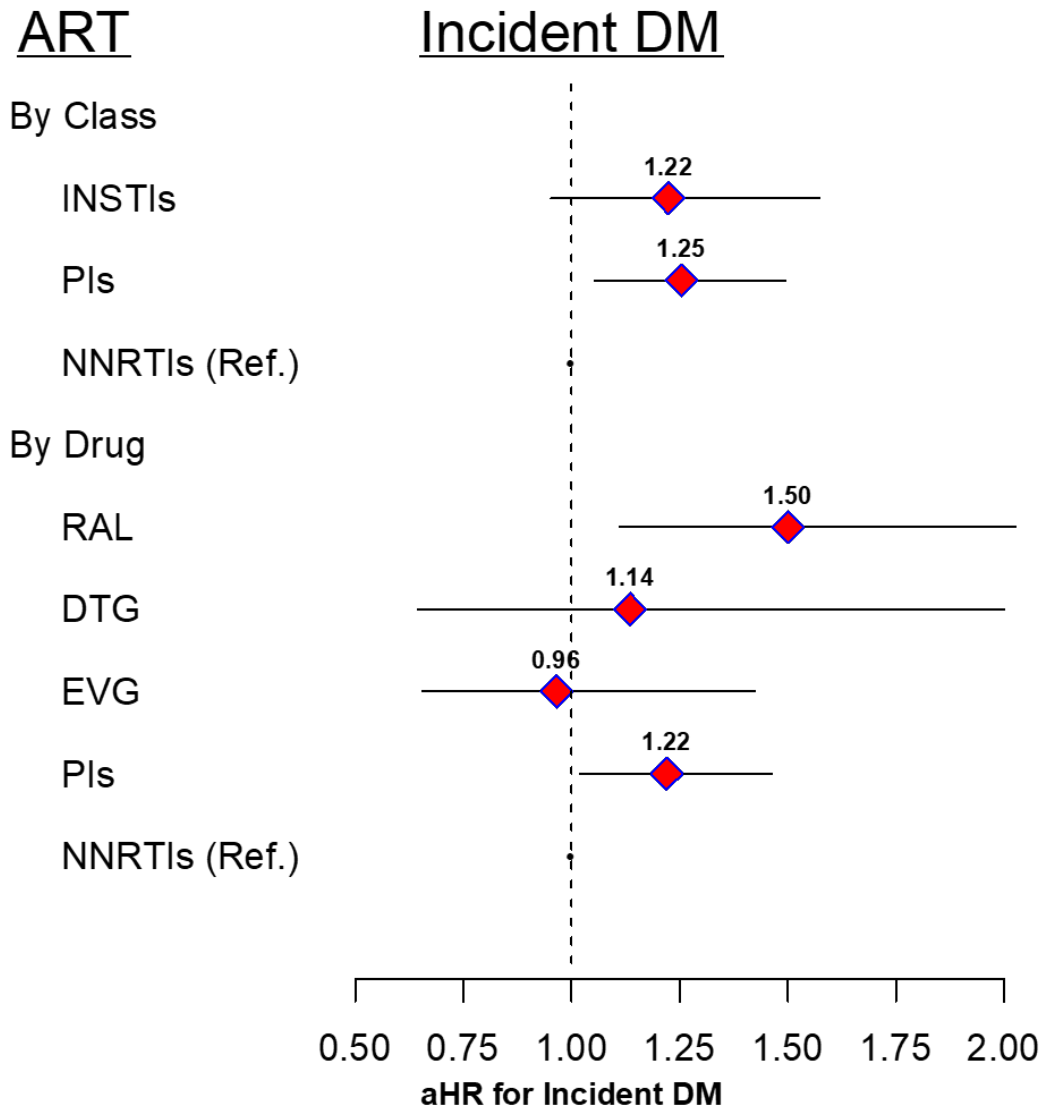
Group	Females		Males		Non-white		White		Age <50		Age ≥50	
	NNRTI	PI	NNRTI	PI	NNRTI	PI	NNRTI	PI	NNRTI	PI	NNRTI	PI
Pre-switch regimen												
Weight over time slope before switch (95% CI)*	0.14 (-0.68 to 0.95)	0.94 (0.42 to 1.46)	0.72 (0.40 to 1.03)	0.77 (0.51 to 1.03)	0.76 (0.30 to 1.22)	1.04 (0.69 to 1.39)	0.60 (0.23 to 0.98)	0.61 (0.31 to 0.92)	0.97 (0.57 to 1.37)	0.87 (0.54 to 1.19)	0.21 (-0.22 to 0.65)	0.70 (0.37 to 1.04)
Change in slope after switch to INSTI (95% CI)	+1.44 (0.78 to 2.11)	-0.45 (-0.92 to 0.03)	+0.32 (0.02 to 0.61)	-0.47 (-0.69 to -0.24)	+1.27 (0.87 to 1.68)	-0.60 (-0.91 to -0.29)	-0.11 (-0.47 to 0.25)	-0.36 (-0.63 to -0.08)	-0.08 (-0.44 to 0.29)	-0.24 (-0.54 to 0.07)	+1.17 (0.78 to 1.57)	-0.66 (-0.94 to -0.38)
p-value for slope change	<0.001	0.07	0.04	<0.001	<0.001	<0.001	0.54	0.01	0.69	0.13	<0.001	<0.001

Greater Weight Gain
After Switch to an INSTI
from NNRTIs vs. PIs in
NA-ACCORD

877 adults with >2 years of consistent viral suppression prior to and following the switch from an NNRTI or PI to an INSTI-based regimen

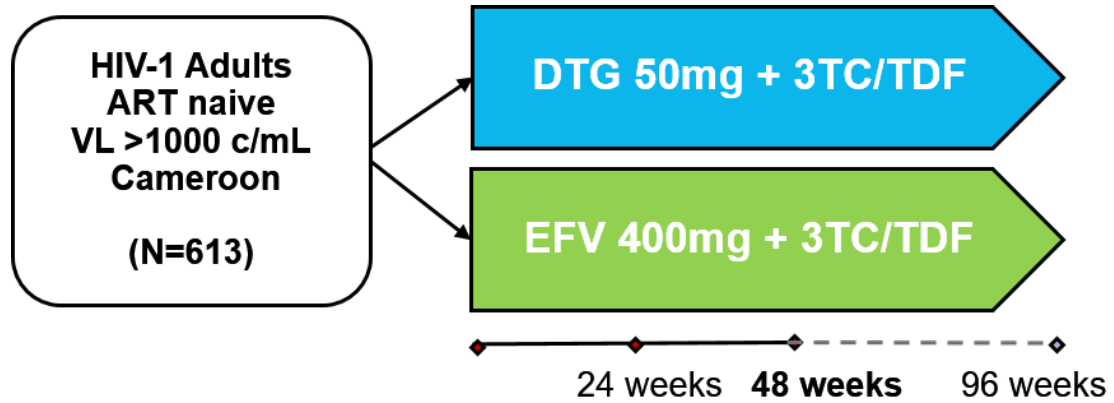
Risk of incident diabetes mellitus after initiation of ART

- 21,516 PWH starting ART in NA-ACCORD



4

Data from Clinical Trials

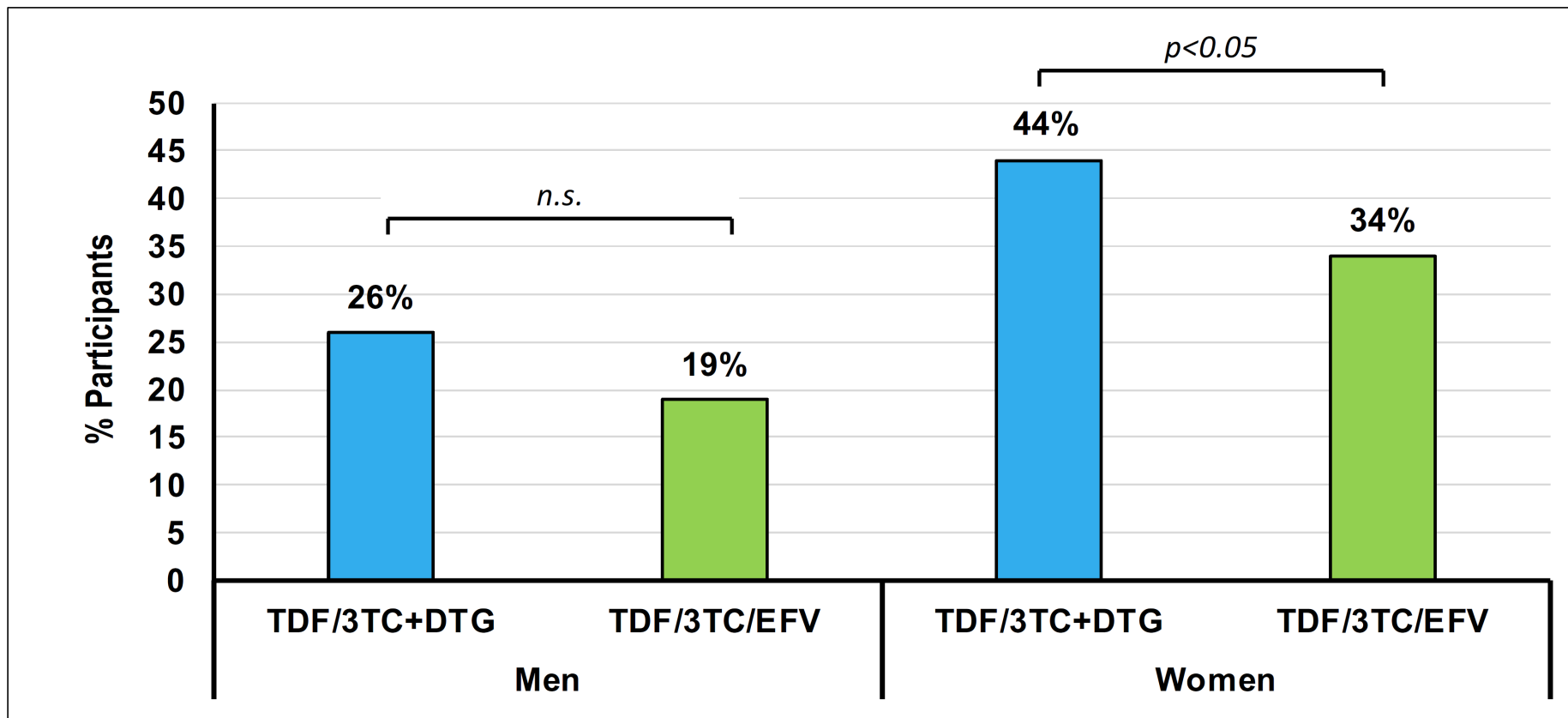


Week 48	TDF/3TC+DTG (n=293)	TDF/3TC+EFV400 (n=278)	p-value for difference
Mean change from baseline:			
Weight (kg)	+5	+3	<0.001
BMI (kg/m ²)	+1.7	+1.2	<0.001
Treatment-emergent overweight (BMI 25 - 29.9), n (%)	16%	17%	n.s.
Treatment-emergent obesity (BMI ≥ 30), n (%)	12%	5%	<0.01

NAMSAL Study

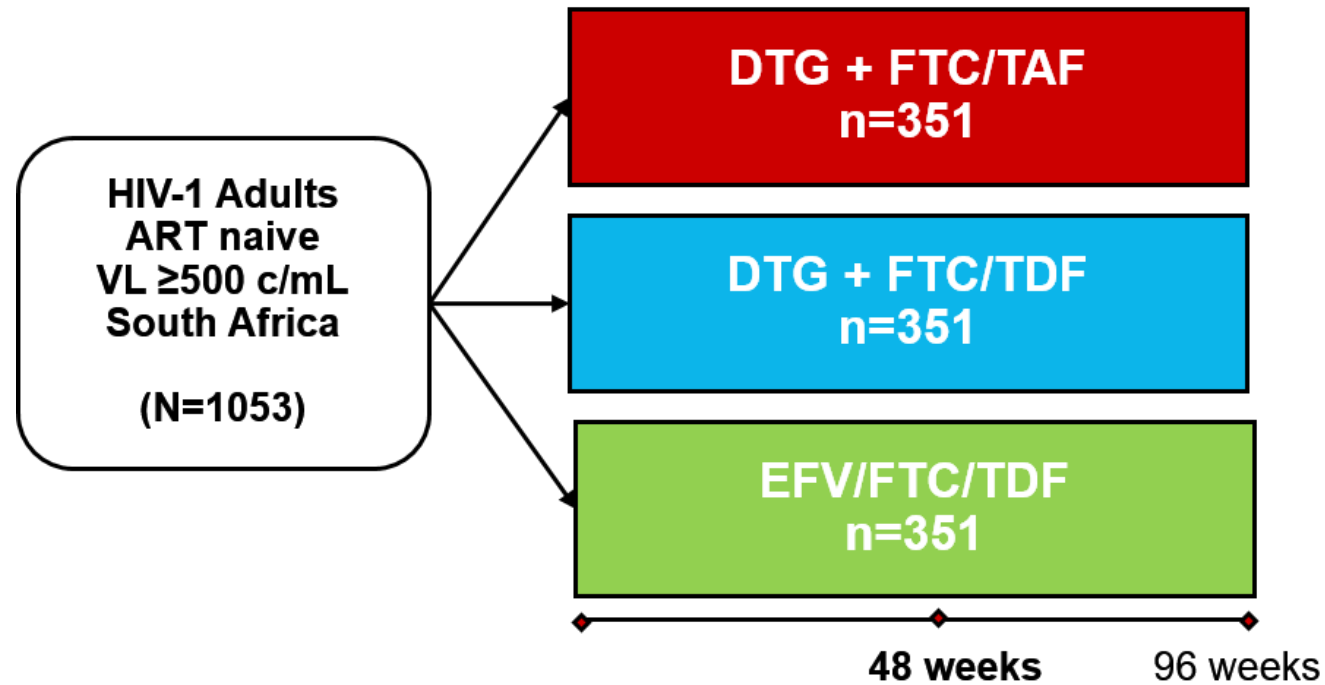
NAMSAL Study

>10% change in weight at 48 weeks



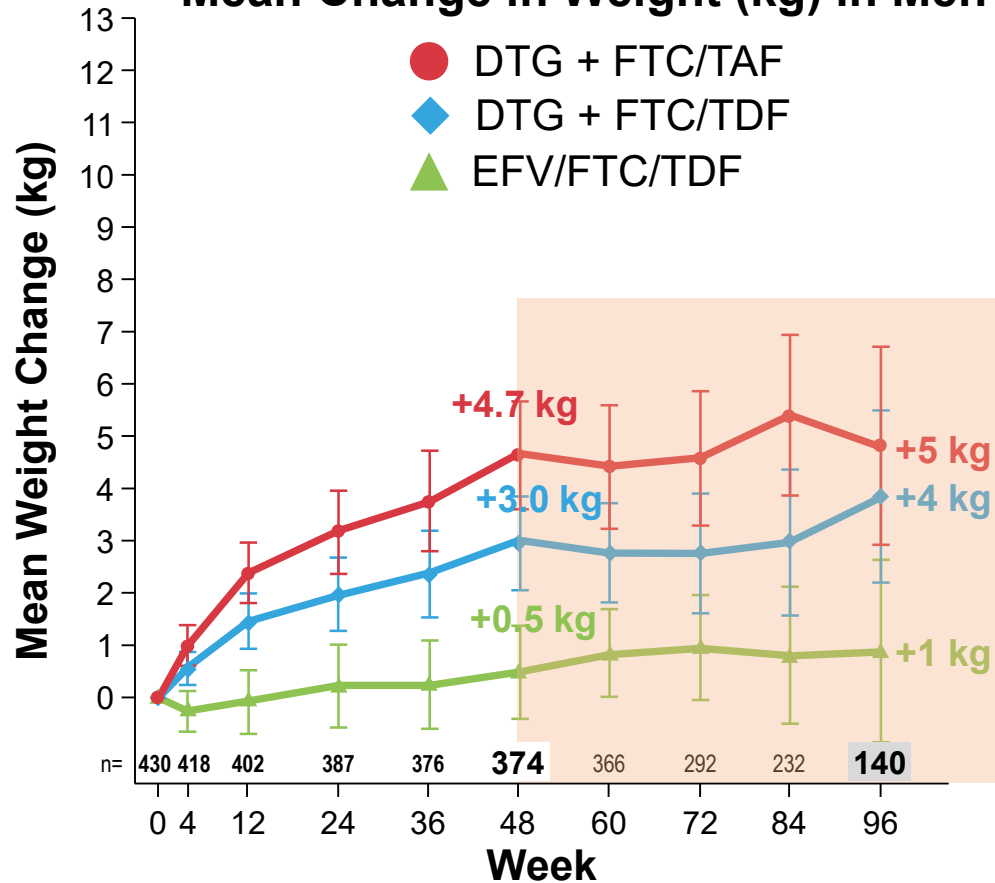
ADVANCE Study

ADVANCE

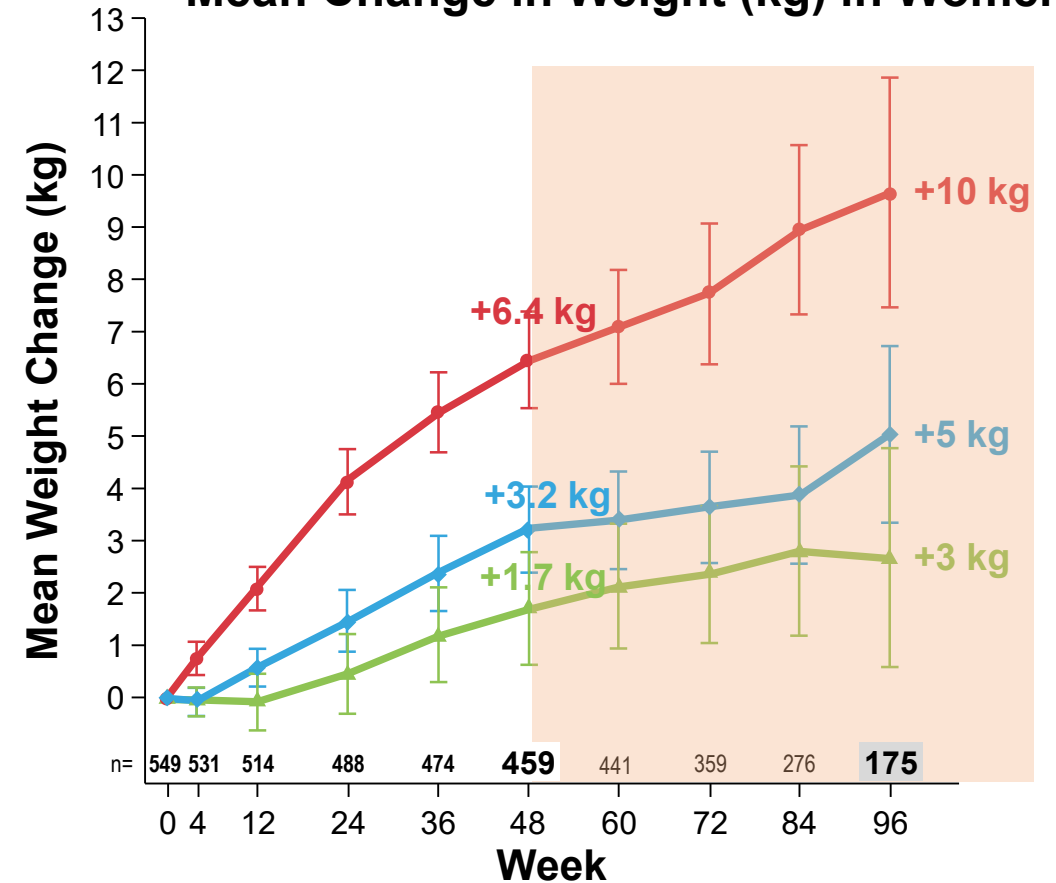


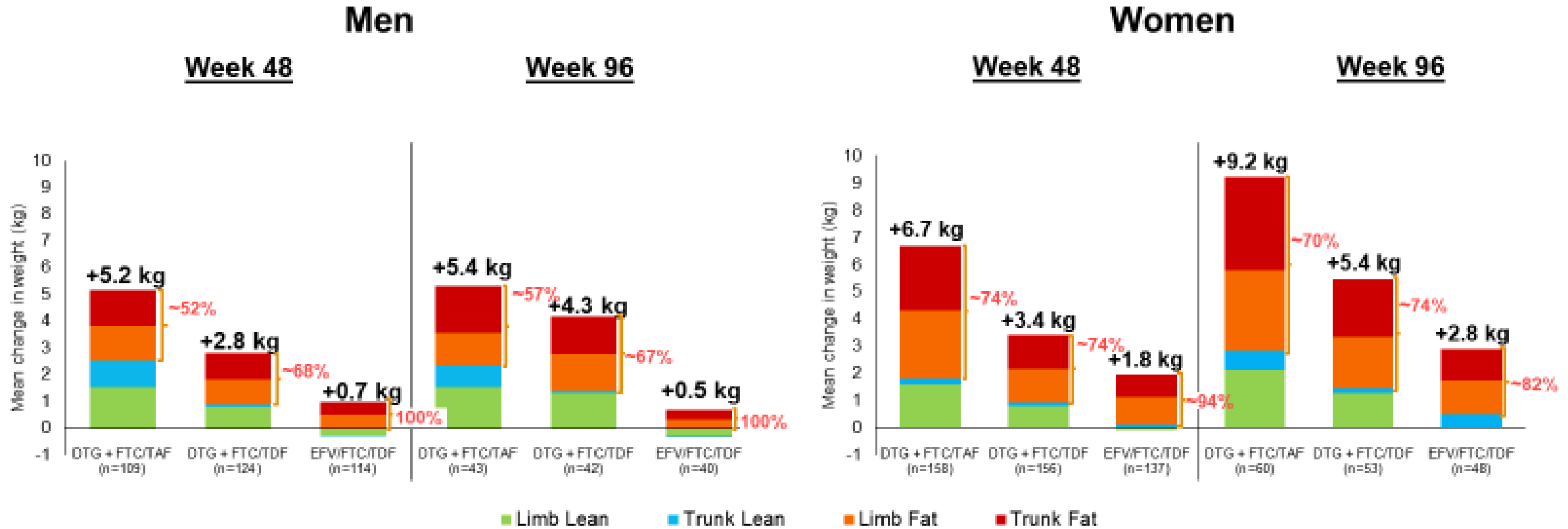
ADVANCE Study

Mean Change in Weight (kg) in Men



Mean Change in Weight (kg) in Women





DTG was associated with increased trunk and limb lean mass and fat vs. EFV

Discussion Areas



Mechanism for
weight gain

Better safety and
efficacy of drugs
Off-target side effects



Impact on clinical practice