

Weight Gain with Antiretroviral Therapy

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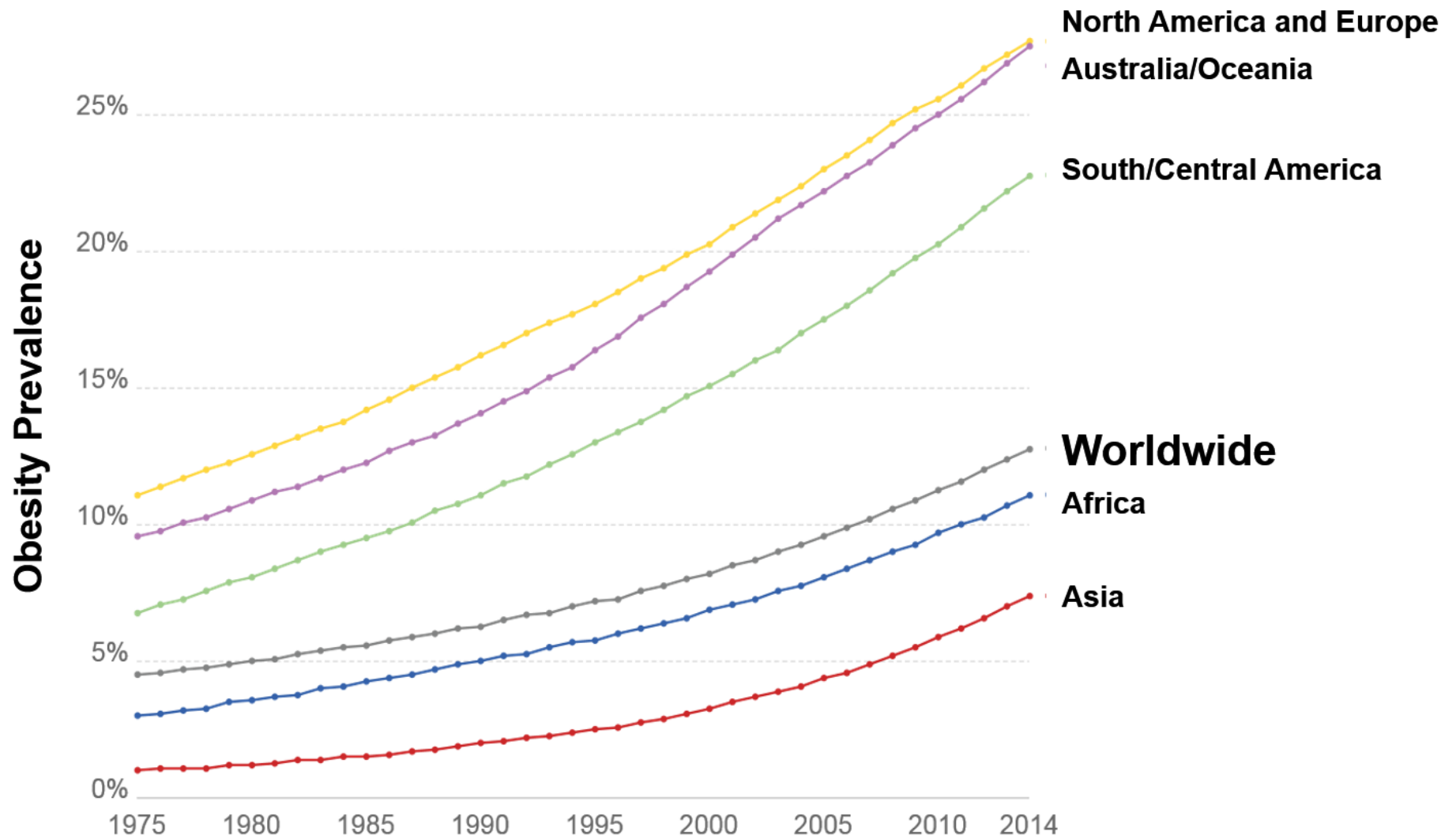
Indiana University, Indianapolis

Disclosures

Scientific advisory board for Gilead Sciences

Scientific advisory board for Theratechnologies

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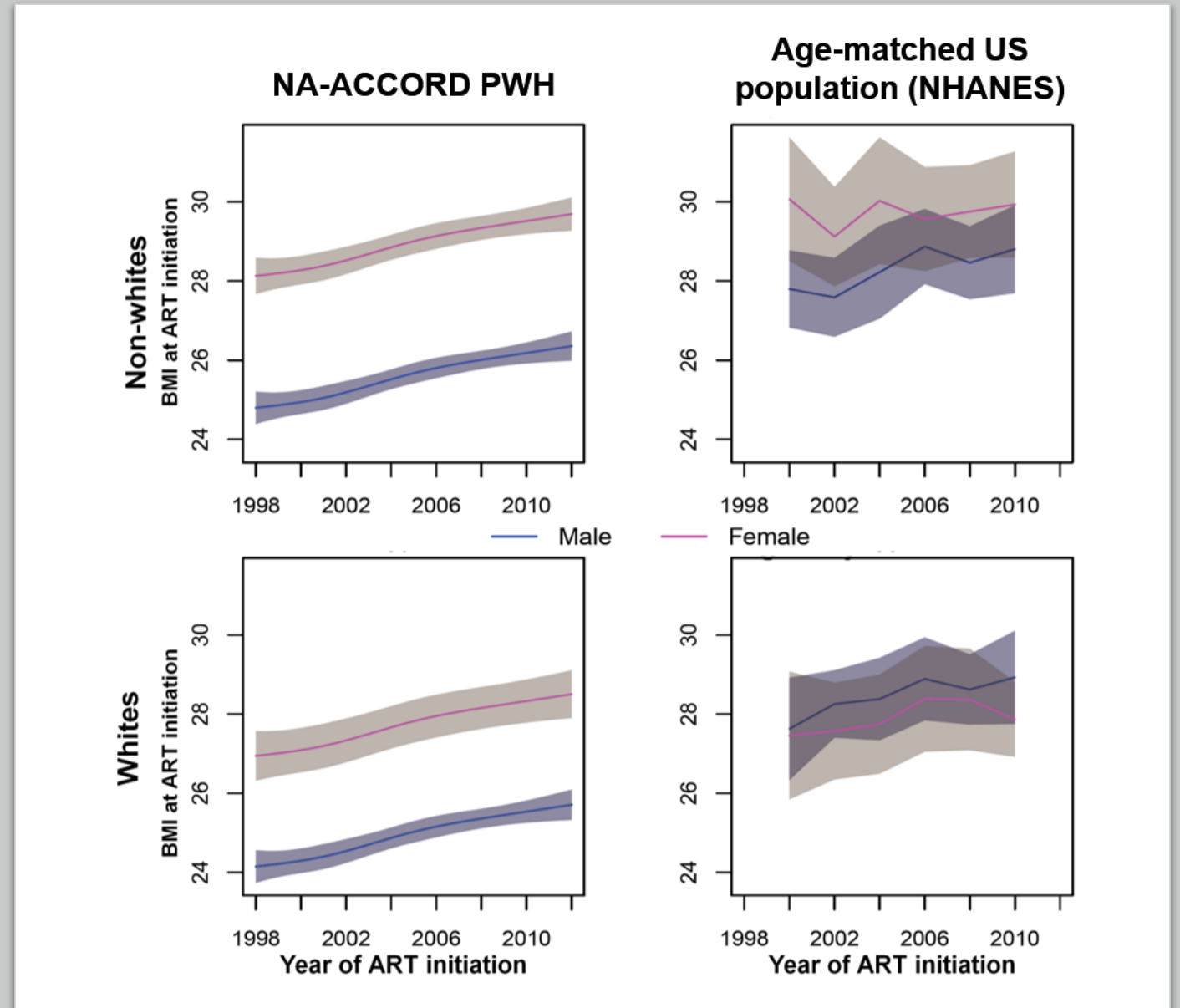


Worldwide Prevalence of Obesity

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



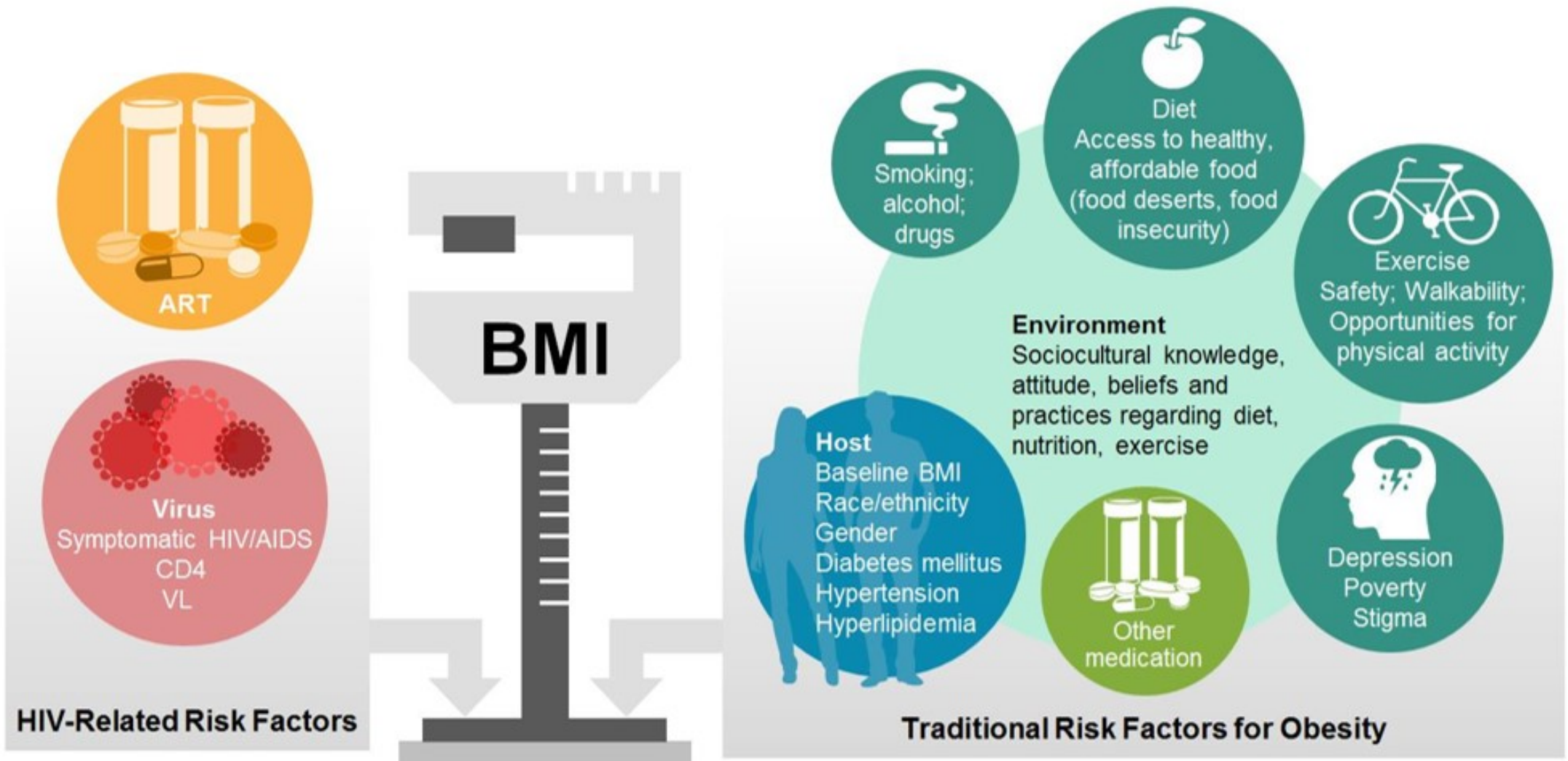
Weight Gain after Starting ART

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

Greatest among white men and non-white women

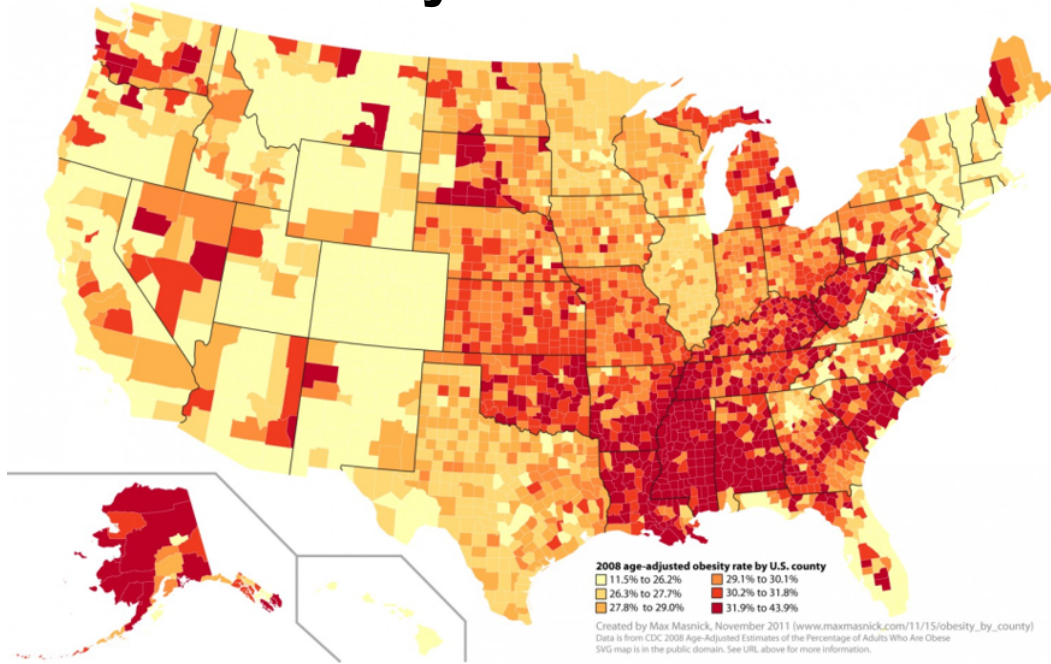
In the first 3 years of ART:

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

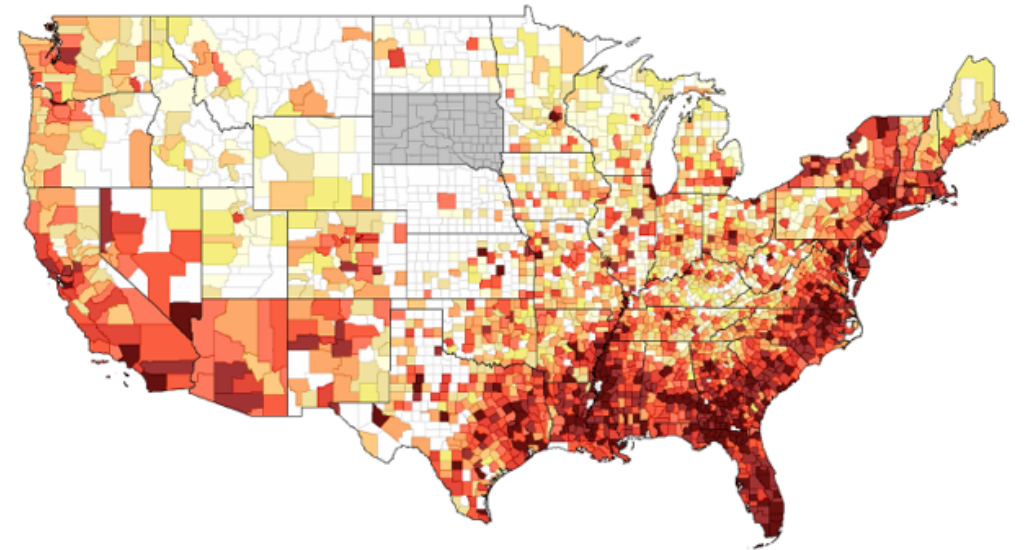


Risk Factors for Weight Gain Among PWH

Obesity Prevalence

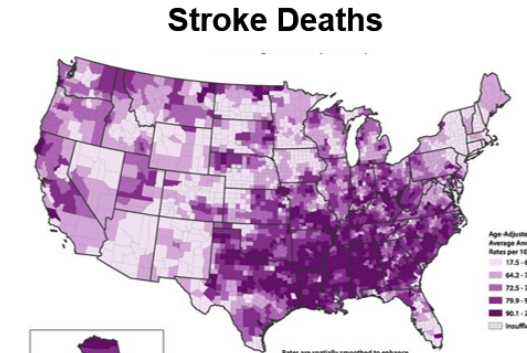
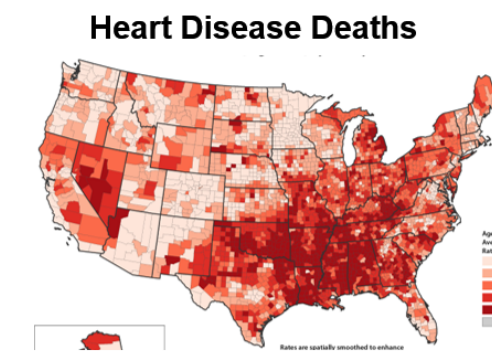
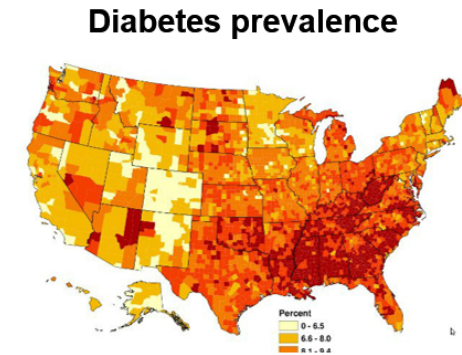
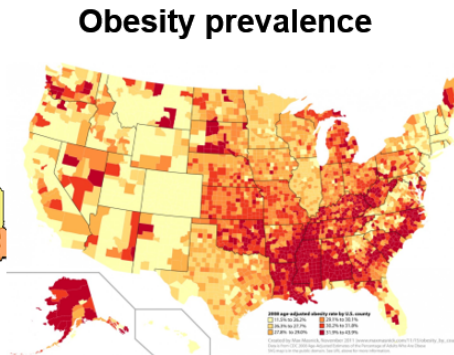
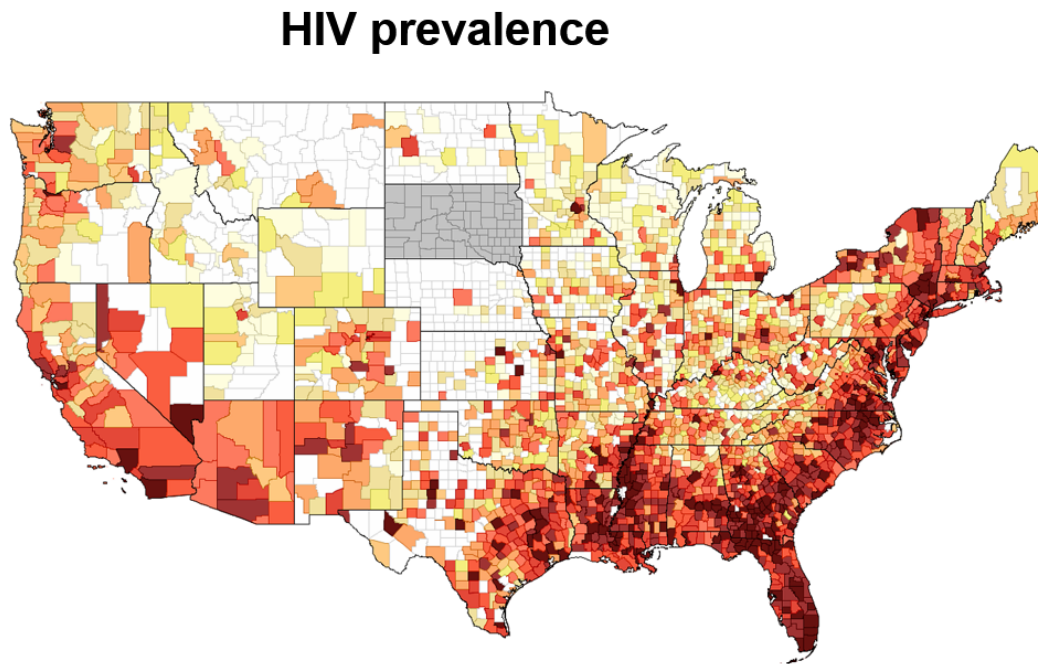


HIV Prevalence



Overlapping HIV and Obesity Epidemics

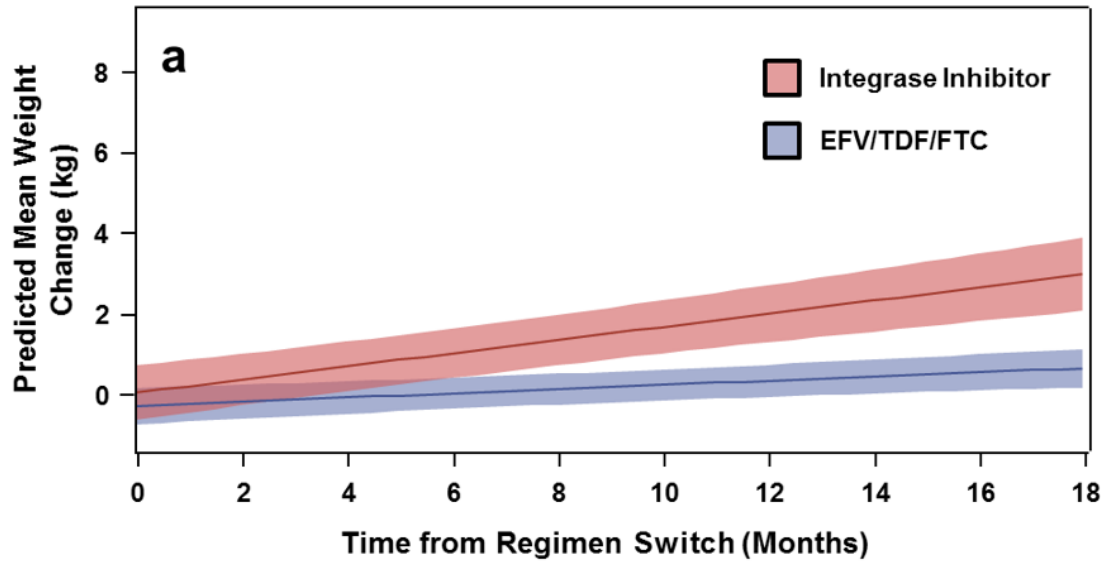
Overlapping Epidemics



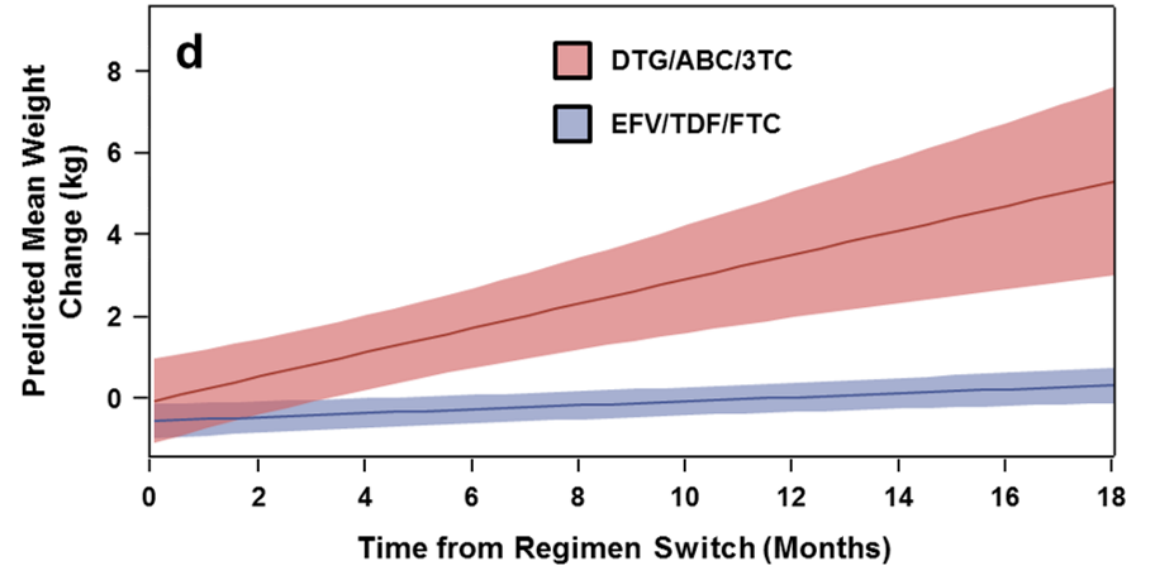
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Early Report of
Increased Weight Gain
with INSTI

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

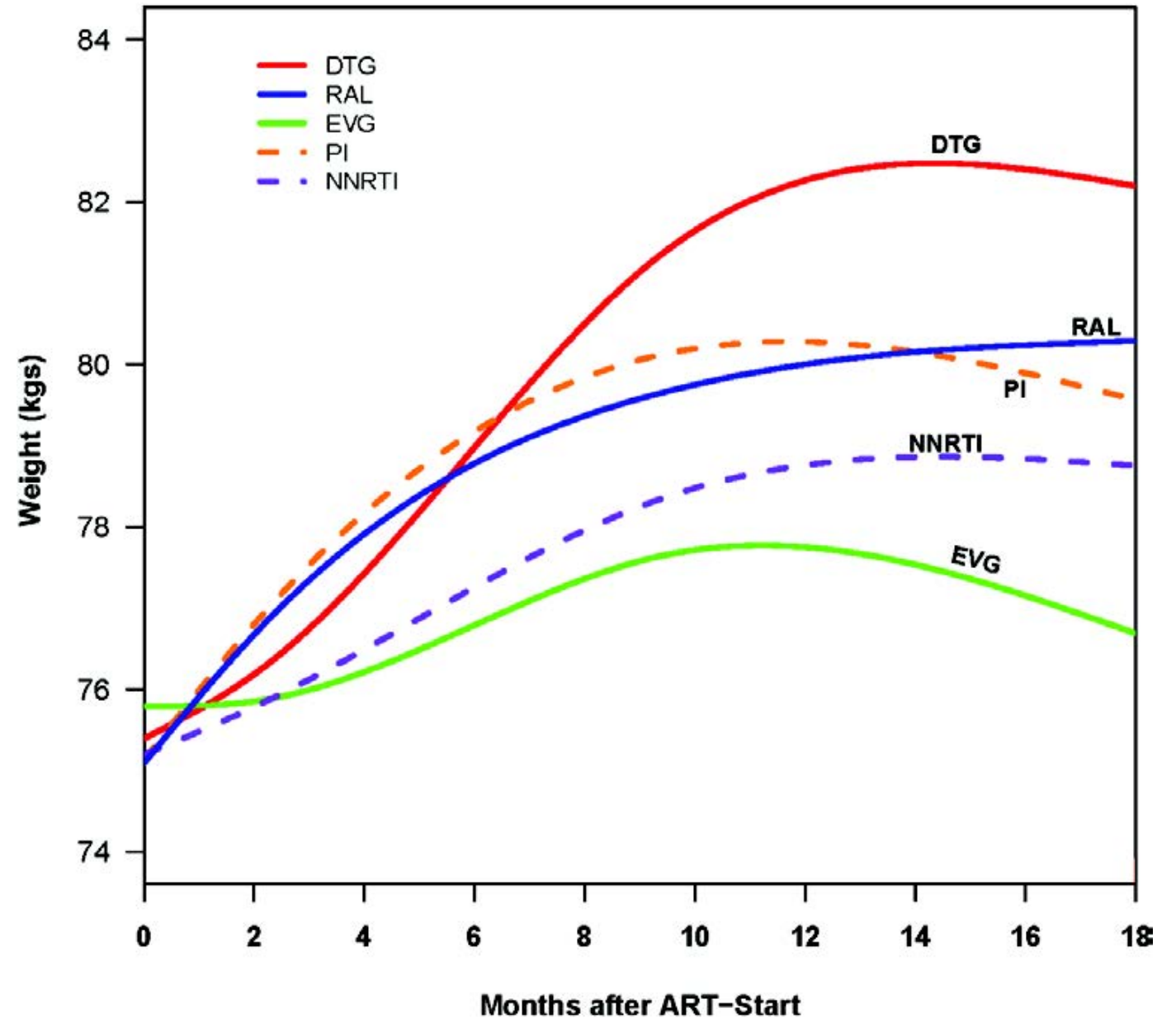
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**Weight Gain by ART
Regimen**

VUMC Cohort

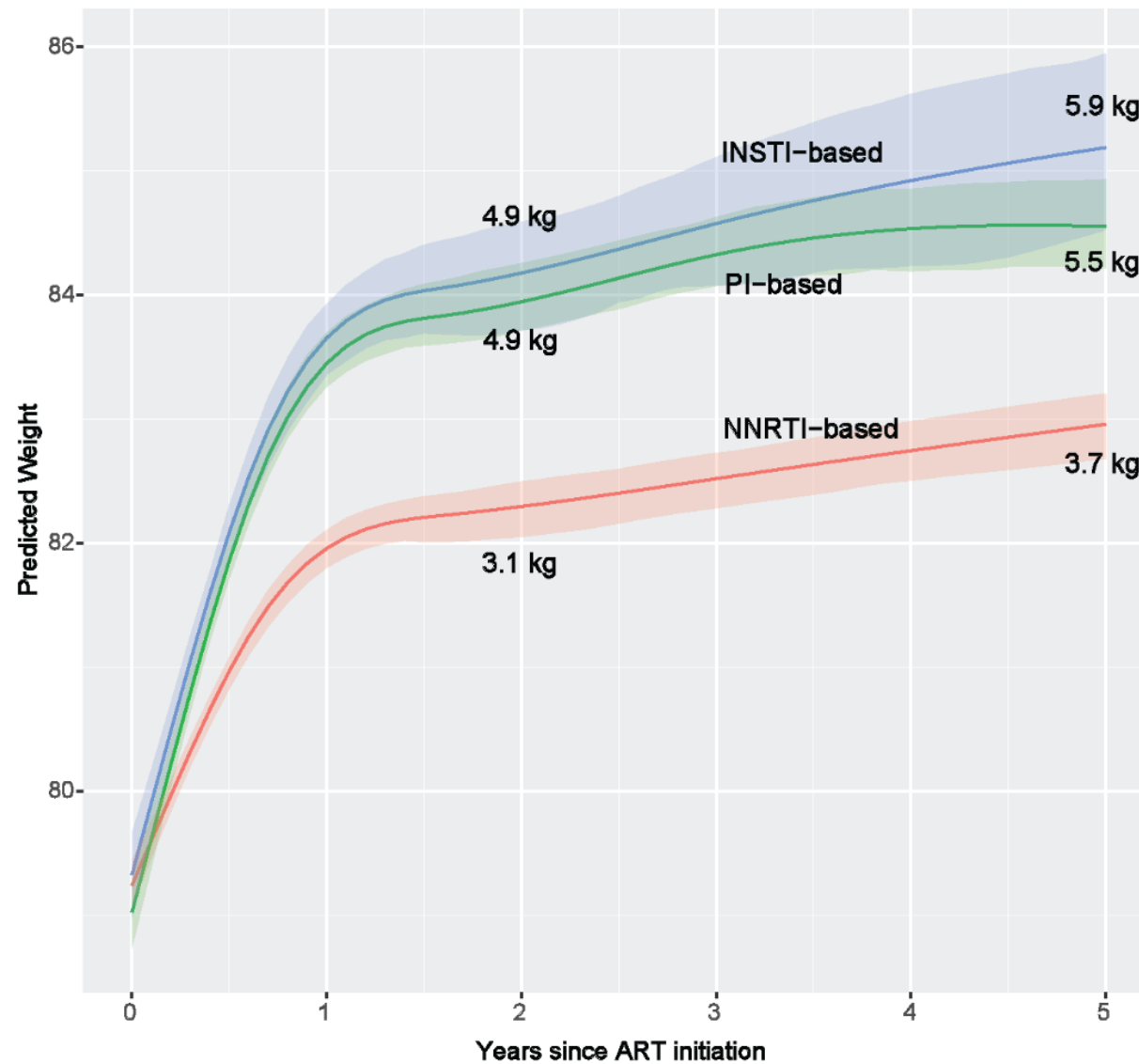
1,152 ART-naive
PWH

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



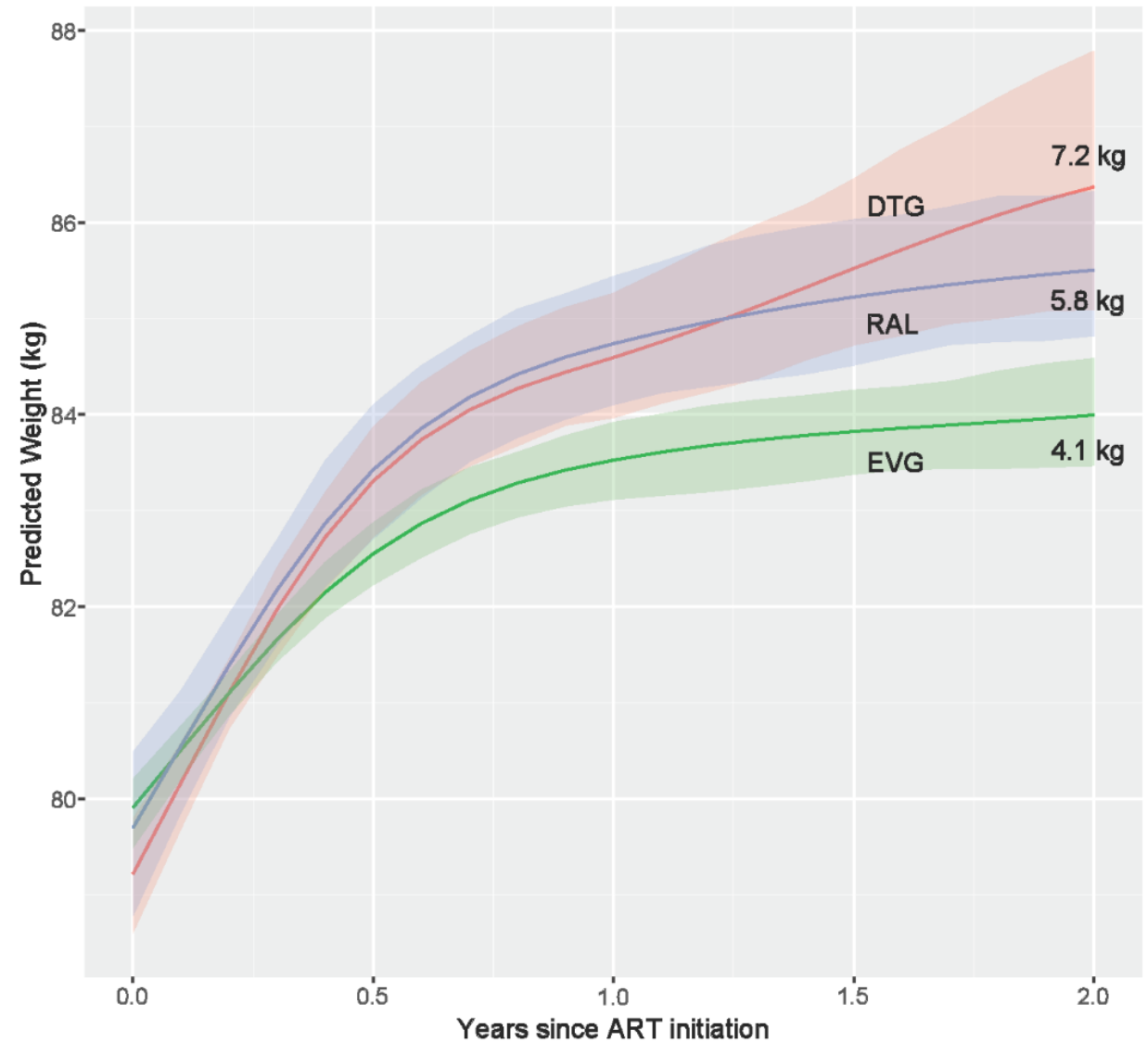
NA-ACCORD Cohort

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

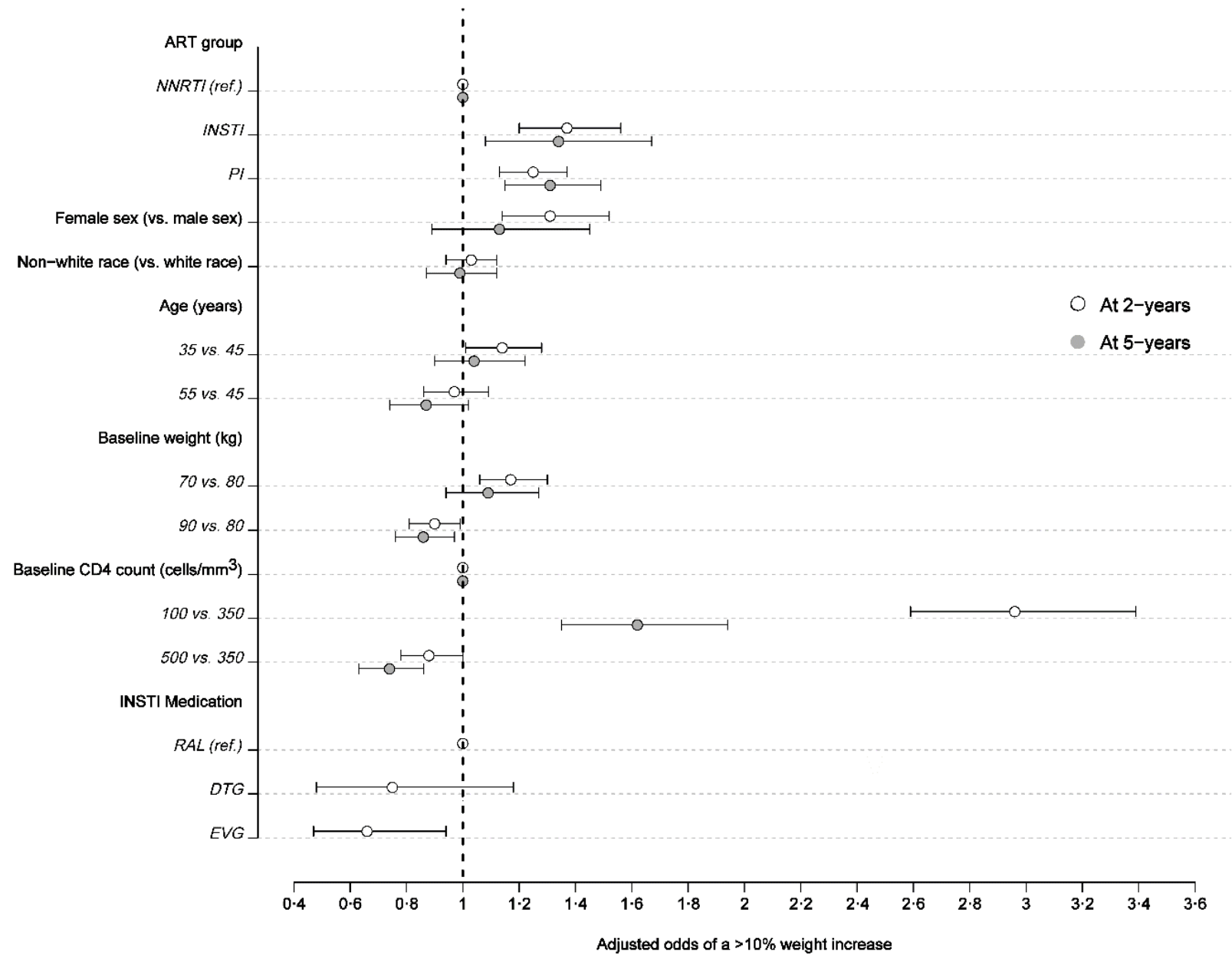


NA-ACCORD Cohort

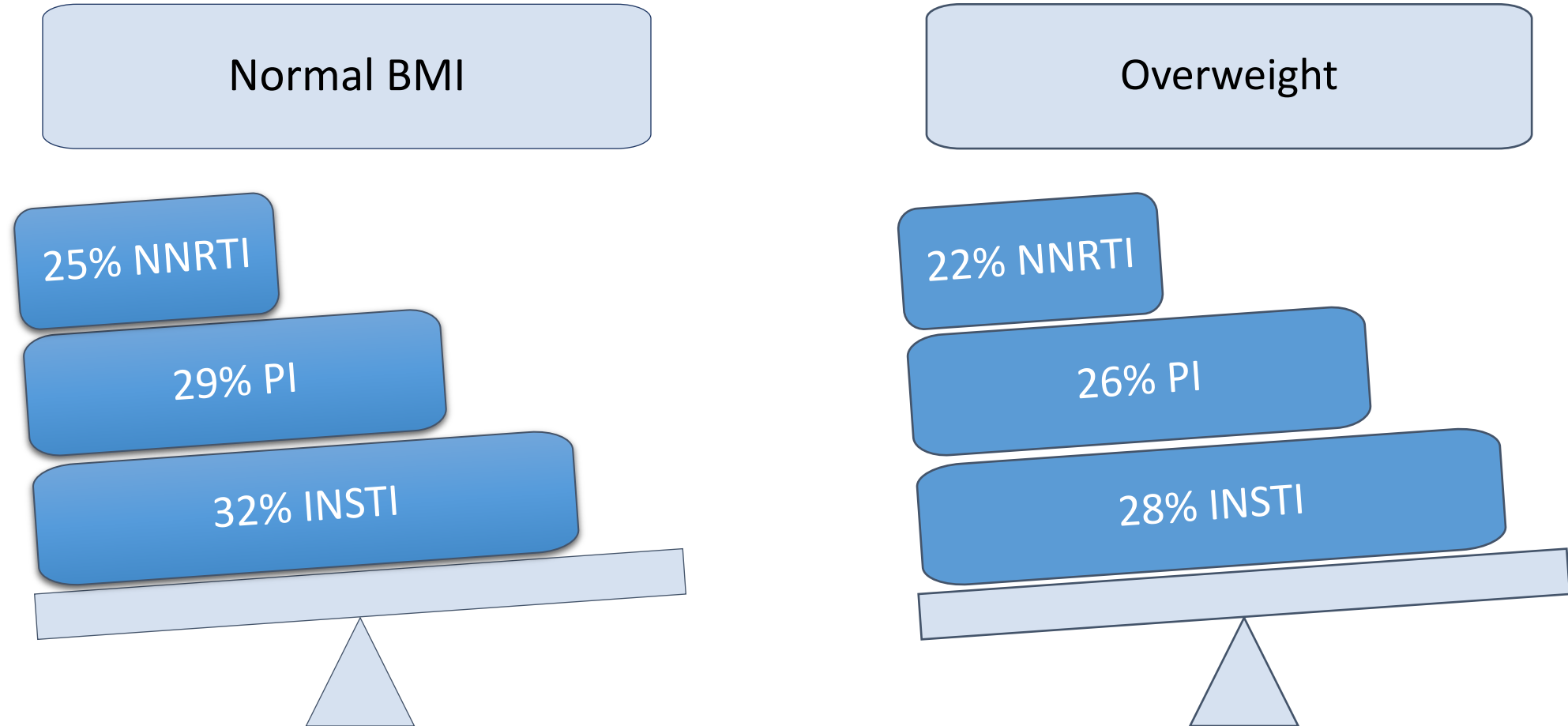
*4,190 patients
starting INSTI drugs
from 2007-2016 in
the US and Canada*



Odds of excessive Weight Gain

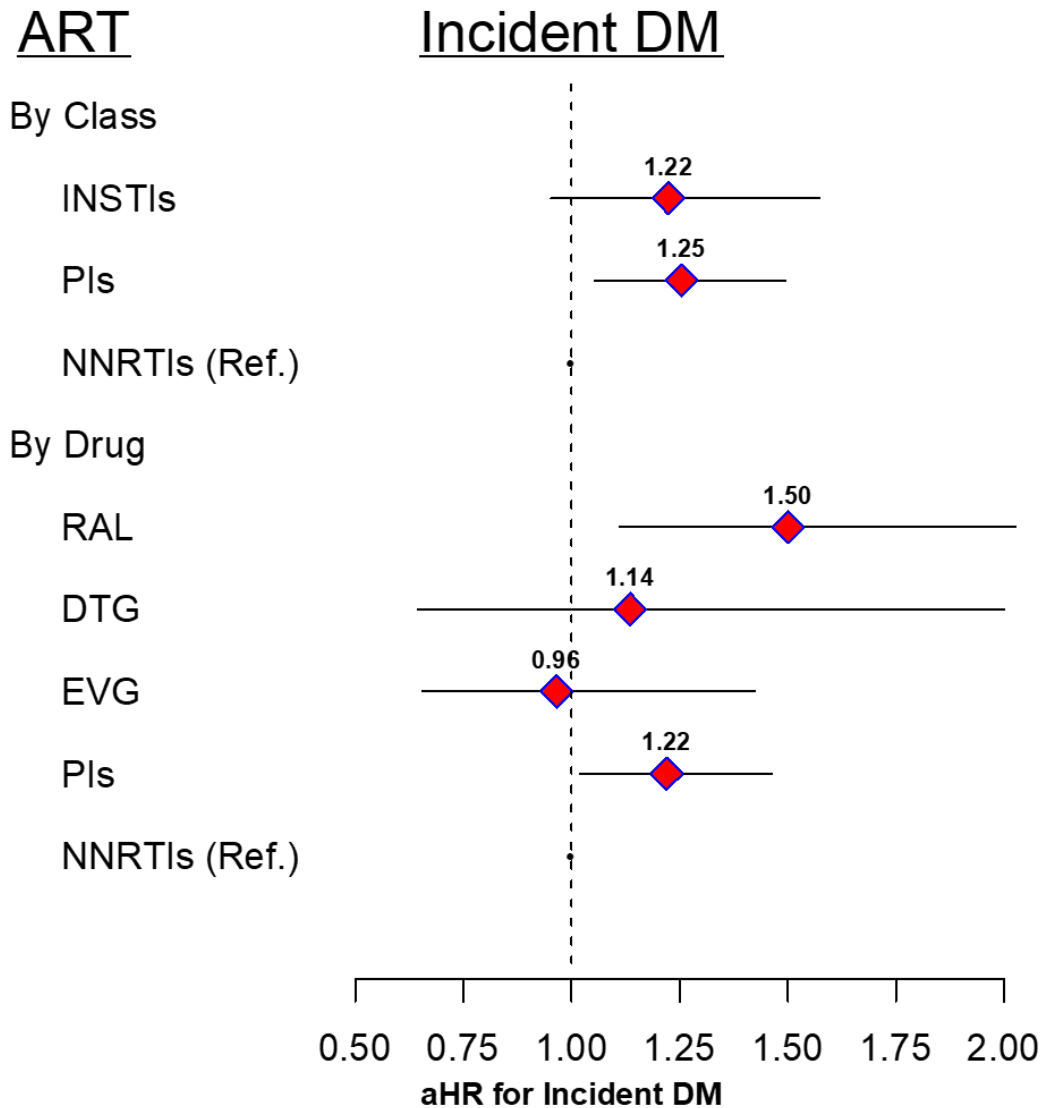


Progression to Obesity



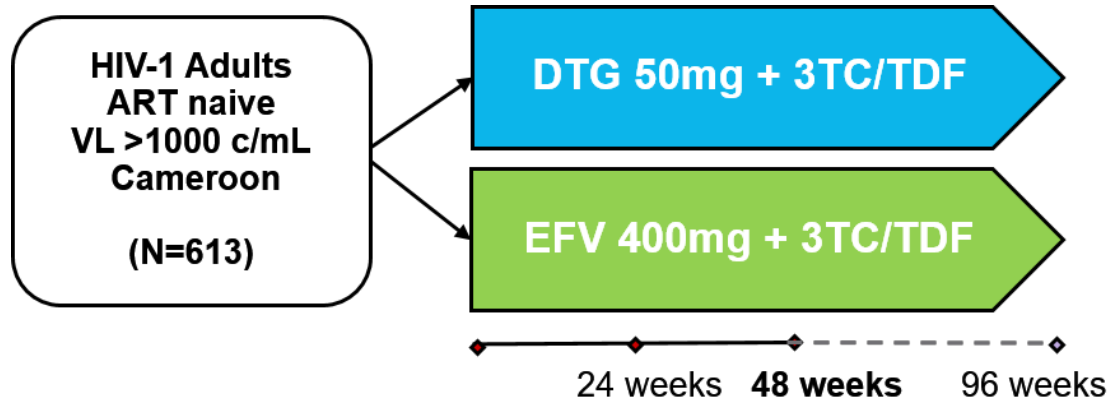
Risk of incident diabetes mellitus after initiation of ART

- 21,516 PWH starting ART in NA-ACCORD



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Data from Clinical Trials

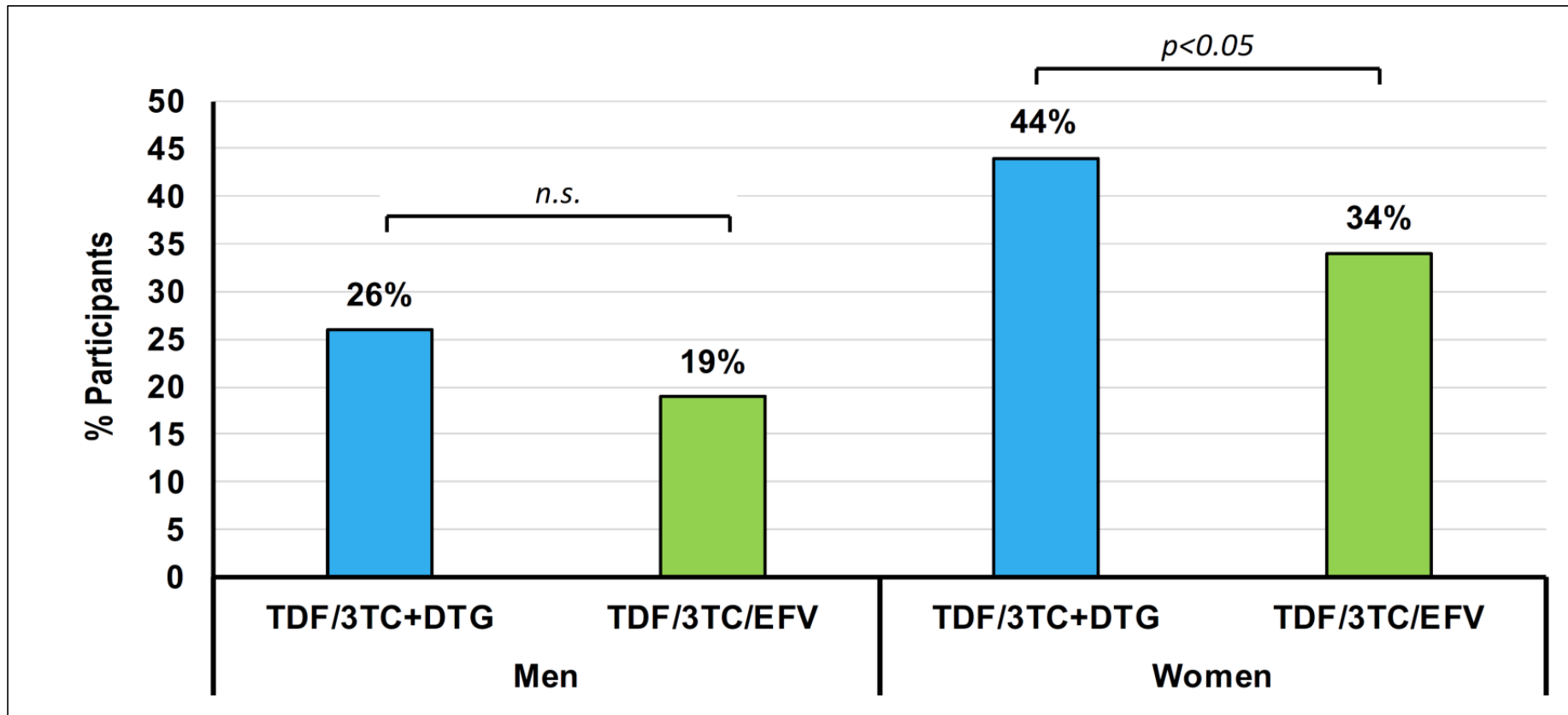


Week 48	TDF/3TC+DTG (n=293)	TDF/3TC+EFV400 (n=278)	p-value for difference
Mean change from baseline:			
Weight (kg)	+5	+3	<0.001
BMI (kg/m ²)	+1.7	+1.2	<0.001
Treatment-emergent overweight (BMI 25 - 29.9), n (%)	16%	17%	n.s.
Treatment-emergent obesity (BMI ≥ 30), n (%)	12%	5%	<0.01

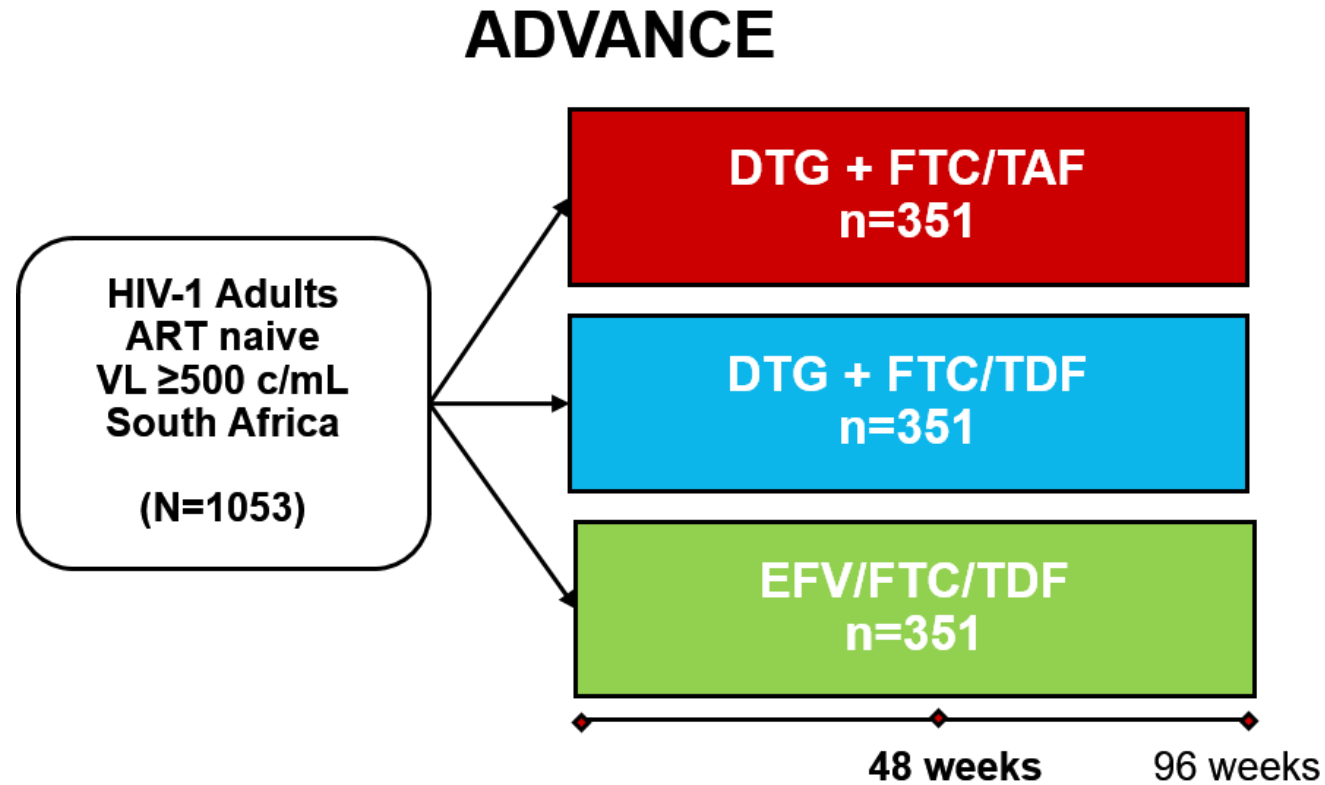
NAMSAL Study

NAMSAL Study

>10% change in weight at 48 weeks

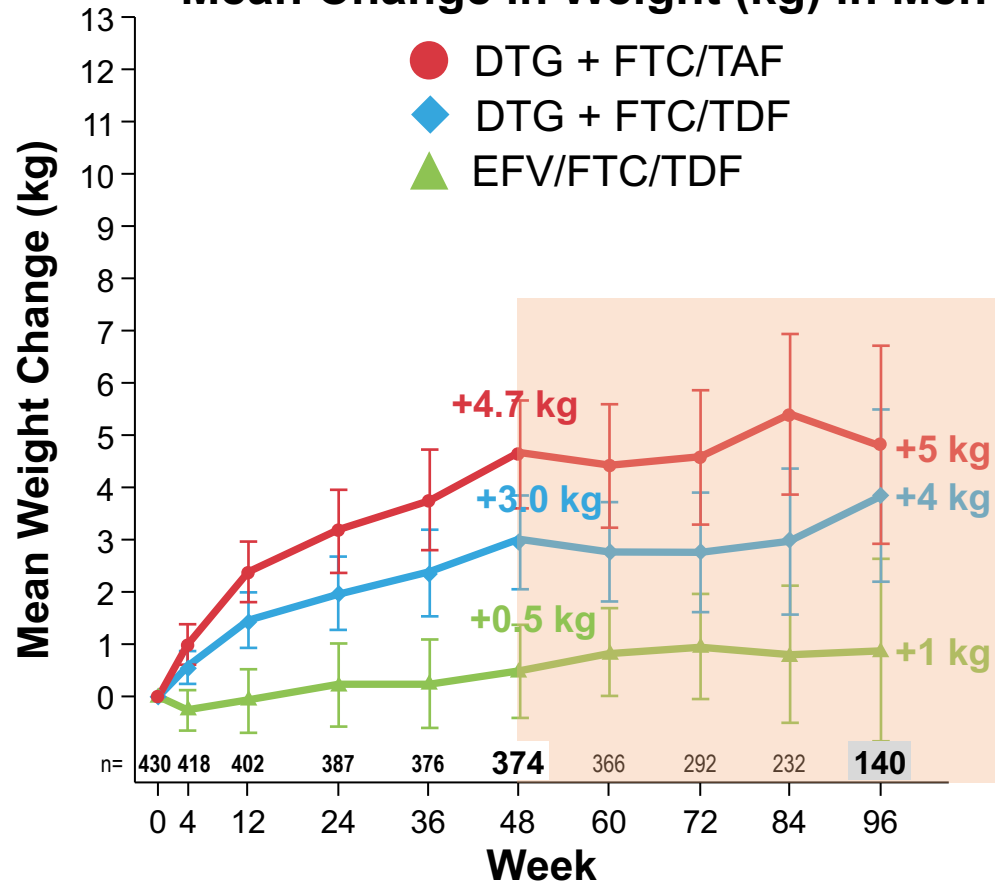


ADVANCE Study

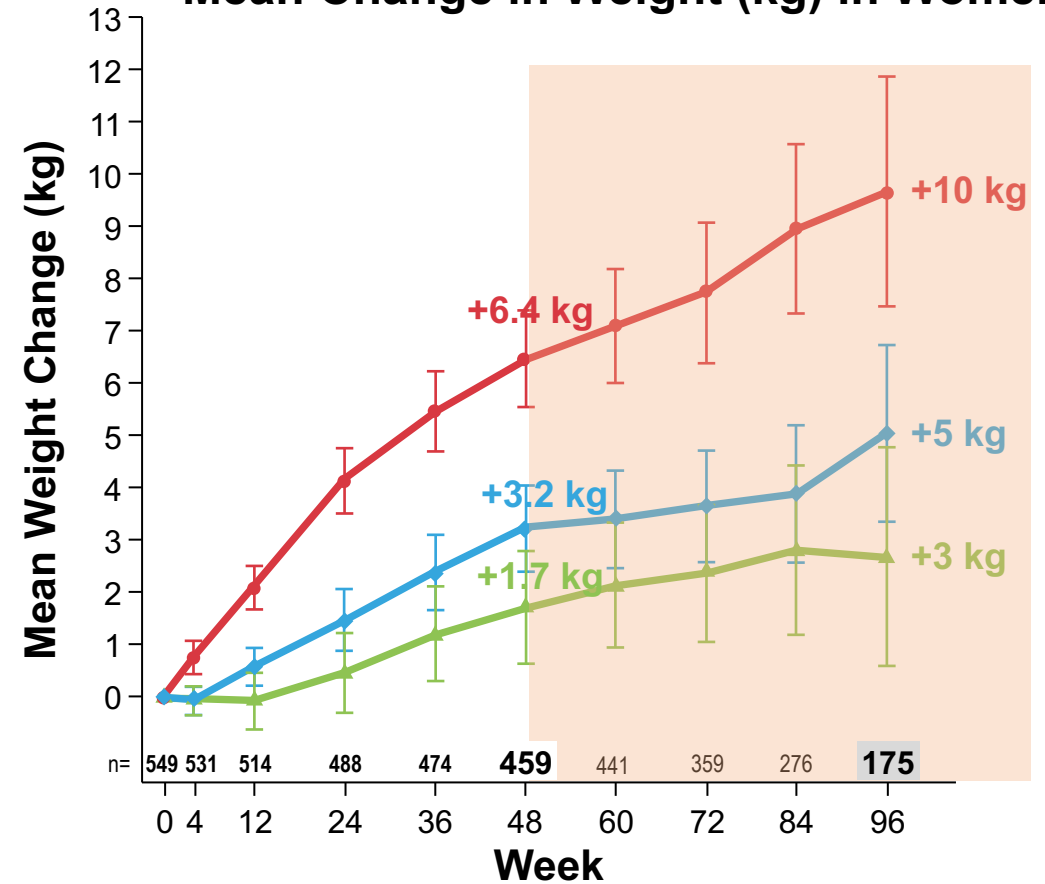


ADVANCE Study

Mean Change in Weight (kg) in Men



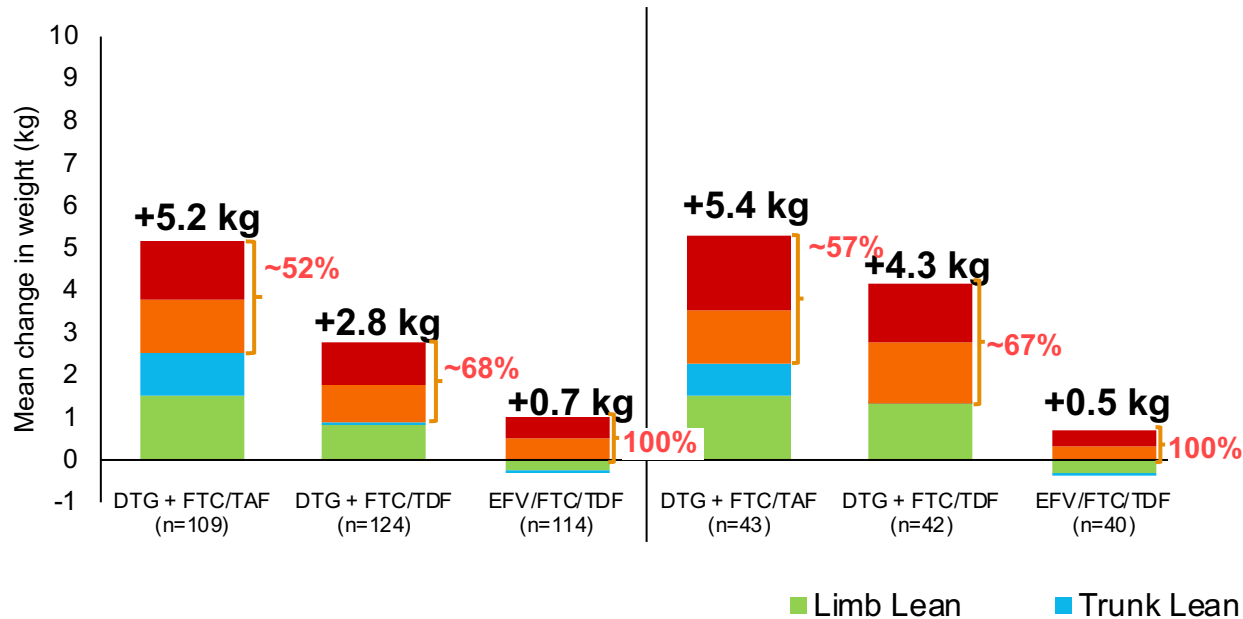
Mean Change in Weight (kg) in Women



Men

Week 48

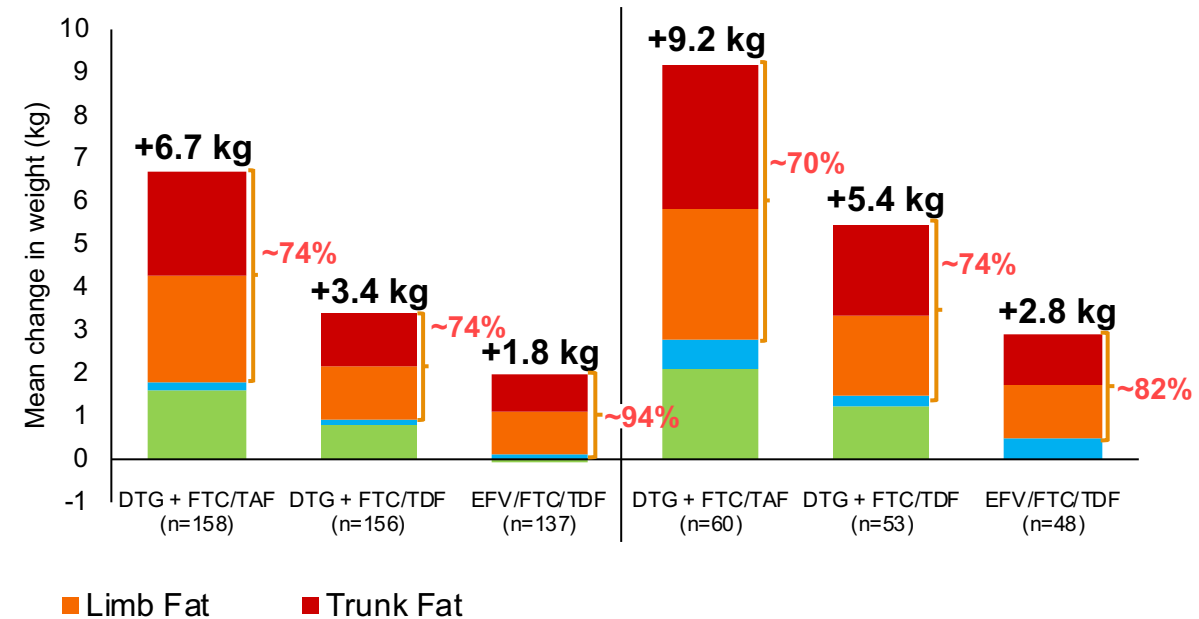
Week 96



Women

Week 48

Week 96

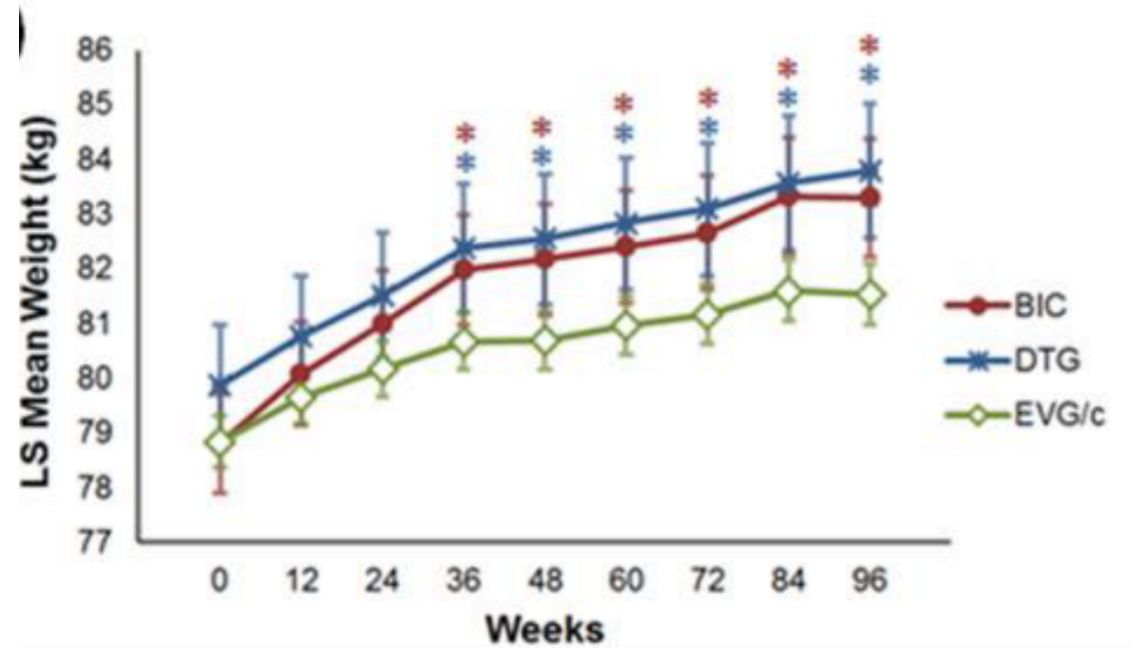
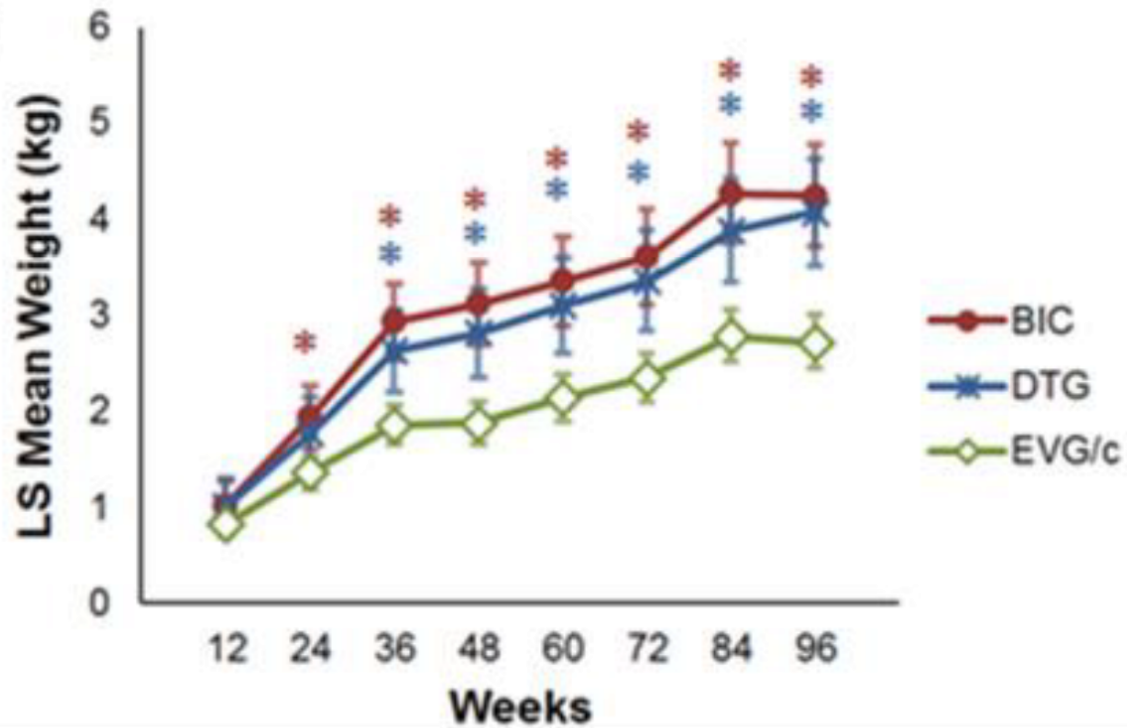


DTG was associated with increased trunk and limb lean mass and fat vs. EFV, with greater increases with FTC/TAF in women, but not in men.

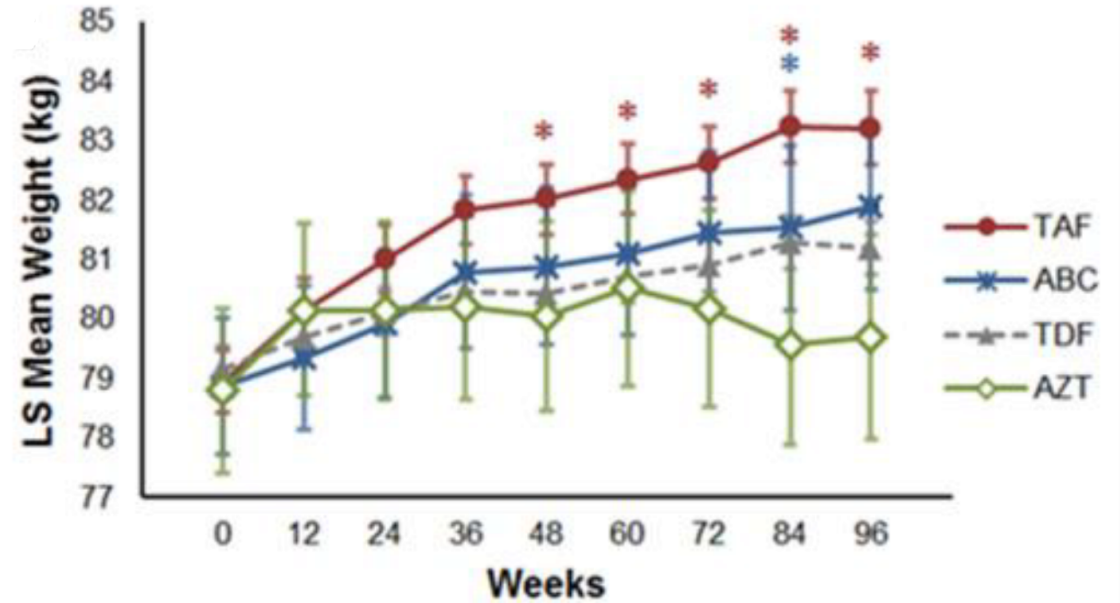
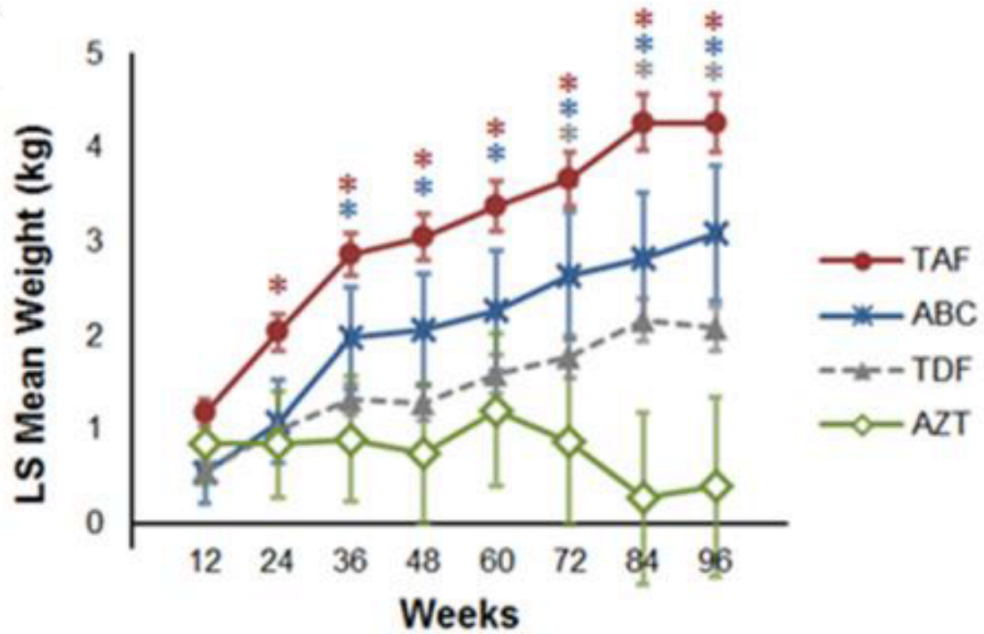
Pooled RCT Analysis

8 RCTs of Treatment naïve PWH between 2003 – 2015 (N=5,000)

Variable	Difference (kg)	95% CI	p value
CD4 (<200 vs. ≥200/μL)	2.97	2.81, 3.13	<0.001
IV drug use (no vs. yes)	1.41	0.97, 1.85	<0.001
Race (black vs. non-black)	0.99	0.87, 1.11	<0.001
HIV RNA (>100k vs. ≤100k c/mL)	0.96	0.84, 1.08	<0.001
Symptomatic HIV (yes vs. no)	0.51	0.36, 0.65	<0.001
Sex (female vs. male)	0.23	0.07, 0.4	0.006
Age (<50 vs. ≥50 years)	0.22	0.07, 0.37	0.004
BMI (obese vs. normal)	0.21	0.06, 0.36	0.005
BMI (overweight vs. normal)	-0.24	-0.36, -0.13	<0.001



How about Bictegravir ?



NRTI backbone and Weight Gain

Discussion Areas



Mechanism for
weight gain

Better safety and
efficacy of drugs
Off-target side effects



Impact on clinical practice