AETC AIDS Education & Training Center Program Southeast

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Antiretroviral Therapy and Weight Gain

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Financial Disclosure

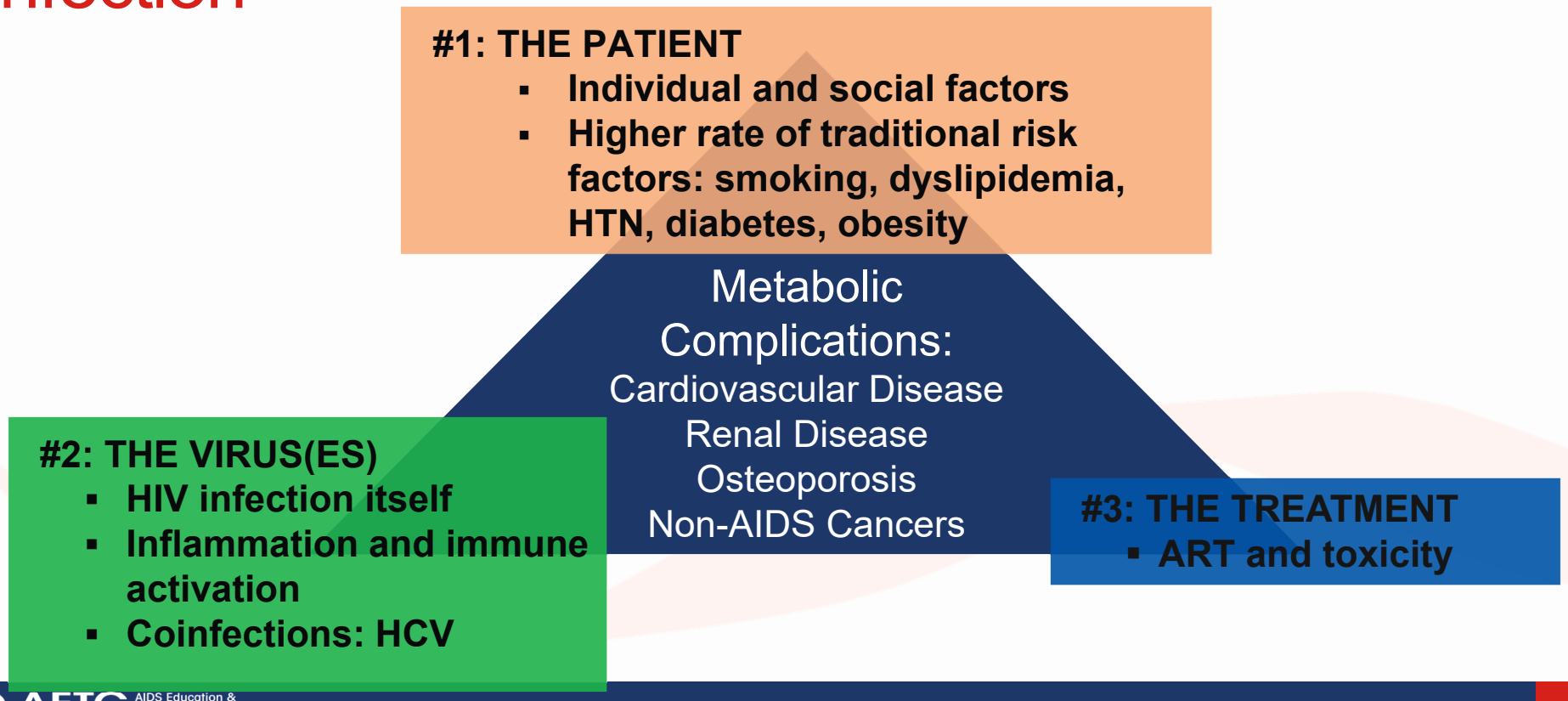
Merck & Co. Advisory Board, research funding
Gilead Sciences Advisory Board
ViiV Healthcare Advisory Board, research funding
Janssen Advisory Board

Learning Objectives

At the end of this presentation, participants will be able to:

- Assess the magnitude of weight gain associated with antiretroviral therapy
- Identify predictors of weight gain on antiretroviral therapy
- List potential mechanisms and metabolic complications of weight gain during antiretroviral therapy

Examining Weight Gain in the Context of Pathogenesis of Chronic Complications of HIV Infection



Case #1: Weight Gain on ART Initiation

- 27 y/o African American woman recently diagnosed with HIV. CD4 count is 198 cells/μL, HIV VL: 649,000 copies/mL. She's HBV immune and HCV antibody negative. She's eager to start antiretroviral therapy but has heard of potential of weight gain. You tell her the greatest potential for weight gain is associated with:
  1. Men and White race
  2. Integrase strand transfer inhibitor-based regimens
  3. Protease inhibitor-based regimens
  4. Nonnucleoside reverse transcriptase inhibitor-based regimens
  5. The jury is still out

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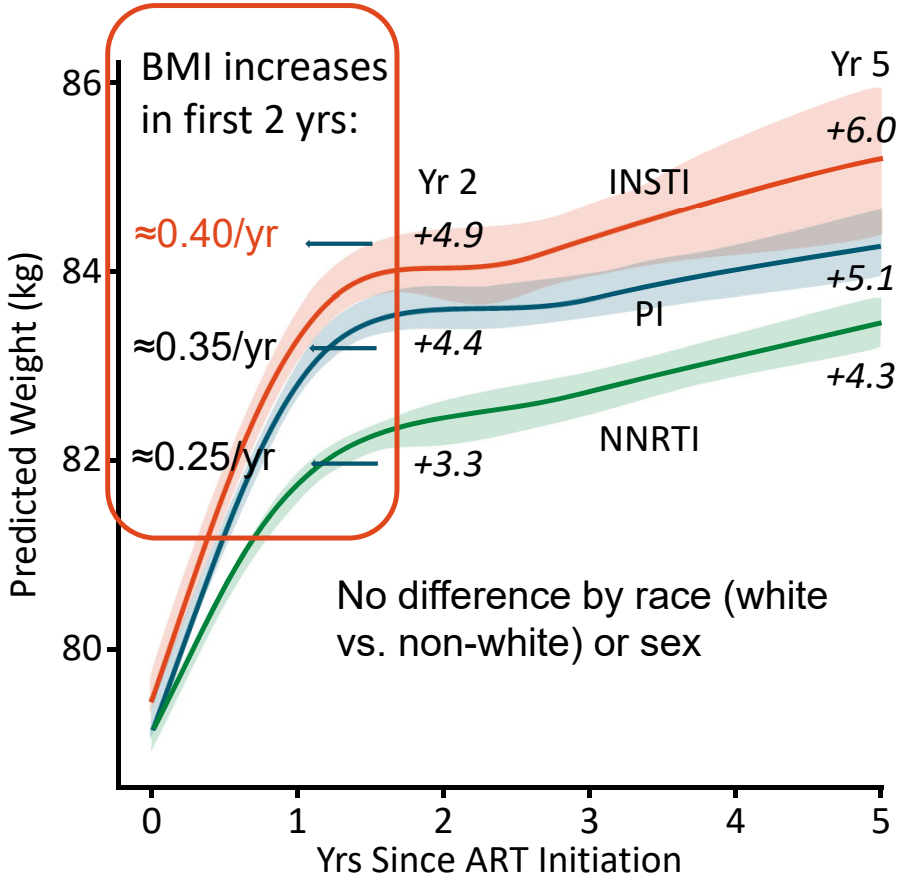
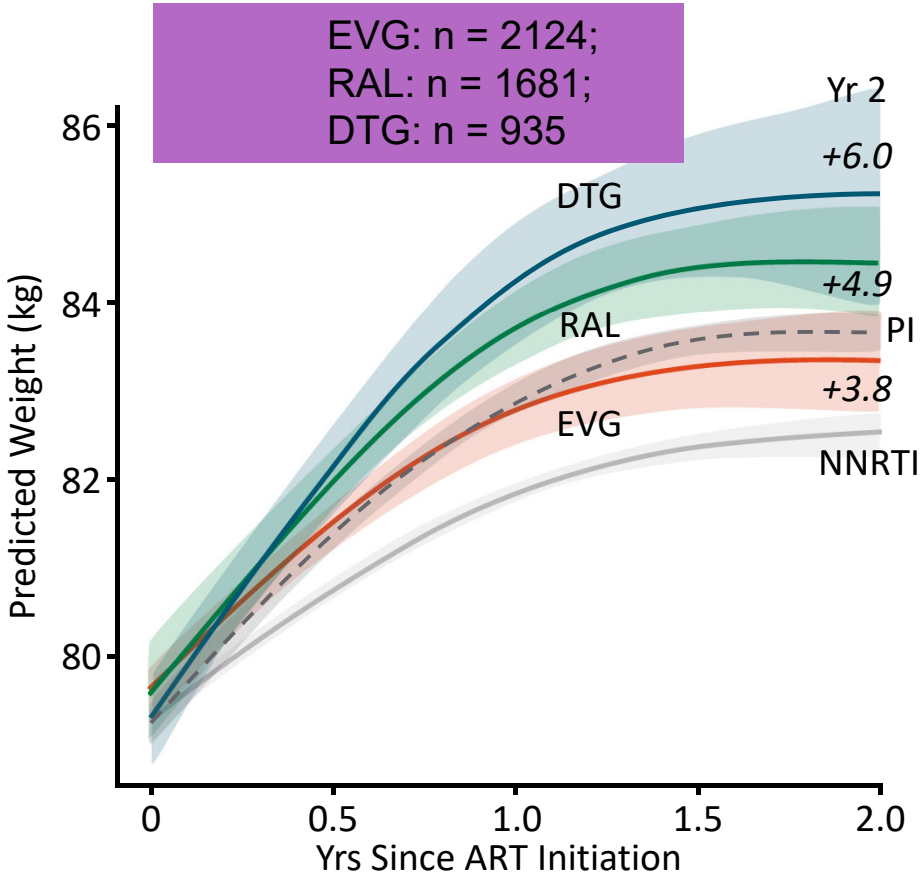
Weight Gain by Class or Specific INSTI: NA-ACCORD

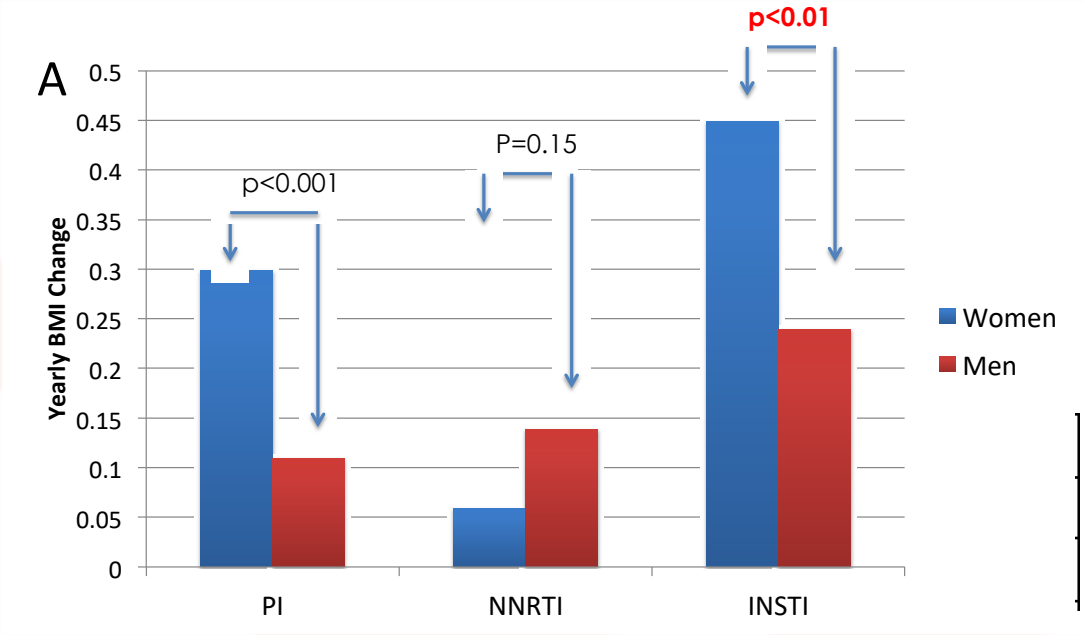


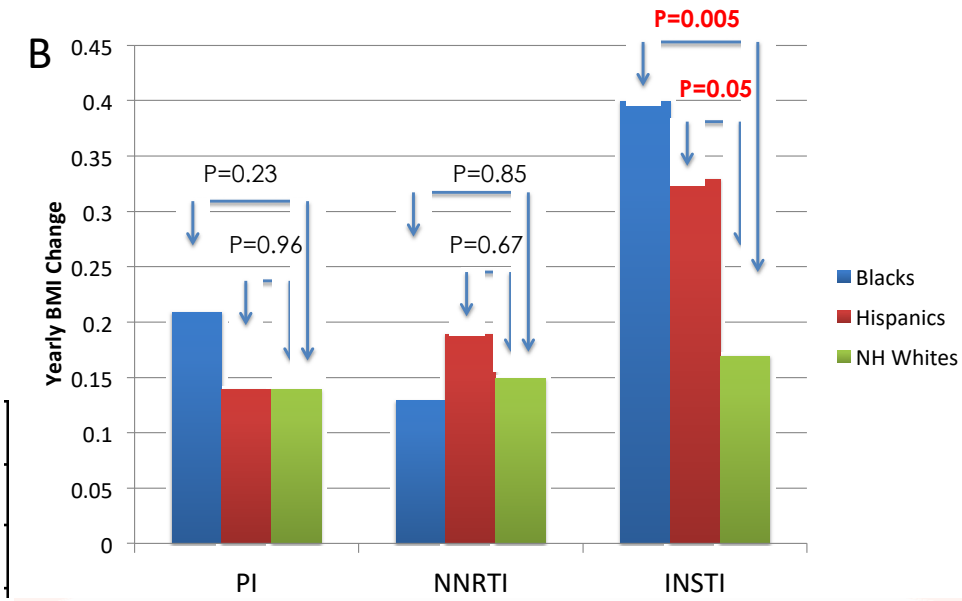


Bourgi. CROI 2019. Abstr 670. ; J Int AIDS Soc. 2020 Apr;23(4):e25484

Weight Gain by Sex and Race/Ethnicity

4,048 patients, 69% male, 53% Black, 28% Hispanic, and 16% non-Hispanic Whites. Mean age was 46.3 years (SD 11.9). Mean baseline BMI: 27.0 kg/m^2 (6.4).

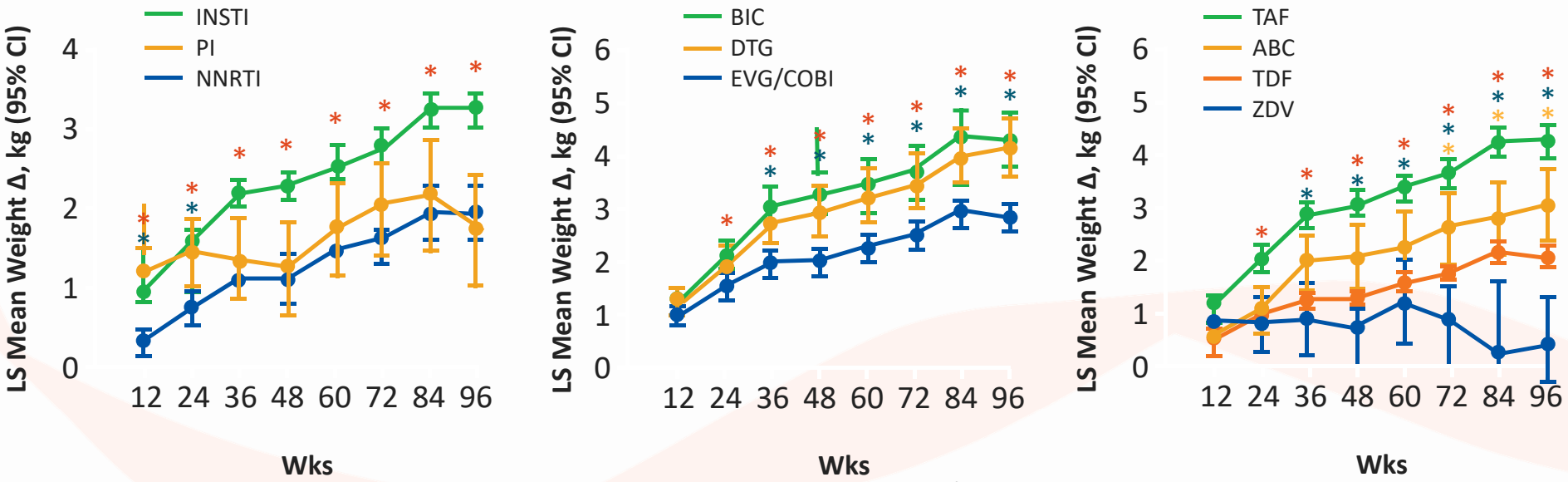




Bedimo. ID Week 2018

Multivariate Analysis of Weight Gain After ART Start

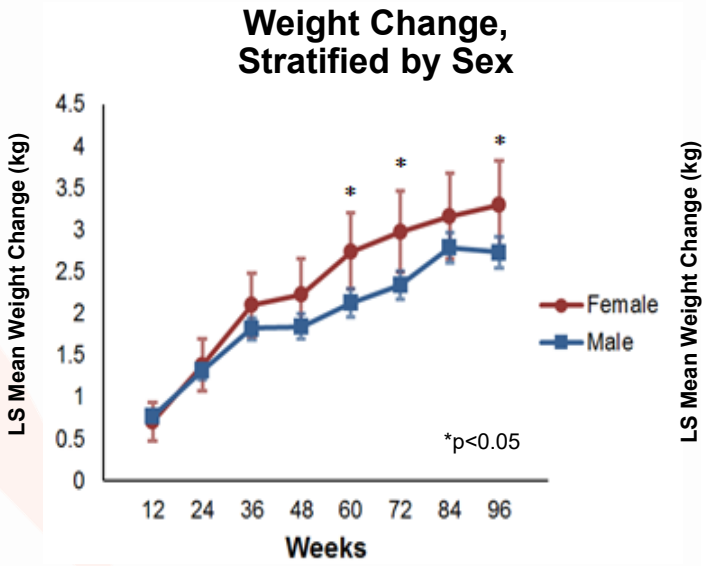
- Pooled analysis of 8 phase III RCTs of first-line ART initiation during 2003-2015 (N = 5680)
  - Baseline factors associated with weight gain: lower CD4+ cell count, higher HIV-1 RNA level, no IDU, female sex, black race, symptomatic HIV, younger age (< 50 vs ≥ 50 yrs), and higher BMI

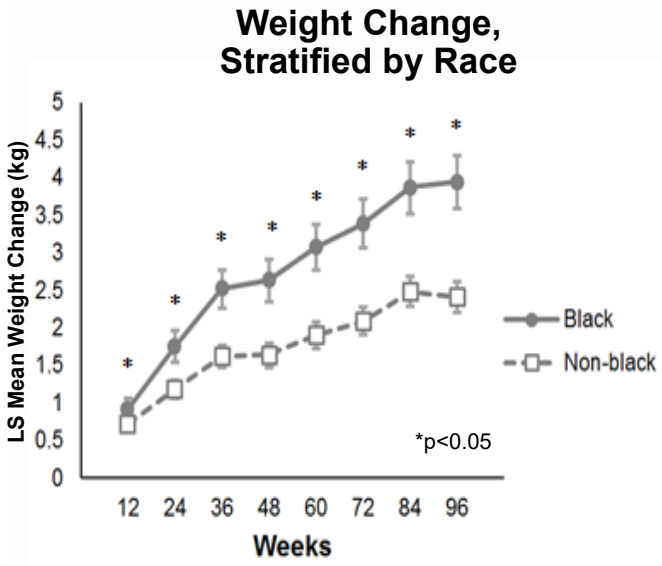


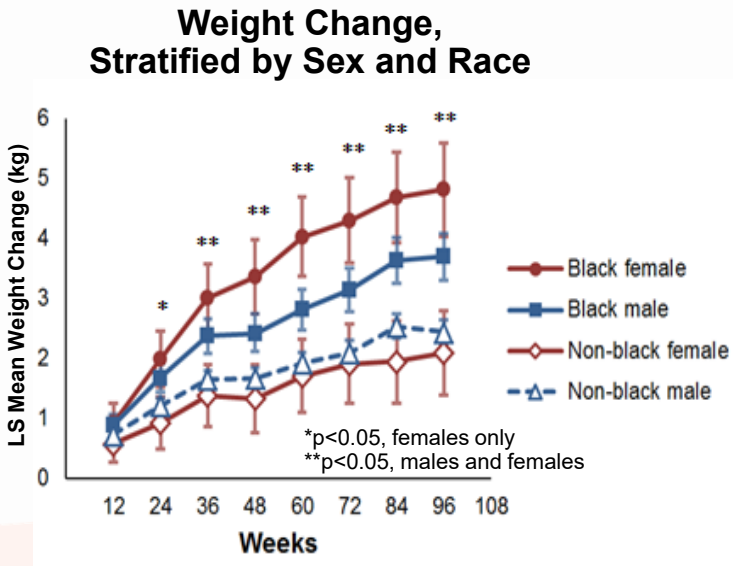
*Color-coded to match respective comparators, denoting *P* ≤ .05 vs NNRTI (first panel), EVG/COBI (second panel), or ZDV (third panel).

Sax et al. Clin Infect Dis. 2020 Sep 12;71(6):1379-1389

Effect of Sex and Race on Weight Change



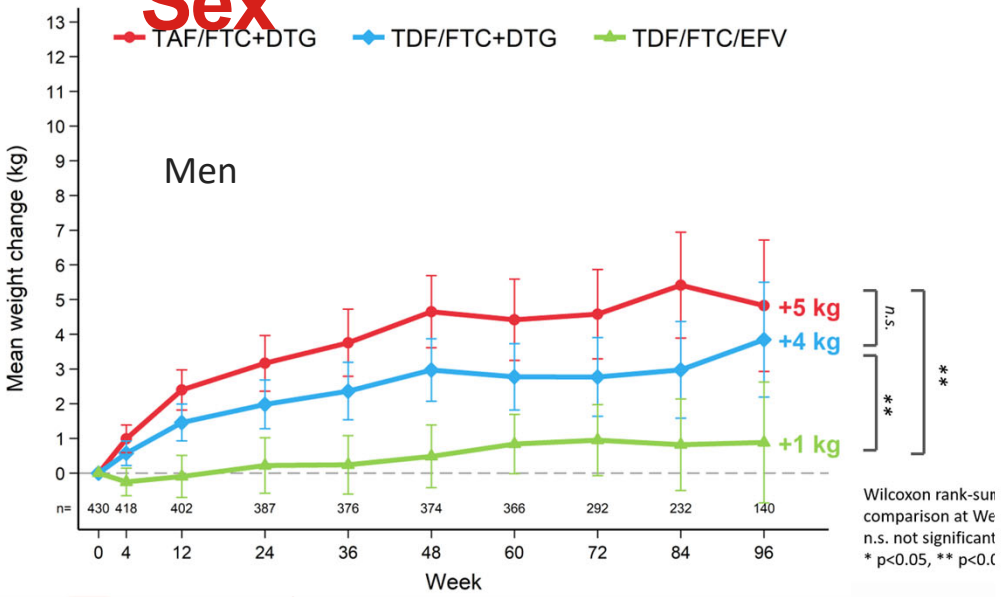


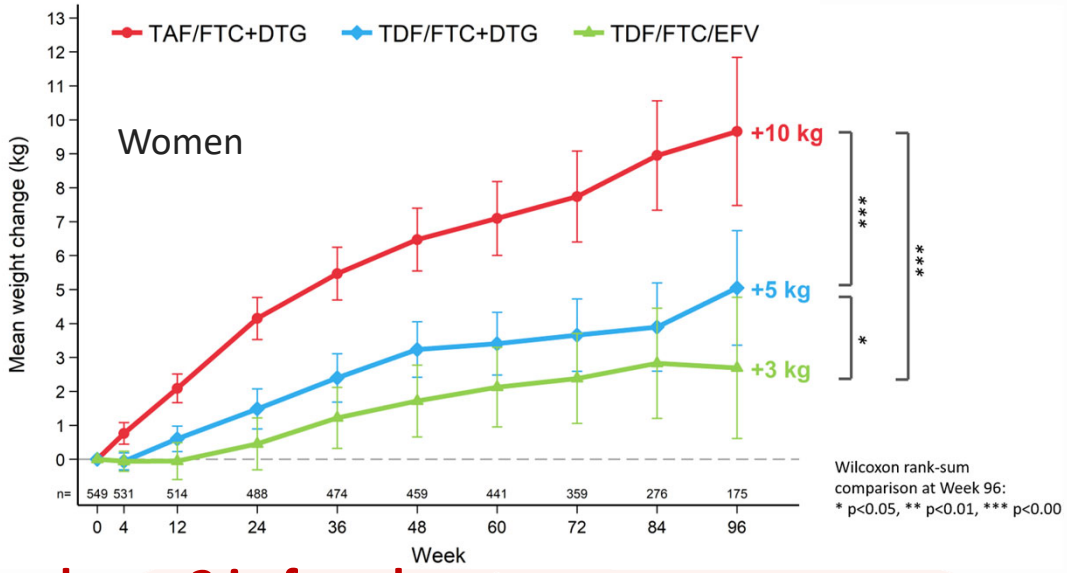


- Females gained more weight than males
- Black participants gained significantly more weight than non-Black participants
- The greatest weight gain was seen among Black females, followed by Black males

Sax et al. Clin Infect Dis. 2020 Sep 12;71(6):1379-1389

Magnitude & Determinants in Africa: ADVANCE - Mean Change in Weight to Wk 96 by Sex



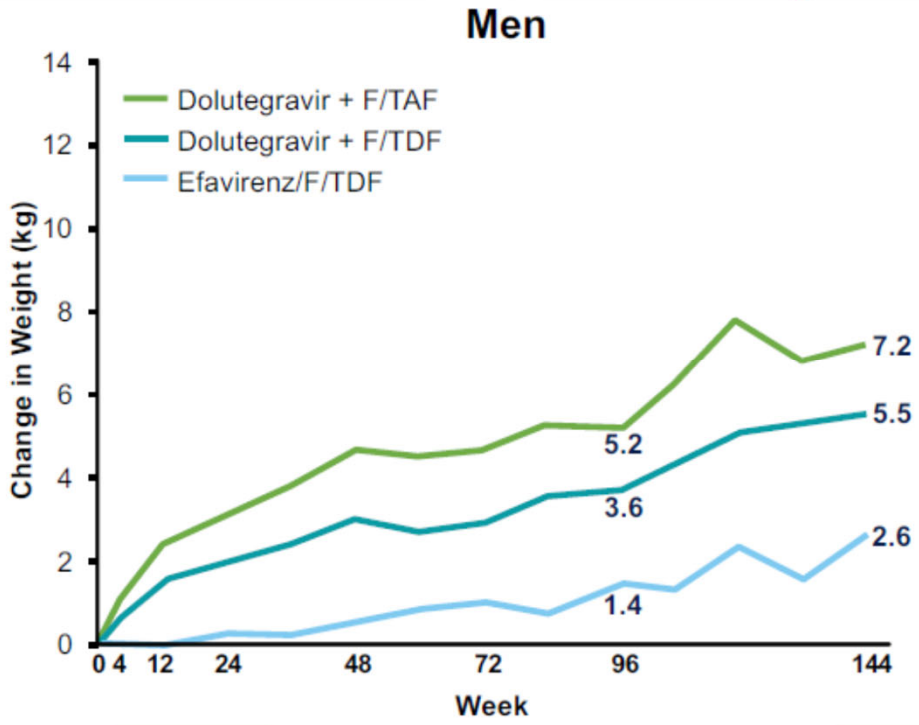


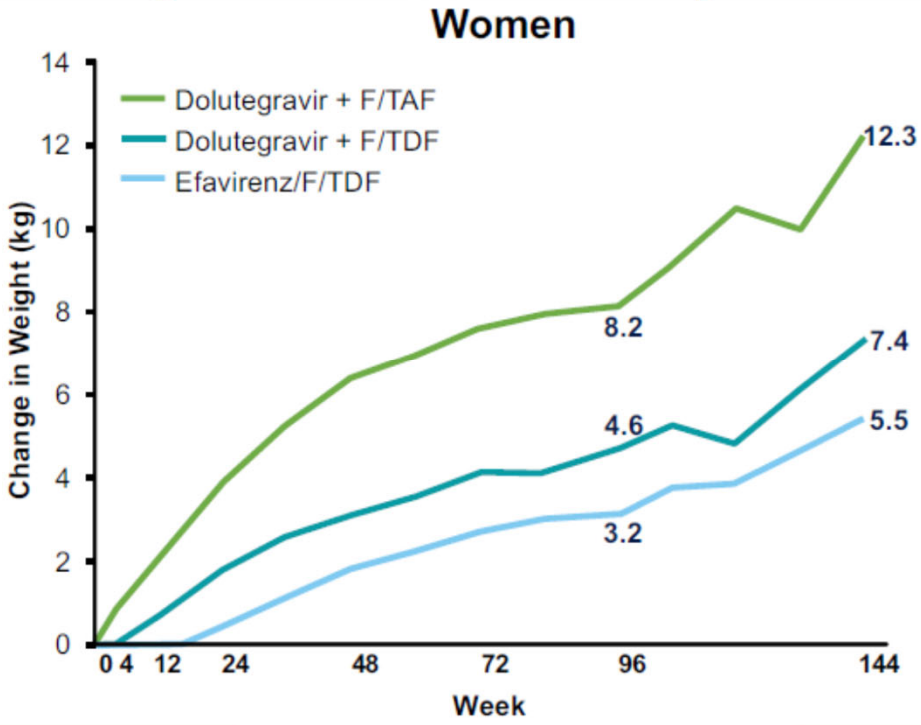
Estimated BMI increase @ 1 year: ≈ 1.5 in males, ≈ 2 in females

	DTG + F/TAF	[illegible]	EFV/F/TDF
≥10% change in body weight (%)	25*†	13*	11
Treatment-emergent obesity (BMI ≥30 kg/m², %)	[illegible]	[illegible]	[illegible]

Venter WF, et al. *N Engl J Med.* 2019;July 24, 2019. [Epub ahead of print]. Hill A, et al. *J Int AIDS Soc.* 2019;22(suppl 5):92. Abstract MOAX0102LB

Magnitude & Determinants in Africa:
ADVANCE - Mean Change in Weight to Wk 144 by Sex



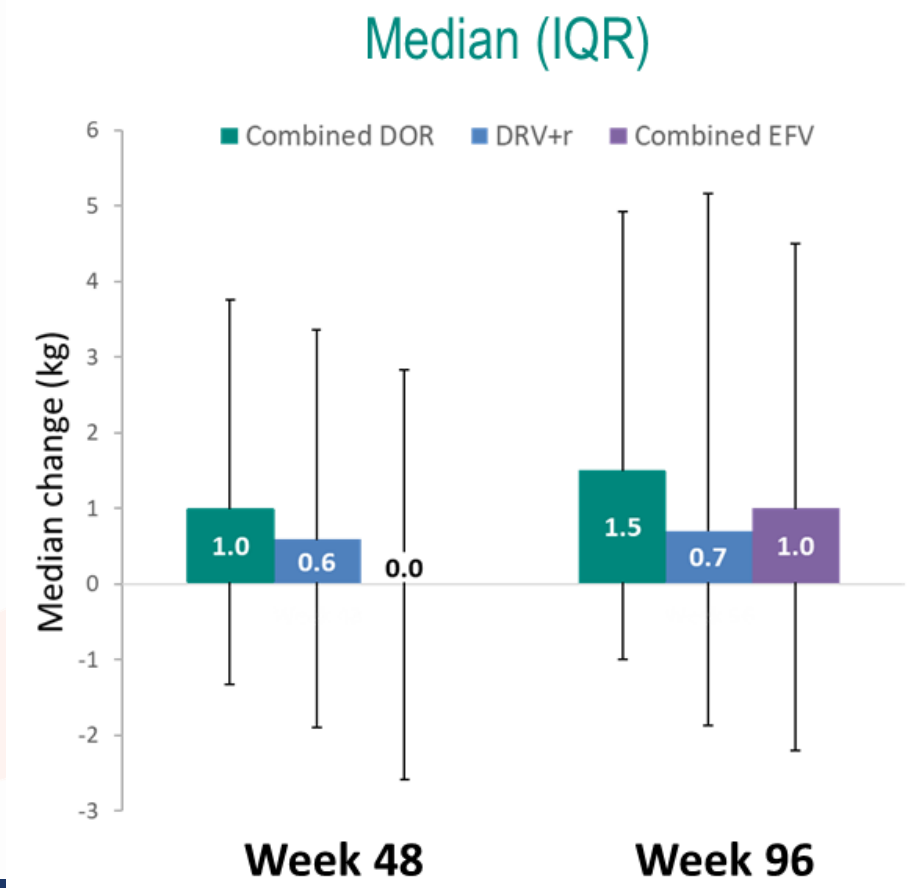


AIDS 2020: 23rd International AIDS Conference Virtual. July 6-10, 2020. Abstract OAXLB0104

Doravirine Weight Gain In Treatment Naïve Individuals

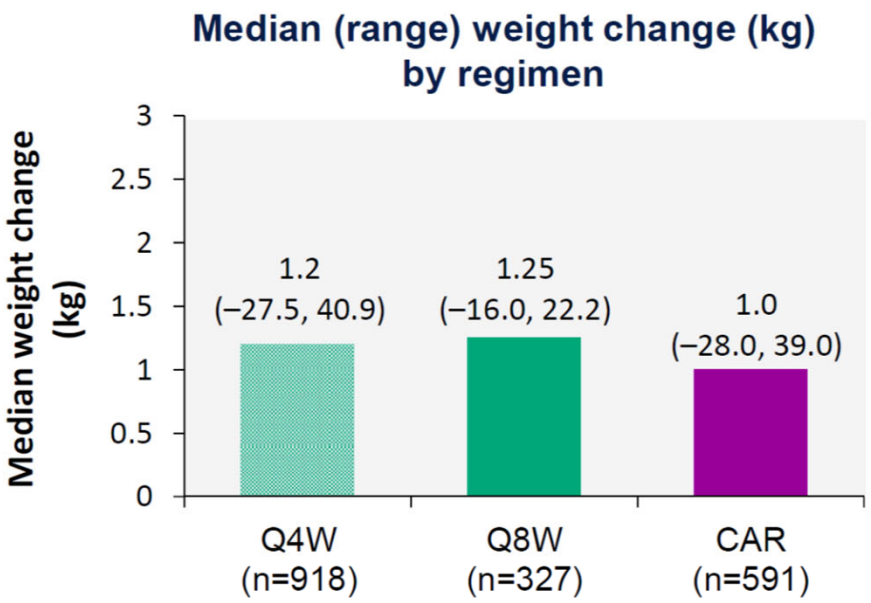
- Post hoc, pooled data analysis of 3 Phase 2/3 clinical trials in treatment naïve patients
  - DOR 100 mg vs EFV 600 mg, with FTC/TDF
  - DOR 100 mg vs DRV+r 800/100, with FTC/TDF or ABC/3TC
  - DOR/3TC/TDF vs EFV/FTC/TDF
- Double blind data through week 96 combined by treatment group

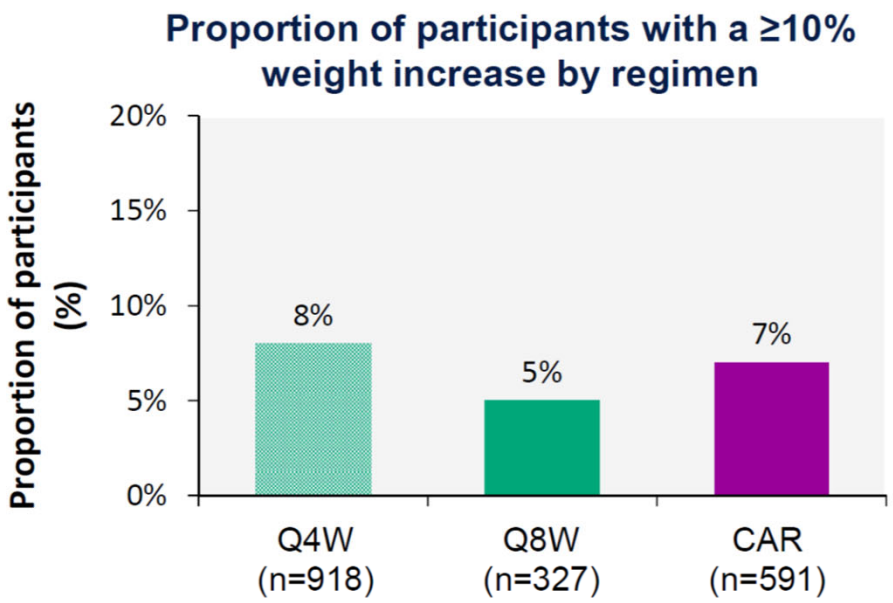
DOR	DRV+r	EFV
N=855	N=383	N=472



Orkin C. EACS 2019; AIDS 2021 Jan 1;35(1):91-99

Weight Change with Cabotegravir/Rilpivirine: Week 48





- Median weight increased from baseline* across all regimens, with slightly higher increases observed in participants receiving CAB + RPV LA vs. those receiving CAR
- The proportion of participants with a ≥10% weight increase was similar for the CAB + RPV LA regimens and CAR

*Median (IQR) weight (kg) at baseline: Q4W, 76.0 (67.0, 85.9); Q8W, 77.0 (68.0, 87.0); CAR, 75.2 (65.4, 85.7).
CAB, cabotegravir; CAR, current antiretroviral regimen; IQR, interquartile range; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

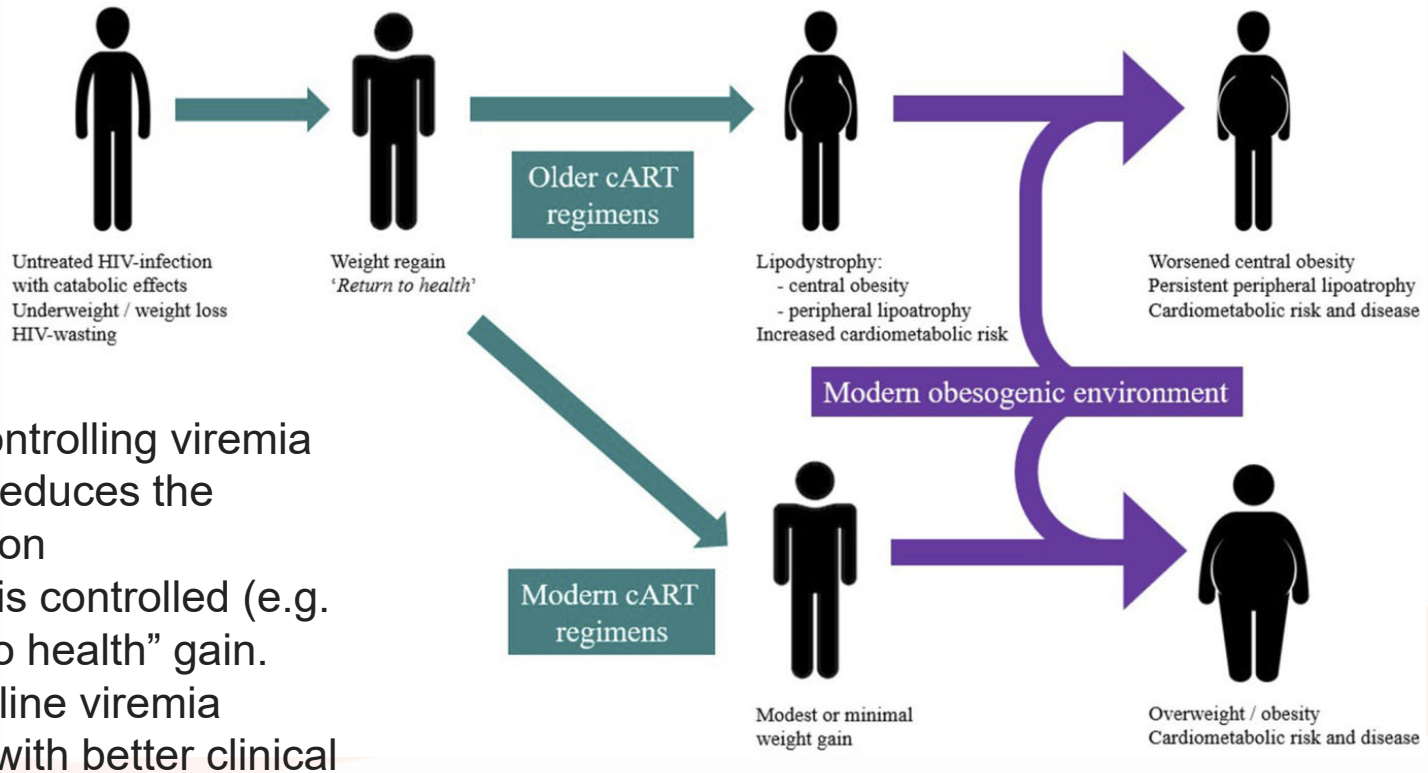
Patel et al. CROI 2021; Virtual. Science Spotlight 1297

Magnitude and Determinants of Weight Gain with ART Initiation in ARV Naïve Patients

- INSTI: Significant weight gain. Greater magnitude of weight gain in people of African descent and women: Probably greater with DTG and BIC than RAL.[4,5,6]
- NRTIs: Greater weight gain with TAF vs. ABC and TDF;[5,6] and greater weight gain with INSTI in conjunction with TAF.[1]
- NNRTI less conducive to weight gain.[5,6,7,8]
- Balance the benefits of INSTIs and TAF with risk of weight gain!

1. Venter. NEJM 2019; 2. Hill. IAS 2019; 3. Bedimo. ID Week 2018; 4. Bourgi. CROI 2019; 5. Bedimo. CROI 2019; 6. Sax. CID 2019; 7. Orkin. EACS 2019; 8. Moestrup. EACS 2019.

Weight Gain with ART Initiation: Return to Health Versus Obesity?



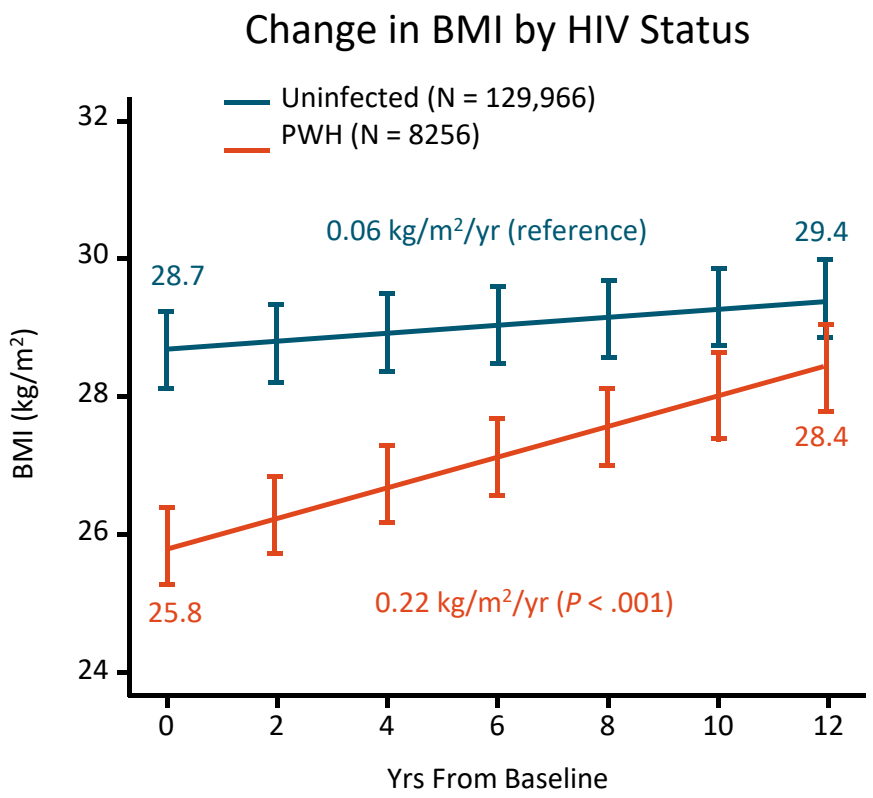
Hypothesis:

- Starting "modern" ART and controlling viremia decreases inflammation and reduces the catabolic effects of HIV infection
- The better and faster viremia is controlled (e.g. with INSTI) the more "return to health" gain.
- Greater gain with higher baseline viremia
- Calorie intake might improve with better clinical status, healthcare services, etc…

Kumar S, et al. *Front Endocrinol.* 2018;9:705.

BMI Changes Over Time in PWH Initiating ART

- Comparison of BMI over time in PWH vs uninfected controls from Kaiser Permanente EMR database (N = 138,222)
  - Study included PWH ≥ 21 yrs of age who initiated ART between 2006-2016 with available baseline BMI
  - Uninfected controls were matched 1:10 by age, sex, race/ethnicity, clinic, yr
- Linear mixed effects modeling* to compare BMI over time by HIV status and baseline BMI



*Potential confounders: sex, age, race/ethnicity, yr, smoking, substance abuse disorder, education/income, insurance, comorbidities.

Silverberg. AIDS 2020. Abtstr OQB0603.

Slide credit: clinicaloptions.com

Case #2: Weight Gain with ART Switch

- MS is a 35 y/o white man on EFV/3TC/TDF for the past 10 years. He has been very reluctant to change a regimen that "saved his life". However, willing to consider, due to persistent insomnia and depressive disorder. CD4 count is 700 cells/μL, VL <20 copies/mL. He's HCV negative and HBV immune. A switch to DTG + FTC/TAF will likely result in:

1. No change in weight, as patient was already virologically suppressed
2. Weight loss, since TAF is associated with fewer metabolic complications
3. Weight gain because of switch from TDF to TAF
4. Weight gain because of switch from EFV to BIC
5. Both 3 and 4

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Magnitude of Weight Gain with INSTI: Rx Experienced

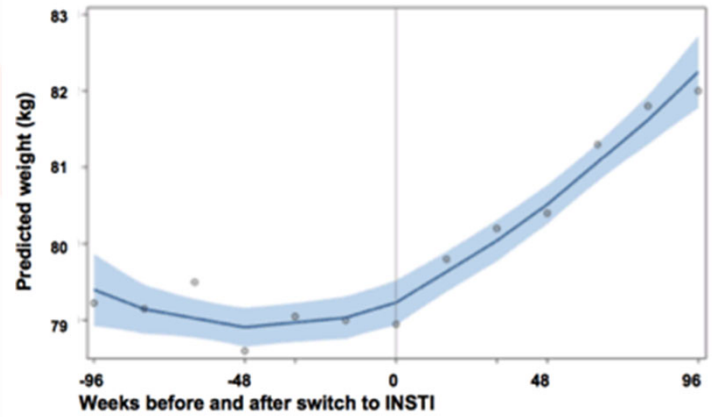
ACTG: A5001 & A5322 (n=691)

Adjusted yearly weight change (Kg/yr):

DTG: 1.0 (p<0.001); EVG: 0.5 (p=0.11); RAL: -0.2 (p=0.37)

In adjusted models, black race, age ≥60 and BMI ≥30 kg/m^2 were associated with greater weight gain

Switch to INSTI + ABC and EVG + TAF predictor (small #s)

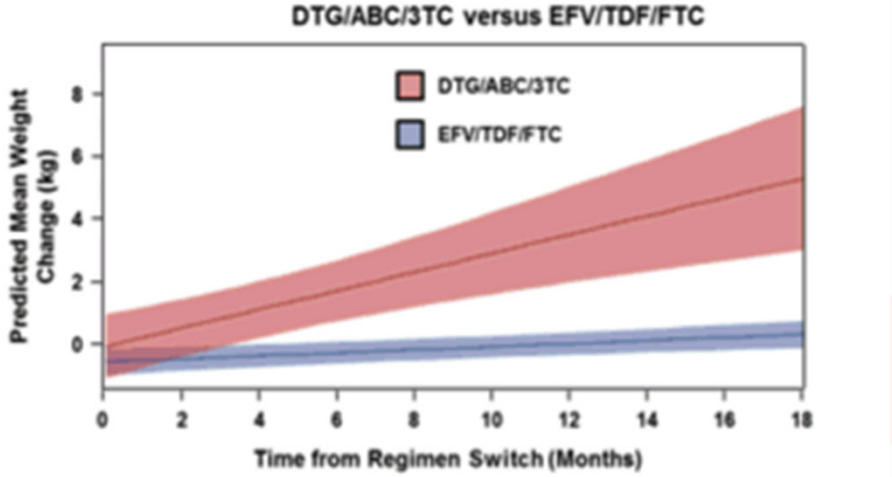


Lake. CROI 2019; Abstract 669; CID 2020 [Epub ahead of print]

Retrospective, single-site study (n=495)

Patients on EFV/TDF/FTC switched to INSTI (DTG/ABC/3TC; RAL/TDF/FTC or EVG/c/TDF/FTC) vs. continued

Weight gain highest with switch to DTG/ABC/3TC



Norwood. JAIDS 2017 Dec 15;76(5):527-531

Weight Gain with Switch to INSTI

NA-ACCORD

INSTI distribution: 870 Total; 431 RAL; 263 EVG; 176 DTG

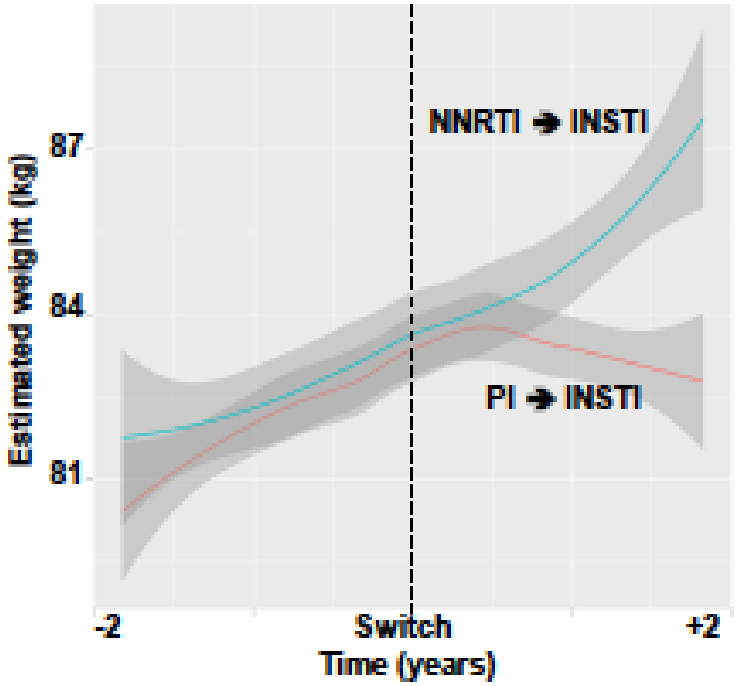


Figure. Unadjusted estimated weight for all persons before and after switch to INSTI by pre-switch regimen

Regimen switch	Pre-switch weight slope (kg/year)	Post-switch weight slope (kg/year)	P-value for slope change
NNRTI → INSTI	0.63	1.13	< 0.001
NNRTI → DTG	0.84	1.73	< 0.001
NNRTI → RAL	0.74	0.97	0.21
NNRTI → EVG	0.56	1.00	0.07
PI → INSTI	0.80	0.34	< 0.001
PI → DTG	0.84	-0.04	< 0.001
PI → RAL	0.74	0.17	< 0.001
PI → EVG	0.56	0.89	0.11

Table 2. Adjusted pre- and post-switch weight slopes by individual INSTI agents

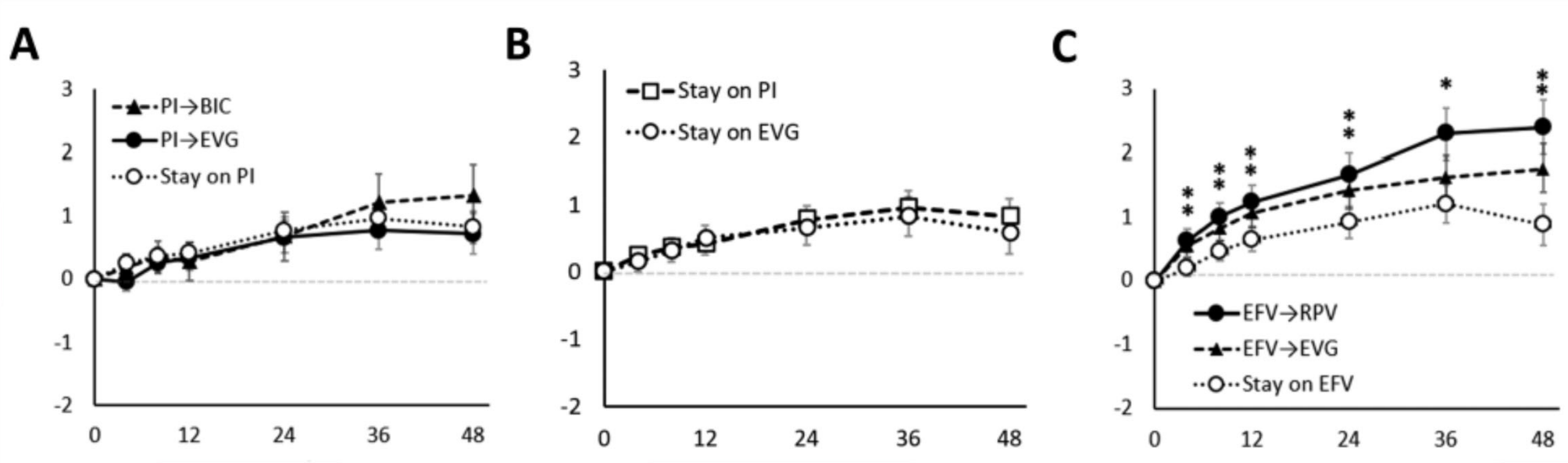
Women, non-whites and older PWH with viral suppression had greater annualized weight gain after switch from NNRTI- to INSTI-based ART; Greatest for DTG

Slowing of weight gain with switch from a PI

Koethe. CROI 2020; Abstract 668

Weight Gain after Switch from PI or NNRTI to INSTI

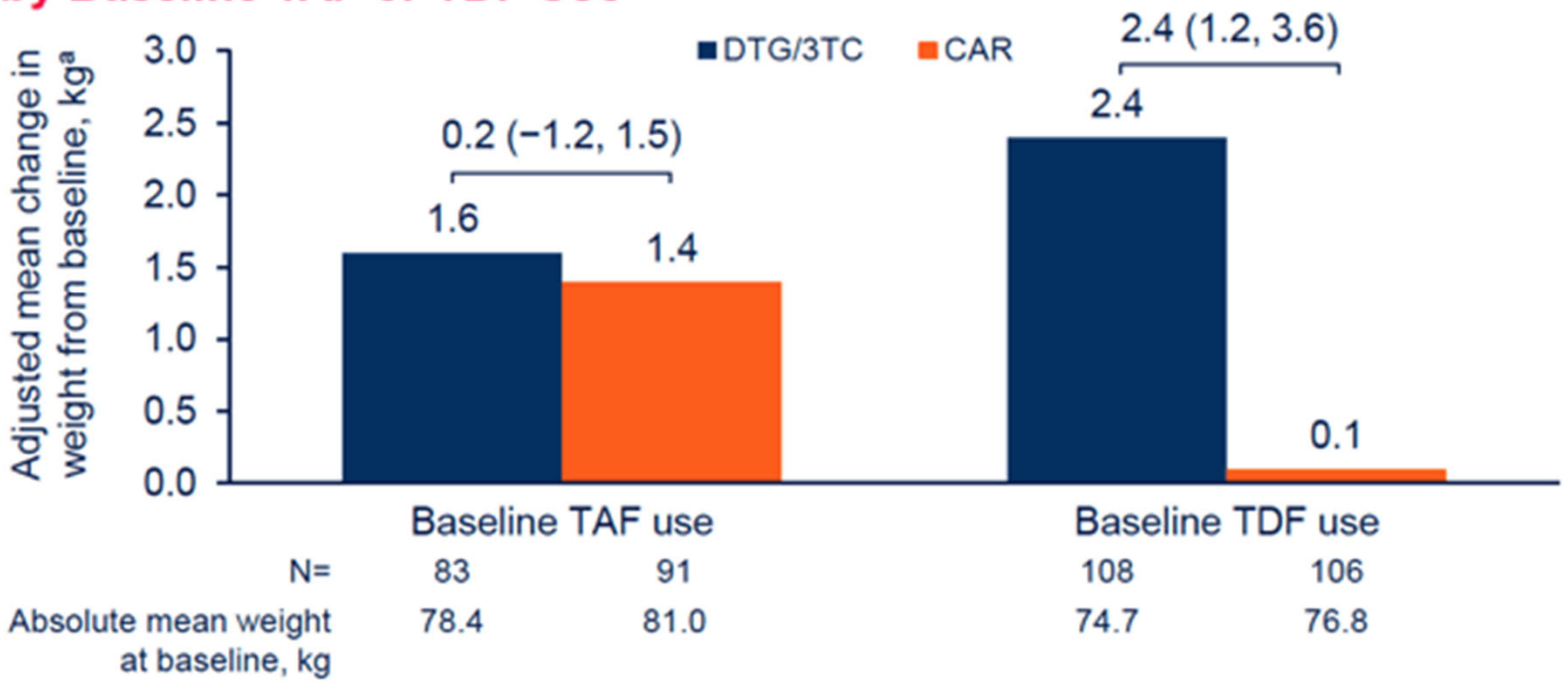
Pooled analysis of 12 prospective clinical trials, wherein virologically suppressed PLWH were randomized to switch or remain on a stable baseline regimen (SBR).



Erlandson. CID. 2021 Oct 20;73(8):1440-1451

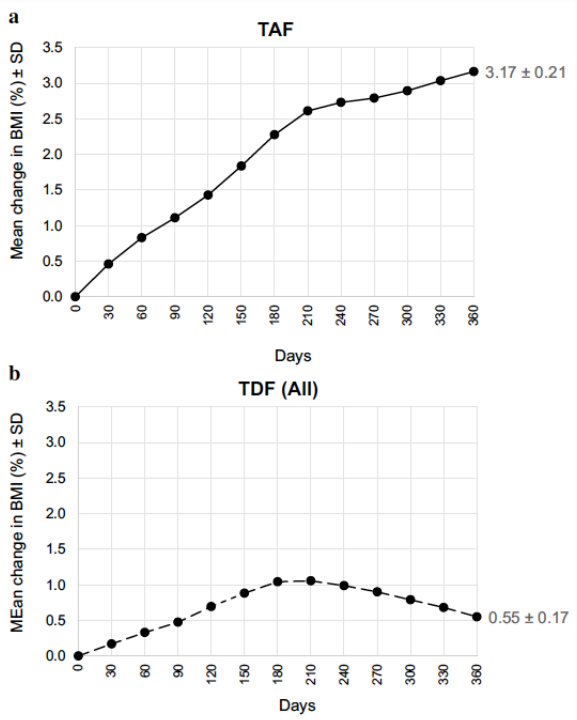
Magnitude of Weight Gain with INSTI: Rx Experienced

Figure 2. Adjusted Mean Change in Weight From Baseline to Week 48 by Baseline TAF or TDF Use



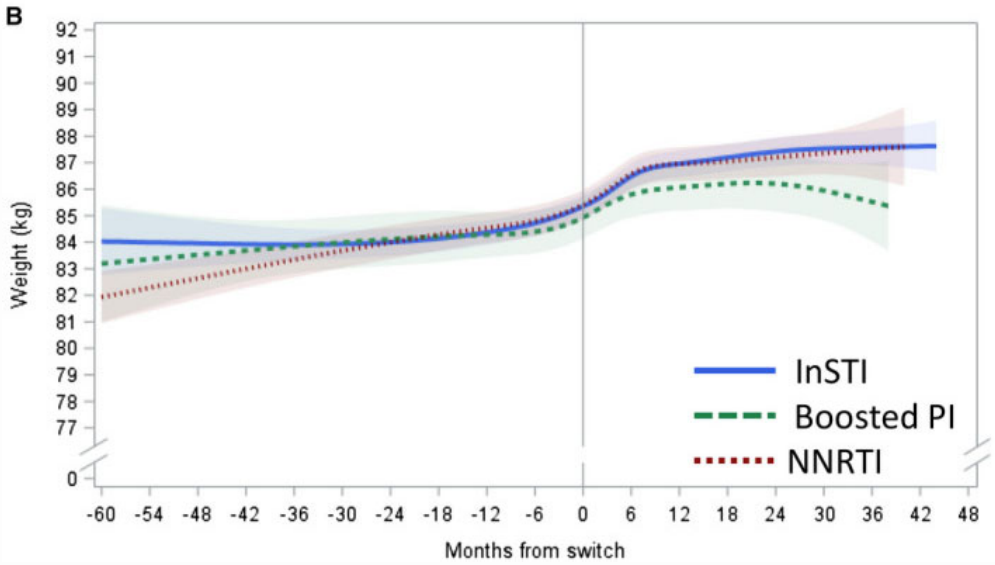
Hagins et al. SALSA trial. CROI 2022; Abstract 603

Weight Gain with NRTI Switch: TDF to TAF



German Cohort:
Switch from TDF to TAF: +2.3 kg.[1]

Gomez. Infection 2019; 47:95-102; 2



OPERA Cohort:

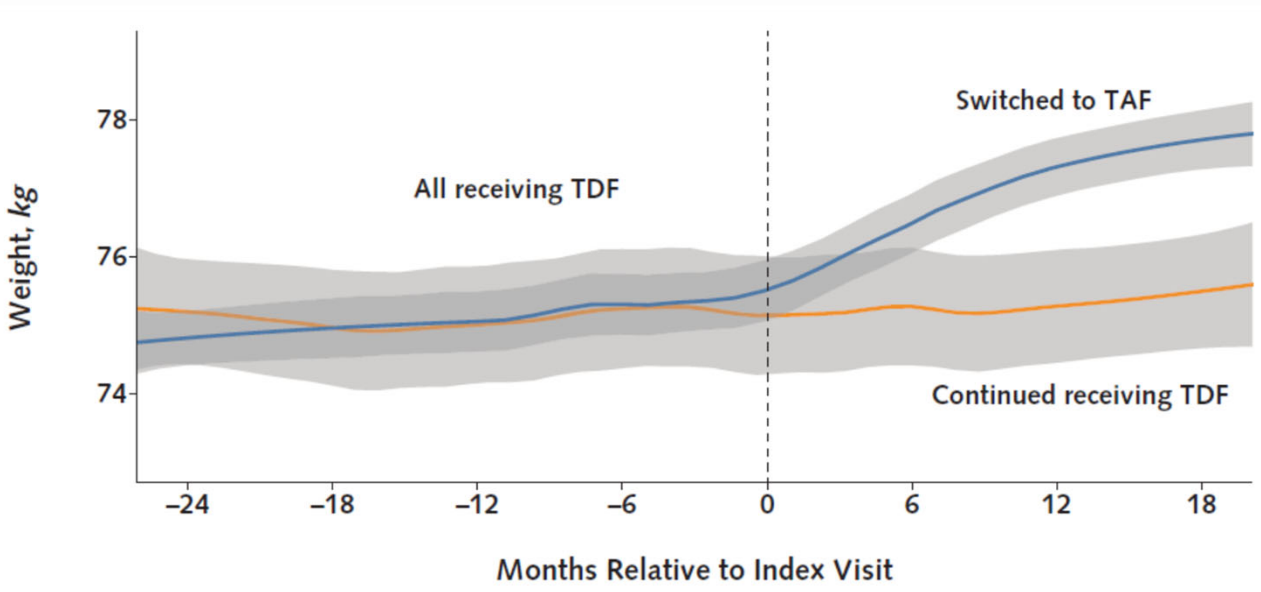
Switching to TAF was associated with early, pronounced weight gain for all (1.80 to 4.47 kg/year).

Weight gain tended to slow down or plateau approximately nine months after switch to TAF.

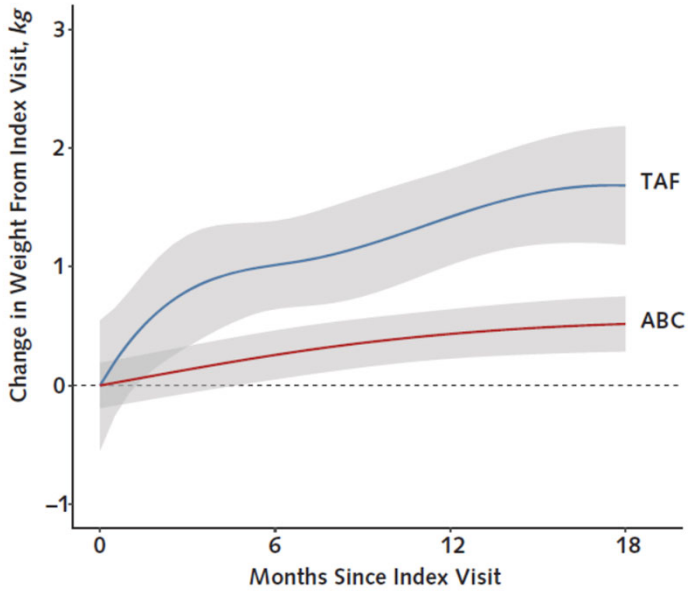
Mallon. J Int AIDS Soc. 2021 Apr; 24(4): e25702.

Weight Gain after Switch from TDF to TAF, or ABC to TAF

Swiss Cohort: 4375 adults living with HIV who received TDF-containing ART for 6 months or longer.



Patients who received ABC and continued ABC (n = 2560) or switched to TAF(n = 427).



Surial. Ann Intern Med 2021 Jun;174(6):758-767

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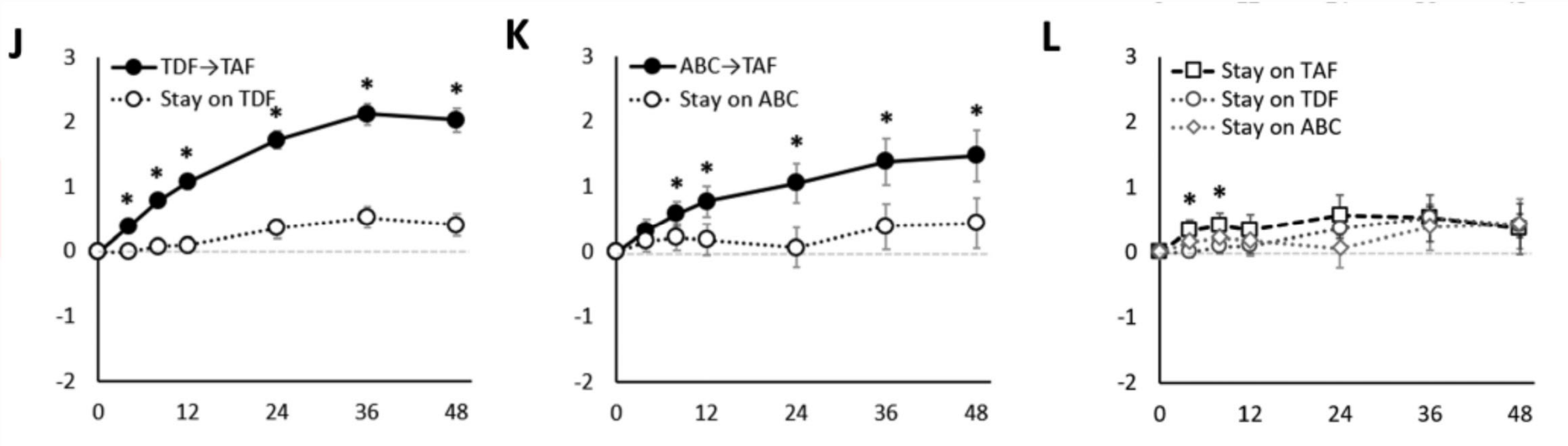


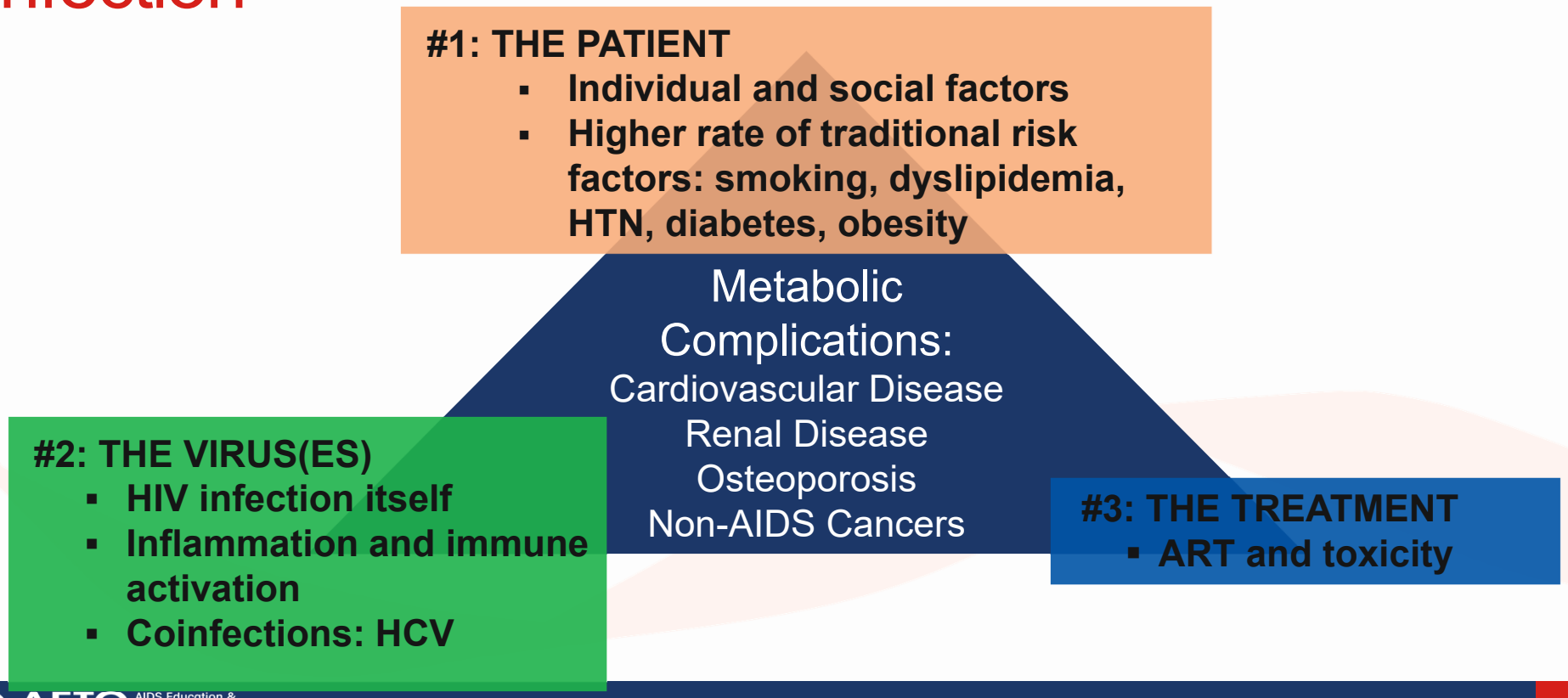
Erlandson. CID. 2021 Oct 20;73(8):1440-1451

Weight Gain with ART-Experienced

- Weight gain occurs in both ARV-naïve and ARV-experienced (INSTI and TAF) and in uninfected (TAF)
  - This suggests different/additional mechanism(s) of action than reversal of catabolism/inflammatory changes in adipose tissue.
  - Phenotypic (pro-inflammatory) modulation of adipose tissue?
- Possible mechanism(s): INSTIs induce adipocyte dysfunction: adipogenesis, lipogenesis, oxidative stress, fibrosis, and insulin resistance.[1]

1. Gorwood.*Cells* **2020**, *9*(4),854;

Examining Weight Gain in the Context of Pathogenesis of Chronic Complications of HIV Infection



#1: The Patient: Intersection of HIV and Obesity Epidemics:

Obesity in the World:

- Worldwide obesity has nearly tripled since 1975.
- In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 650 million were obese.
- 39% of adults aged 18 years and over were overweight in 2016, and 13% were obese.

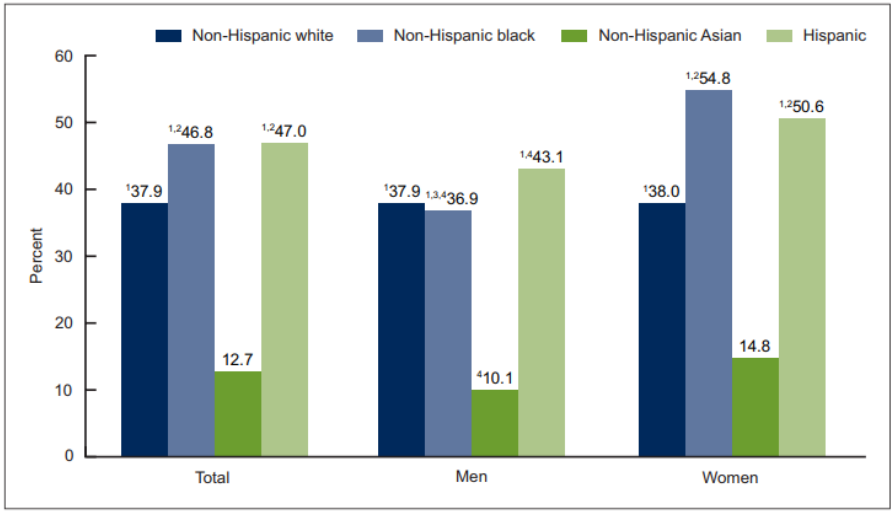
https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight

Obesity in the US:

- The prevalence of 39.8% in 2016.

Affected mostly Blacks and Hispanics

Figure 2. Age-adjusted prevalence of obesity among adults aged 20 and over, by sex and race and Hispanic origin: United States, 2015–2016

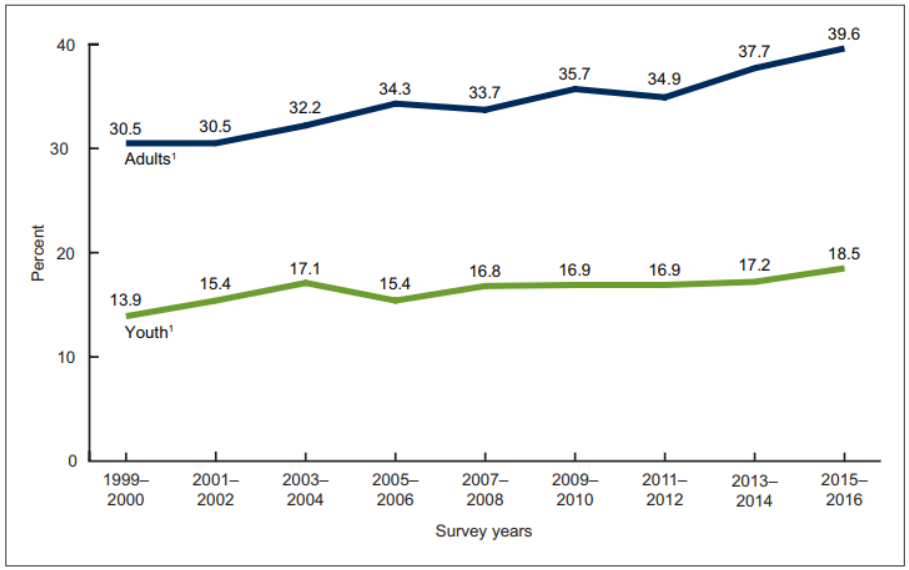


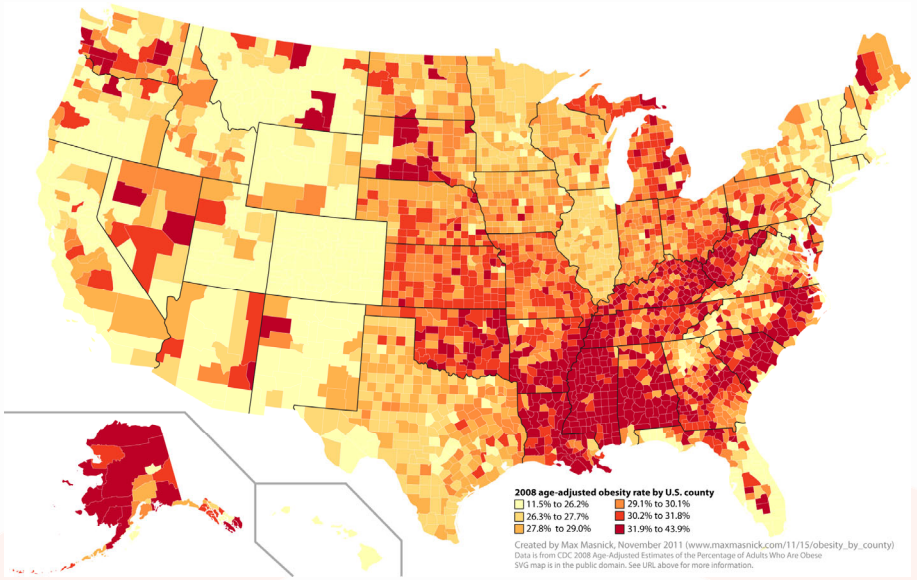
https://www.cdc.gov/nchs/data/databriefs/db288.pdf

Obesity is getting worse

And overlaps with poverty and HIV

Figure 5. Trends in obesity prevalence among adults aged 20 and over (age adjusted) and youth aged 2–19 years: United States, 1999–2000 through 2015–2016

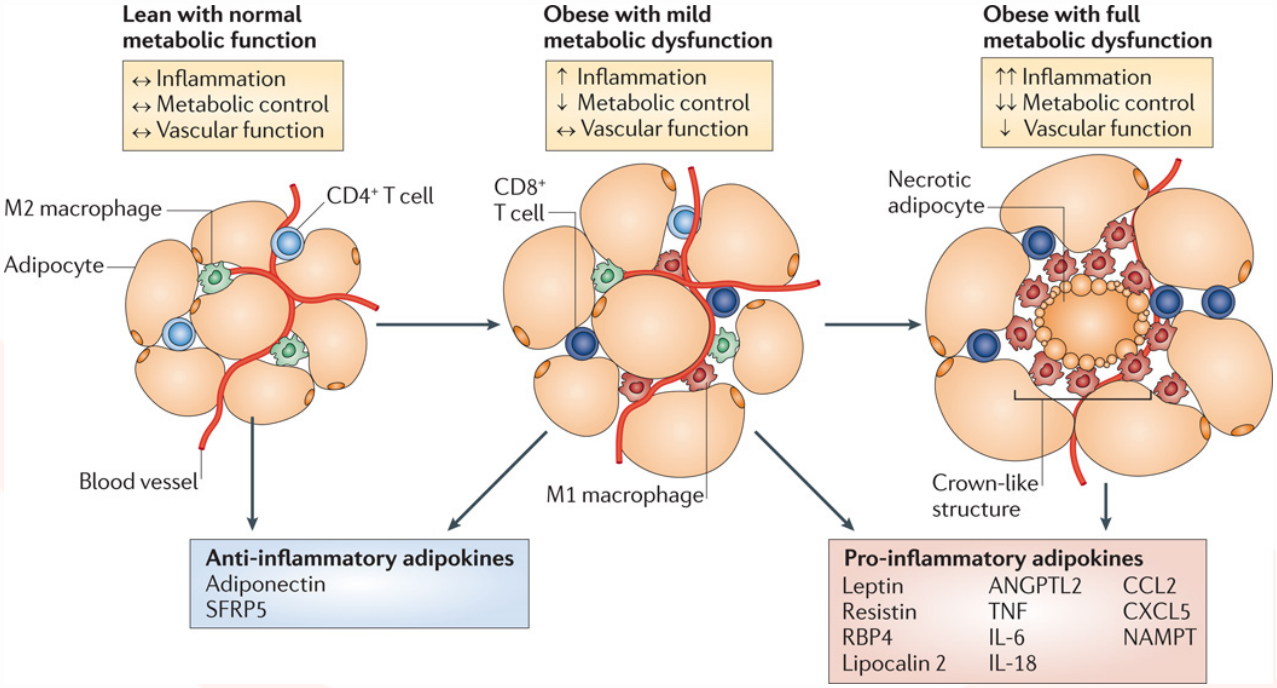




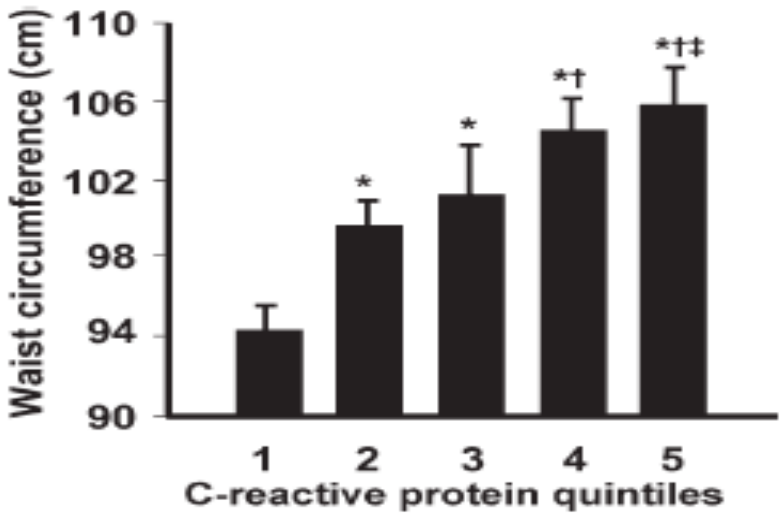
Like HIV, higher prevalence of obesity in the South, in Blacks & Hispanics, in low income households

https://www.cdc.gov/nchs/data/databriefs/db288.pdf

Obesity-Induced Inflammatory Changes in Adipose Tissue – Phenotypic Modulation



Ouchi et al. Nat Rev Immunol. 2011 Feb;11(2):85-97

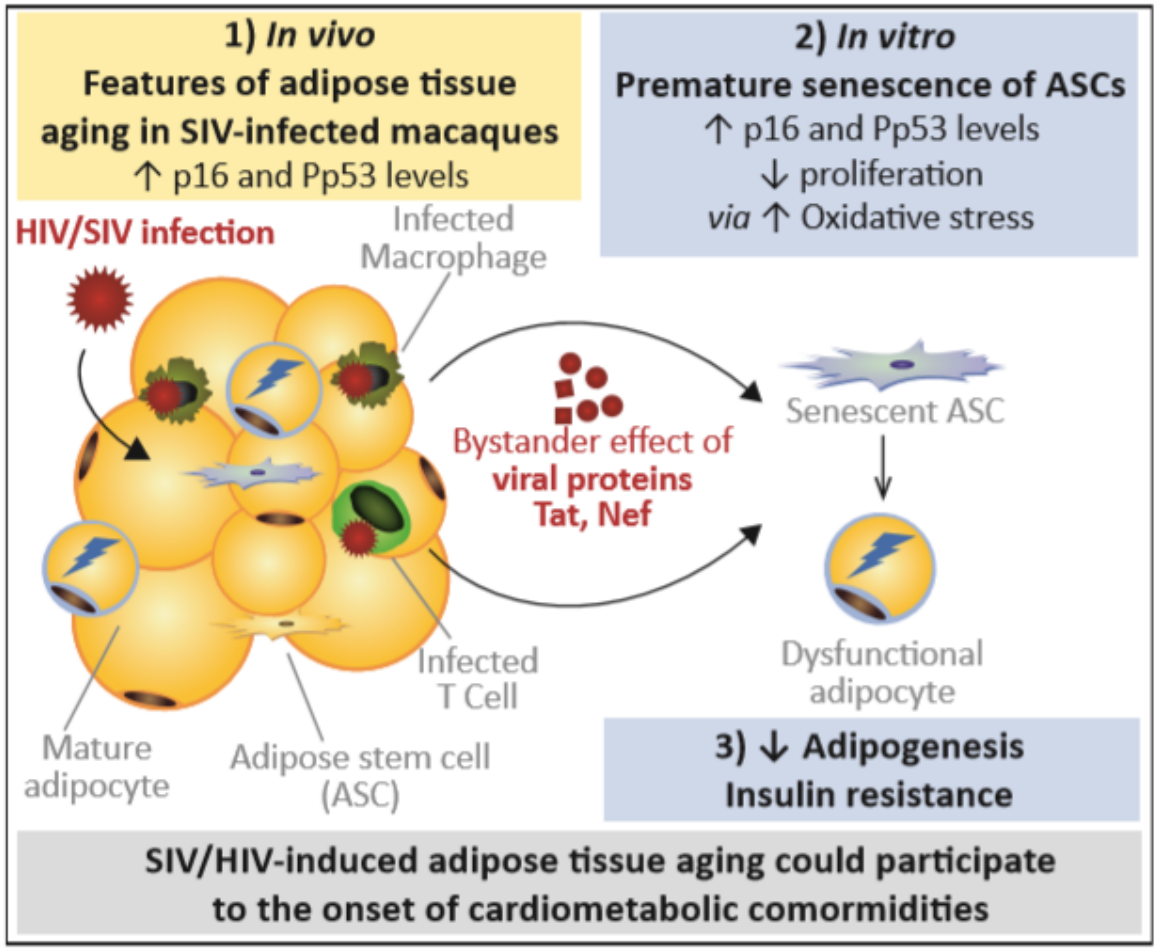


Samaras K et al. Obesity 2008;17:53-59

Need to understand mechanisms and metabolic implications of weight gain in HIV

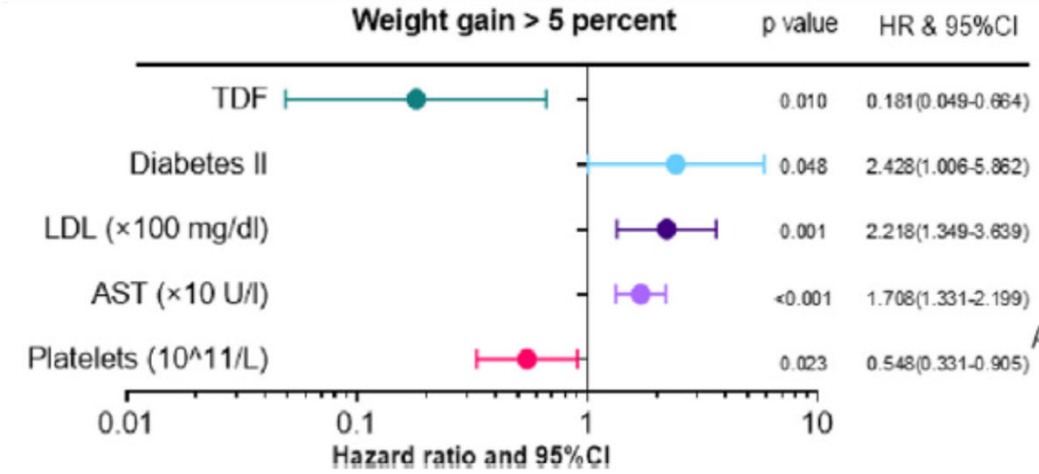
#2: The Virus: HIV Induces Adipocyte Dysfunction

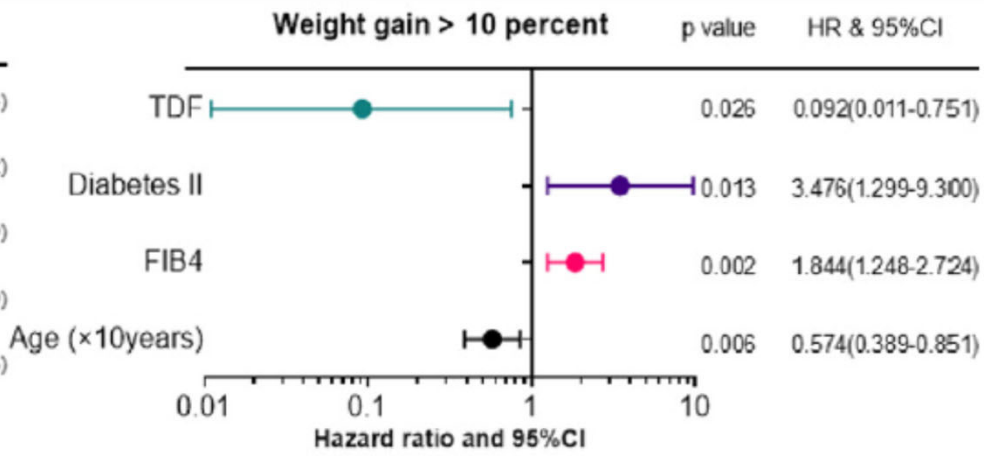
Gorwood.*Cells* **2020**, *9*(4),854; https://doi.org/10.3390/cells9040854



#2 The Patient or the Treatment?: Weight Change on ART

- Prospective cohort of 319 HIV mono-infected on ART;
  - 64 (25%) and 34 (13%) gained >5% of and >10% of weight, respectively
- Predictors of weight gain:
  - Exposure to INSTIs or TAF did not predict weight increase. TDF predicted weight loss (caveat: mean exposure to INSTIs and TAF were 31 and 33 months resp; Weight gain is "front loaded" in most cohort)

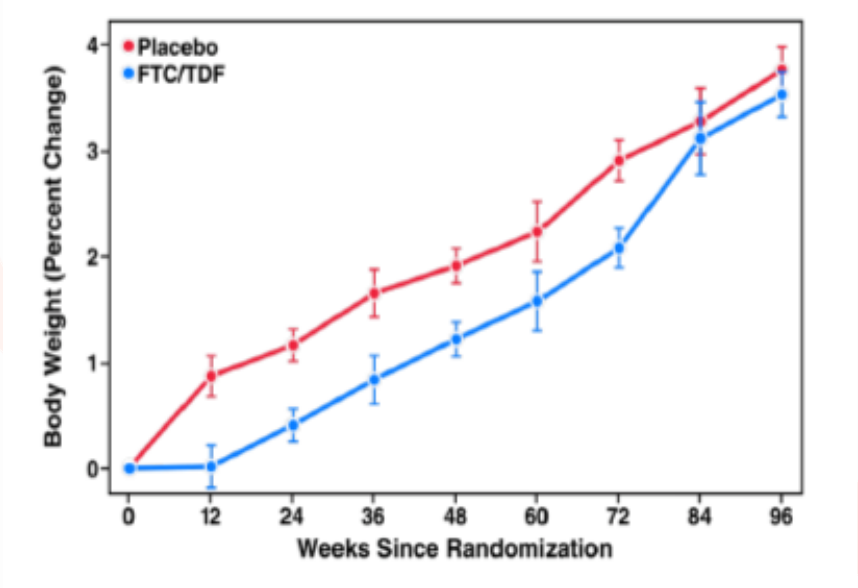




Bischoff. EClinicalMedicine 2021 Sept 5;40:101116

#3: The Treatment: Weight Gain on PrEP Studies: iPrEX: FTC/TDF vs. Placebo HPTN 083

- Placebo (n=1225)
- TDF/FTC (n=1226)
- Delayed weight gain in treatment group



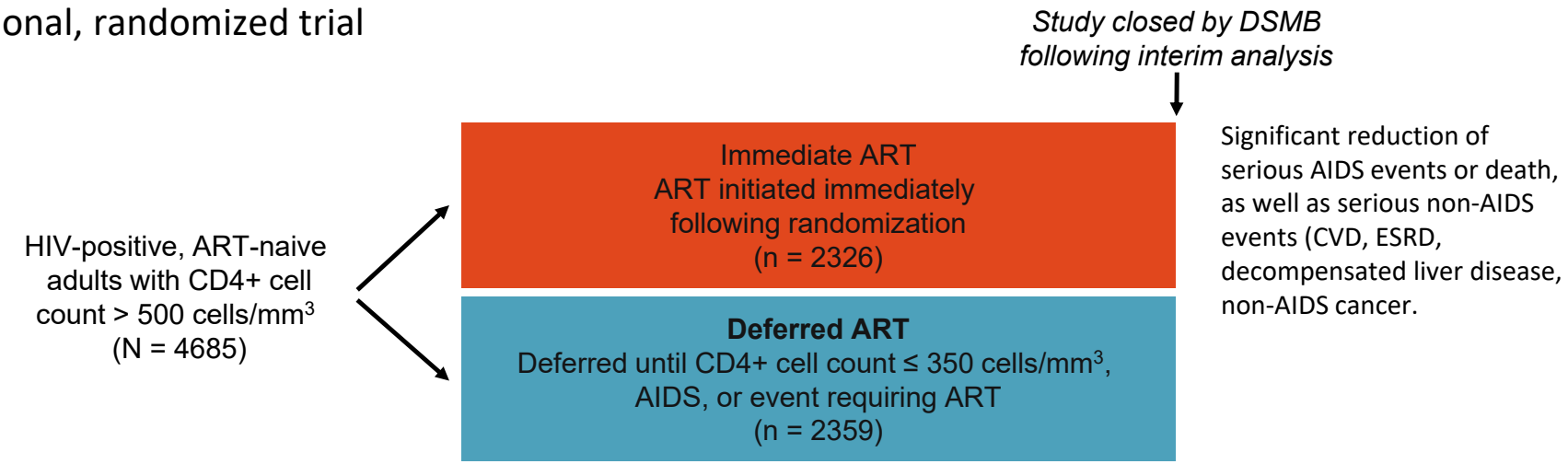
Grant. NEJM 2010;363: 2587-99

- Overall, significantly greater median weight increase from BL with CAB vs FTC/TDF ($P < .001$)
  - CAB: +1.30 kg/yr (95% CI: 0.99-1.60)
  - FTC/TDF: +0.31 kg/yr (95% CI: -0.12 to -0.49)

Landovitz. AIDS 2020. Abstr OAXLB0101

START: Immediate vs Deferred Therapy in ART-Naïve

- International, randomized trial



Mean percent change in weight from baseline:

Immediate: 1.1% (95% CI: 0.9 – 1.5)

Deferred: 1.9% (95% CI: 1.7 – 2.2)

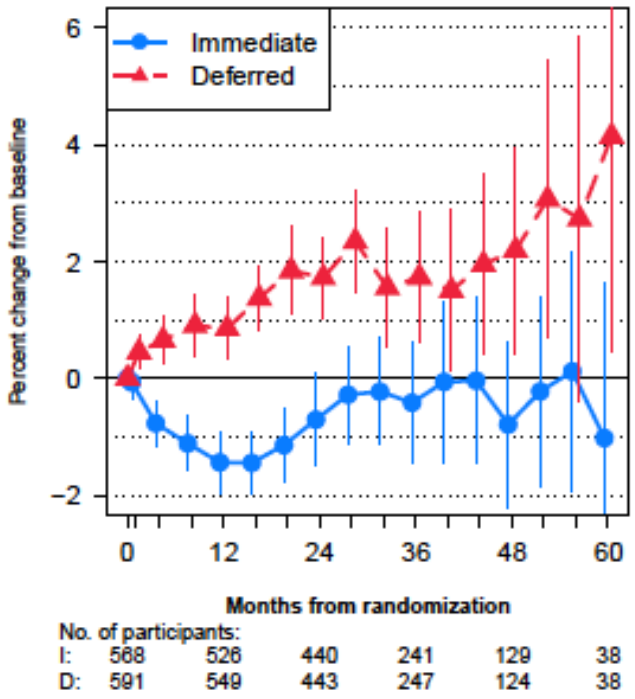
Important to note:

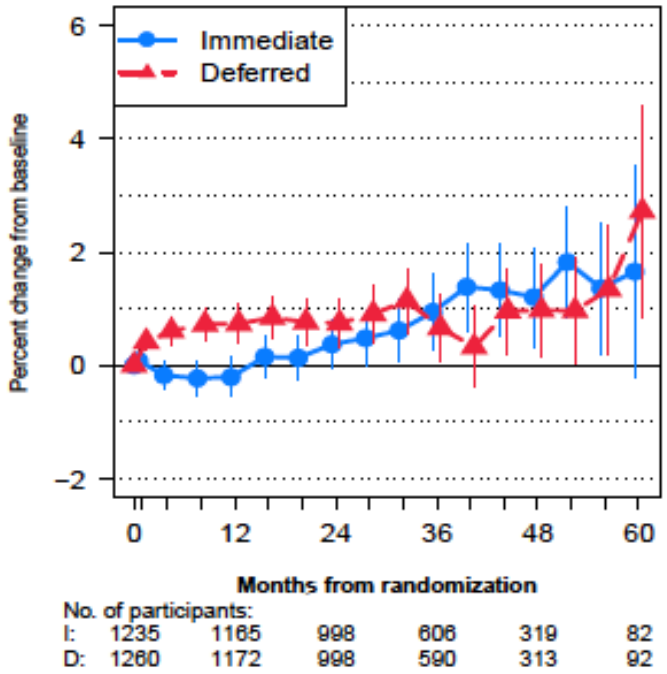
Most patients (80%) are on NNRTI; <4% on INSTI

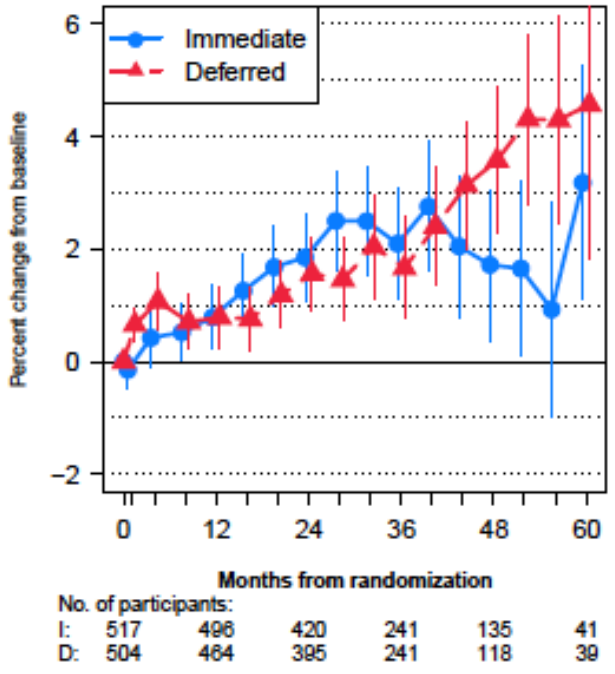
Very high median CD4 count (650), and rather low median viremia (12.7K).

INSIGHT START Group. N Engl J Med. 2015;373:795-807. Lundgren J, et al. IAS 2015. Abstract MOSY0302.; Moestrup. EACS 2019

START: Weight Change by Baseline Viremia



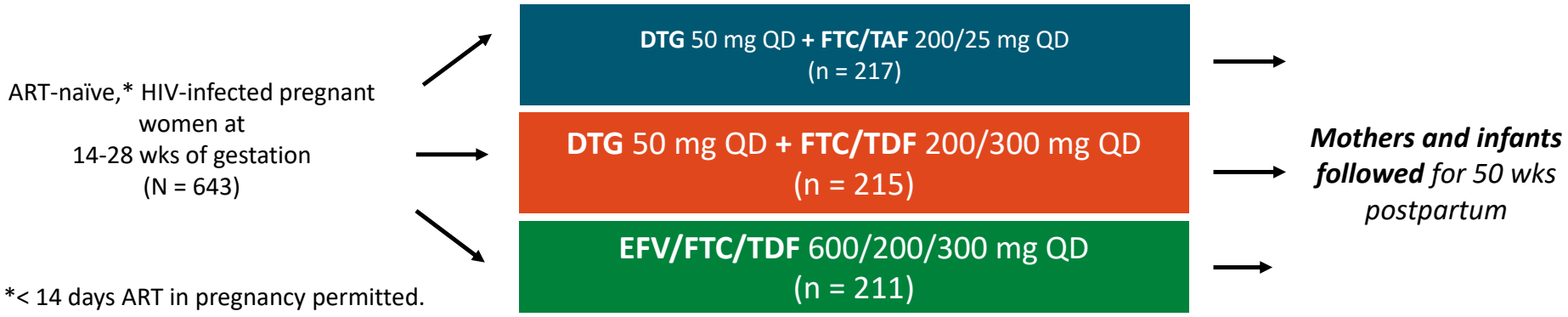




ART with NNRTI might actually prevent weight gain that would have occurred; especially if b/l CD4 is high and b/l viremia is low…

IMPAACT 2010: Average Weekly Maternal Weight Gain

- Randomized, open-label, international, phase III noninferiority trial



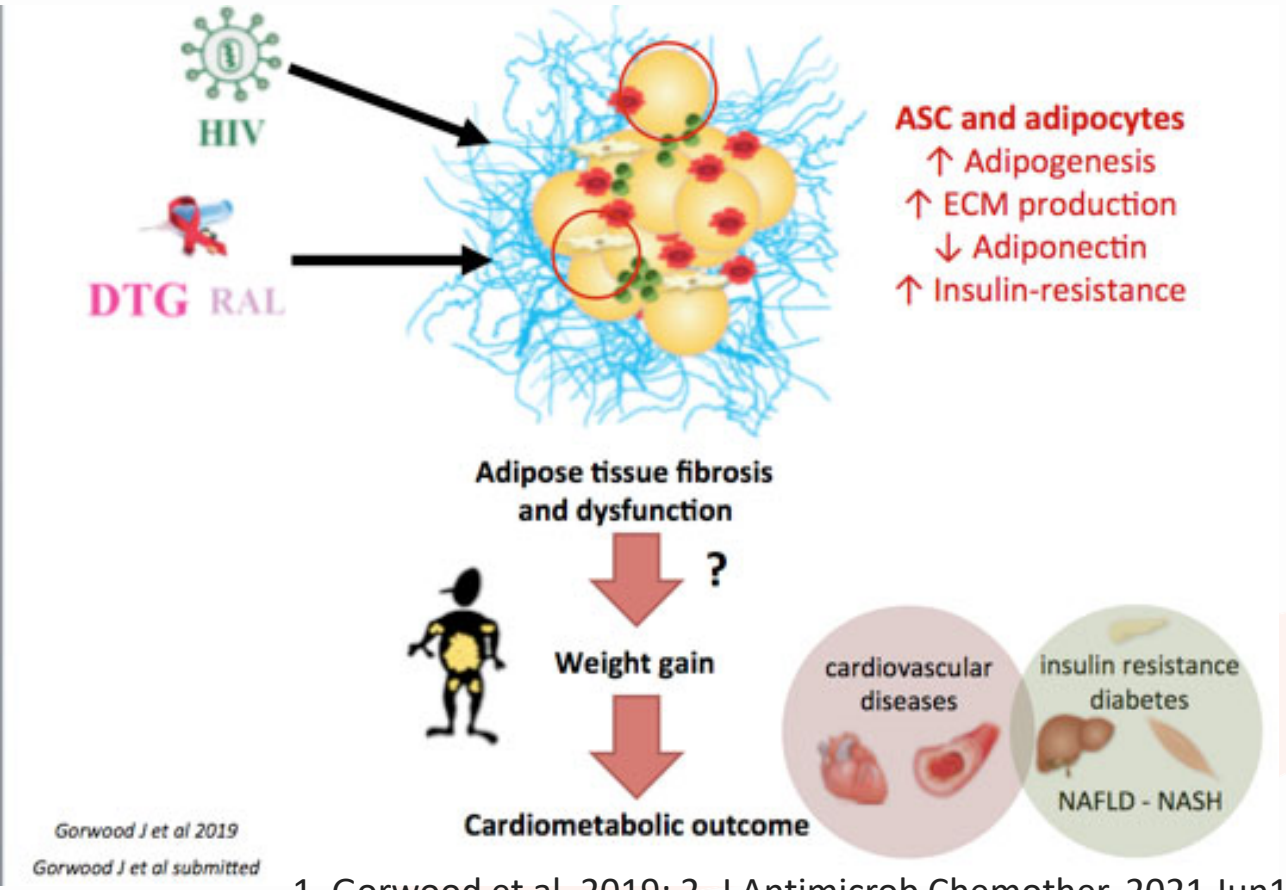
Maternal Weight Gain[1]	DTG + FTC/TAF	DTG + FTC/TDF	EFV/FTC/TDF
Average weekly maternal weight gain, kg	0.378*	0.319	0.291

**P* = .011 vs DTG + FTC/TDF and *P* < .001 vs EFV/FTC/TDF.

- Recommended maternal weekly weight gain in second and third trimesters, according to IOM: 0.45 kg[2]
- Also, post-partum mean weight was 4.35 kg greater with DTG vs EFV, in DolPHIN-2 [3] and 5 Kg greater in Tshilo Dikotla cohort study. but DTG weight gain similar to that of women without HIV [4]

1. Chinula. CROI 2020. Abstr 130LB. 2. IOM Pregnancy Weight Guidelines. 2009.; 3. Malaba CROI 2020; abstract 771; 4. Jao. CROI 2020; abstract 771

Potential Mechanisms of Weight Gain on ART?



- DTG and RAL increased ECM production in ASCs and adipocytes. They induced adipocyte dysfunction and insulin resistance.[1]
- NEAT 022: Switch from PI to INSTI associated with decreased LDL, TC/HDL, CRP & sCD14, but decreased adiponectin.[2]
  - Percent change in adiponectin correlated inversely with percent change in BMI.

1. Gorwood et al. 2019; 2. J Antimicrob Chemother. 2021 Jun13;dkab158. doi: 10.1093/jac/dkab158

Case #3: Cardiometabolic Risk of Weight Gain on ART

- WG is a 30 y/o white woman who has been on DTG + TAF/FTC for the past 2 years. VL <20 copies/mL. CD4 count: 640 cells/μL. Since ART initiation, she gained 30 lbs (210 lbs to 240 lbs). Her fasting blood glucose increased from 99 to 135 mg/dL. She reports no change in diet or exercise level. Studies so far have shown which of the following cardiovascular or metabolic risk of her weight gain?

1. There is no risk for metabolic complications. Most of the weight gain is lean, not fat mass
2. Decreased risk of insulin resistance
3. Increased risk of metabolic syndrome
4. Increased risk of cardiovascular disease

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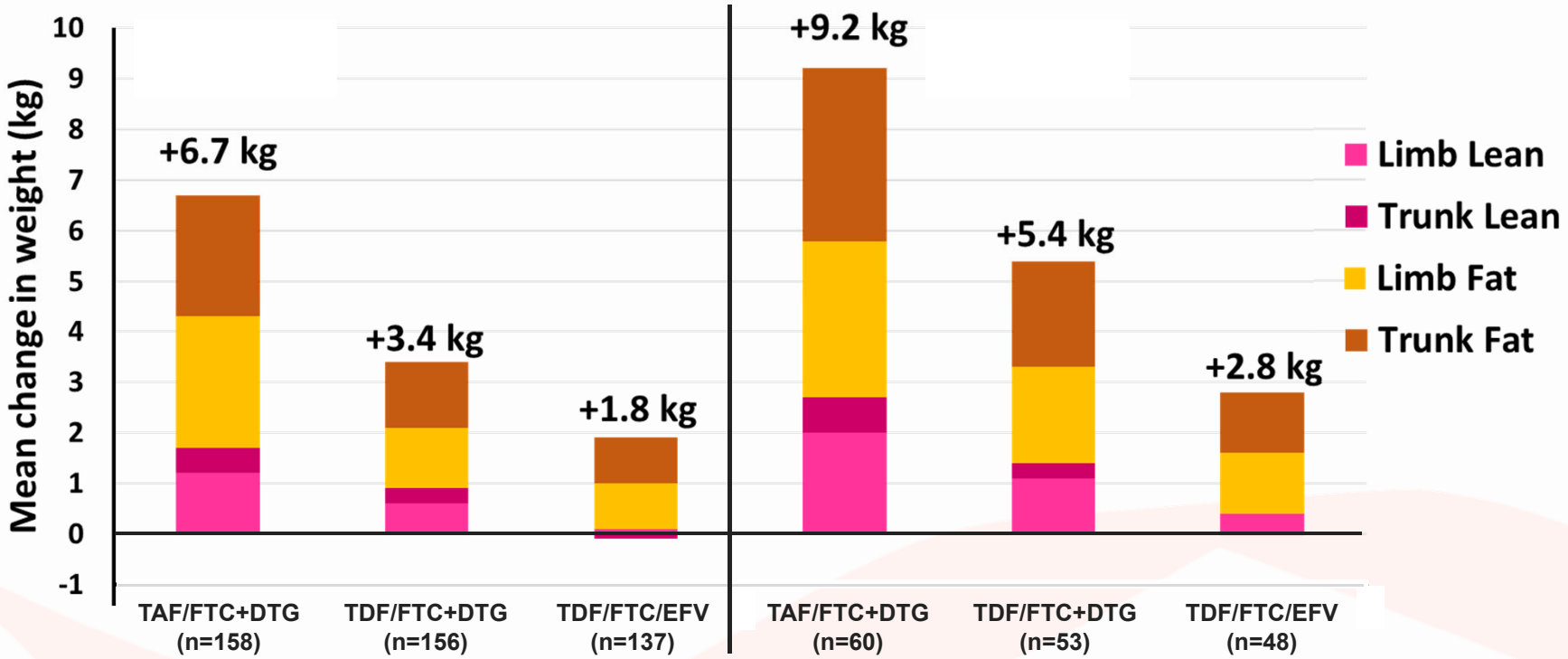
4. Increased risk of cardiovascular disease

Implications of obesity in the general population

- High BMI accounted for 4.0 million deaths globally, nearly 40% of which occurred in persons who were not obese.[1]
- More than two thirds of deaths related to high BMI were due to cardiovascular disease.
- Raised BMI is a major risk factor for non-communicable diseases such as[2]:
  - ASCVD, DM, Musculoskeletal disorders (especially osteoarthritis);
  - Some cancers (including endometrial, breast, ovarian, prostate, liver, and colon).
- These are the leading causes of morbidity and mortality in virologically suppressed PWH.
- DM risk with weight gain at ART initiation is greater than comparable gain in non-HIV comparators.[3]
  - 5 lbs weight gain → 15% increased risk of DM in PWH vs. 8% in controls

1. The GBD 2015 Obesity Collaborators*N Engl J Med 2017;377:13-27. 2. https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight ; 3. Herring. JAIDS. 2016 Oct 1;73(2):228-36

ADVANCE: Changes in body composition: women

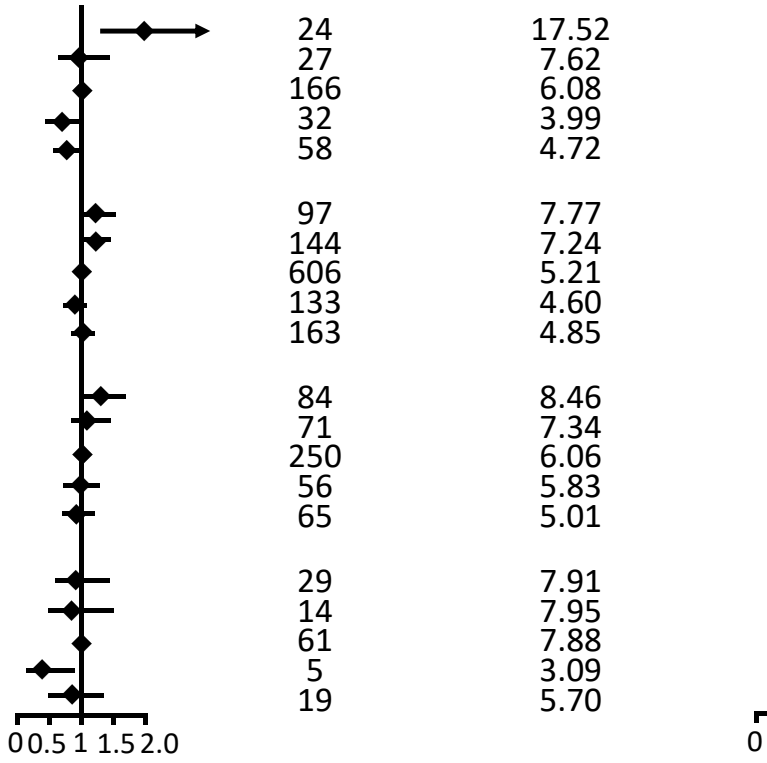


Most of the weight gain in DTG arms is fat gain, both trunk and limb. Higher with TAF

Increases in lean mass (both limb and trunk) also higher in DTG arms vs. EFV

D:A:D Study: Risk of CVD After BMI Changes on ART

	CVD Events	Rate/1000 Yrs	DM events	Rate/1000 Yrs
Baseline BMI < 20				
BMI decrease > 2	24	17.52	2	1.44
BMI decrease 1-2	27	7.62	12	3.34
BMI stable ± 1	166	6.08	48	1.76
BMI increase 1-2	32	3.99	16	1.99
BMI increase > 2	58	4.72	38	3.11
Baseline BMI 20-25				
BMI decrease > 2	97	7.77	35	2.82
BMI decrease 1-2	144	7.24	48	2.43
BMI stable ± 1	606	5.21	324	2.82
BMI increase 1-2	133	4.60	93	3.26
BMI increase > 2	163	4.85	162	4.93
Baseline BMI 25-30				
BMI decrease > 2	84	8.46	60	6.43
BMI decrease 1-2	71	7.34	65	7.14
BMI stable ± 1	250	6.06	266	6.81
BMI increase 1-2	56	5.83	80	8.88
BMI increase > 2	65	5.01	131	11.08
Baseline BMI 30+				
BMI decrease > 2	29	7.91	29	9.65
BMI decrease 1-2	14	7.95	16	10.32
BMI stable ± 1	61	7.88	89	12.69
BMI increase 1-2	5	3.09	22	15.68
BMI increase > 2	19	5.70	50	17.35



CVD: Adjusted for age, race, transmission mode, sex, recent ABC and other NRTI use, cumulative protease inhibitor use, CD4+ count, family history of CVD, smoking status
DM: Adjusted for age, race, mode of transmission, sex, stavudine use, triglycerides, CD4+ count, smoking status, and HDL

Petoumenos. CROI 2020. Abstr 83.; **Petoumenos. J Acquir Immune Defic Syndr. 2021 Apr 15;86(5):579-586.**

ADVANCE Study: Weight Gain and Metabolic Syndrome Through Wk 96

- Gained weight was predominantly fat mass rather than lean mass; women gained significantly more fat mass than men ($P < .001$)

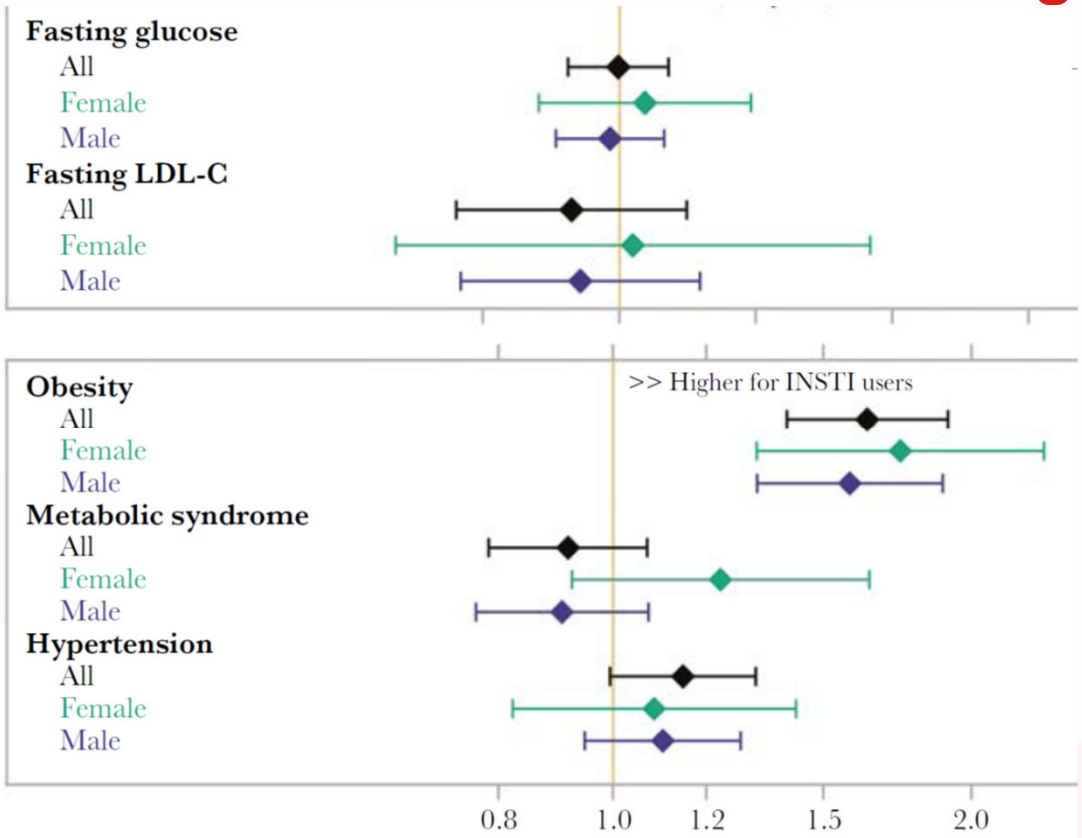
Outcome	DTG + FTC/TAF (n = 351)	DTG + FTC/TDF (n = 351)	EFV/FTC/TDF (n = 351)
Mean weight gain from BL, kg			
Women			
▪ Wk 96	8.2	4.6	3.2
▪ Wk 144*	12.3	7.4	5.5
Men			
▪ Wk 96	5.2	3.6	1.4
▪ Wk 144*	7.2	5.5	2.6
Treatment-emergent metabolic syndrome at Wk 96, %			
All patients	8.4†	5.9	3.9†
Women	10.9	8.1	5.6
Men	4.6	3.3	1.8

*Data after Wk 96 are incomplete. †$P = .03$ for comparison between DTG + FTC/TAF and EFV/FTC/TDF. All other comparisons were not significant.

Sokhela. AIDS 2020. Abstr OAXLB01.

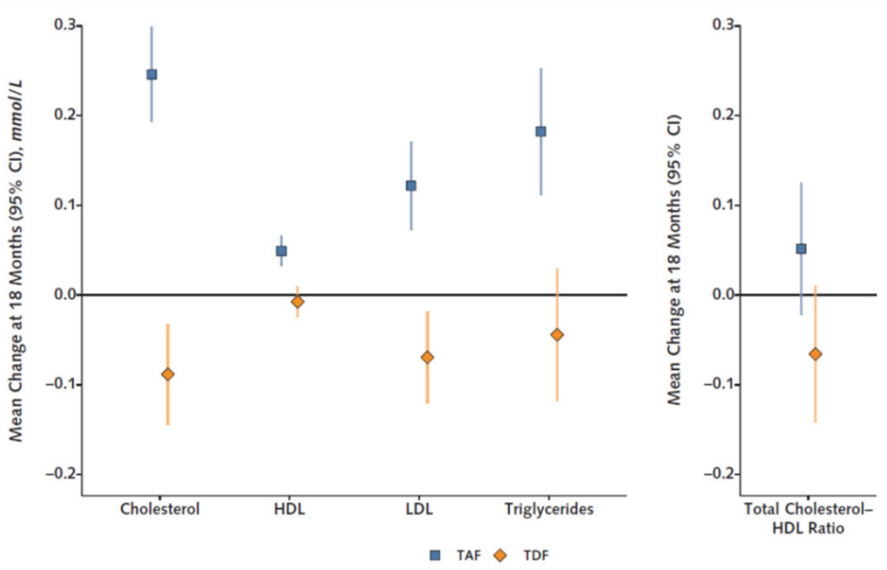
Slide credit: clinicaloptions.com

Metabolic Associations of Weight Gain on INSTI and TAF



REPRIEVE: Odds of metabolic changes on INSTI vs. non-INSTI

Kileel. OFID; 2021 Nov 20;8(12):ofab537



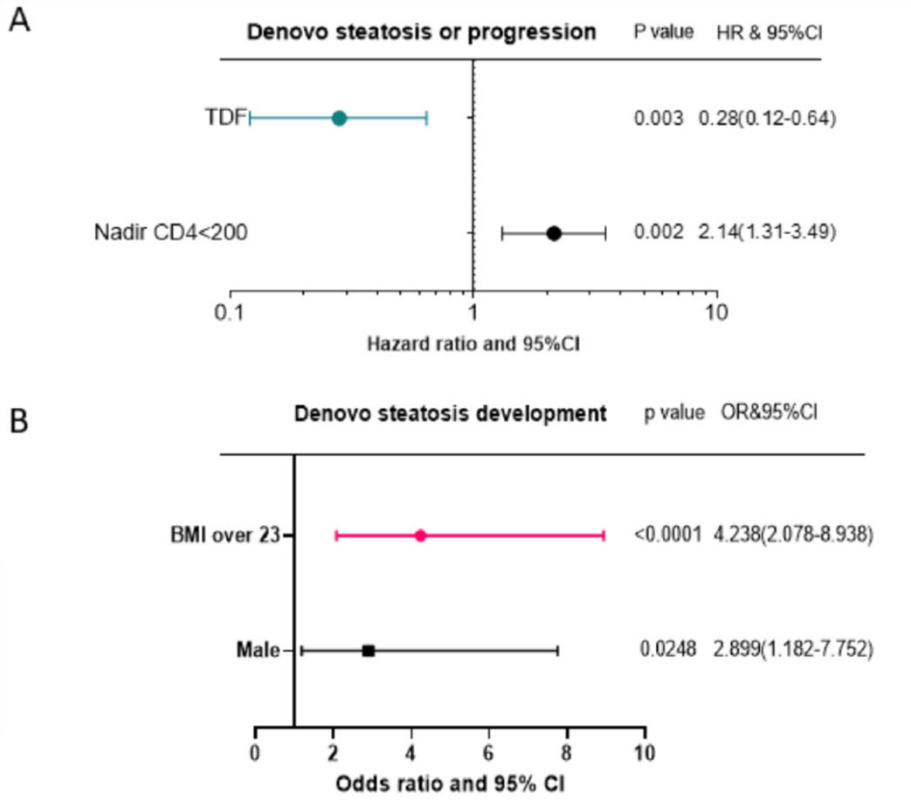
Swiss Cohort:

Switching to TAF led to increases in total cholesterol, HDL, LDL, and TG after 18 months.

Surial B, et al. Ann Intern Med. 2021;174(6):758-767.

De-Novo Hepatic Steatosis with Weight Gain After ART Initiation

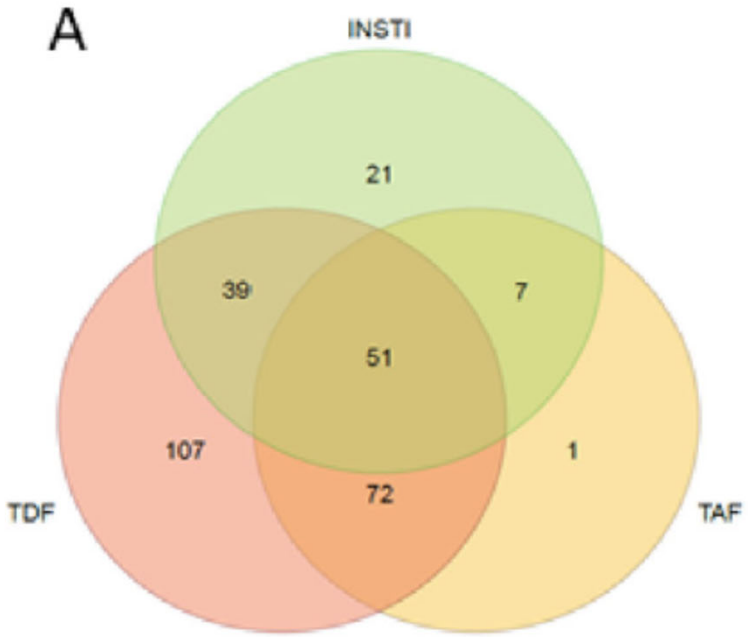
- Prospective cohort of 319 HIV mono-infected on ART;
  - 155 (52%) with no b/l steatosis → 69 (45%) developed steatosis on f/u
- BMI of >23 kg/m^2 for males is significantly associated with development of de novo steatosis (68% risk vs. 25% for females)
- TDF associated with lower risk of de-novo steatosis.
  - Steatosis (CAP value) decrease for those on TDF; regardless of weight trajectory…)

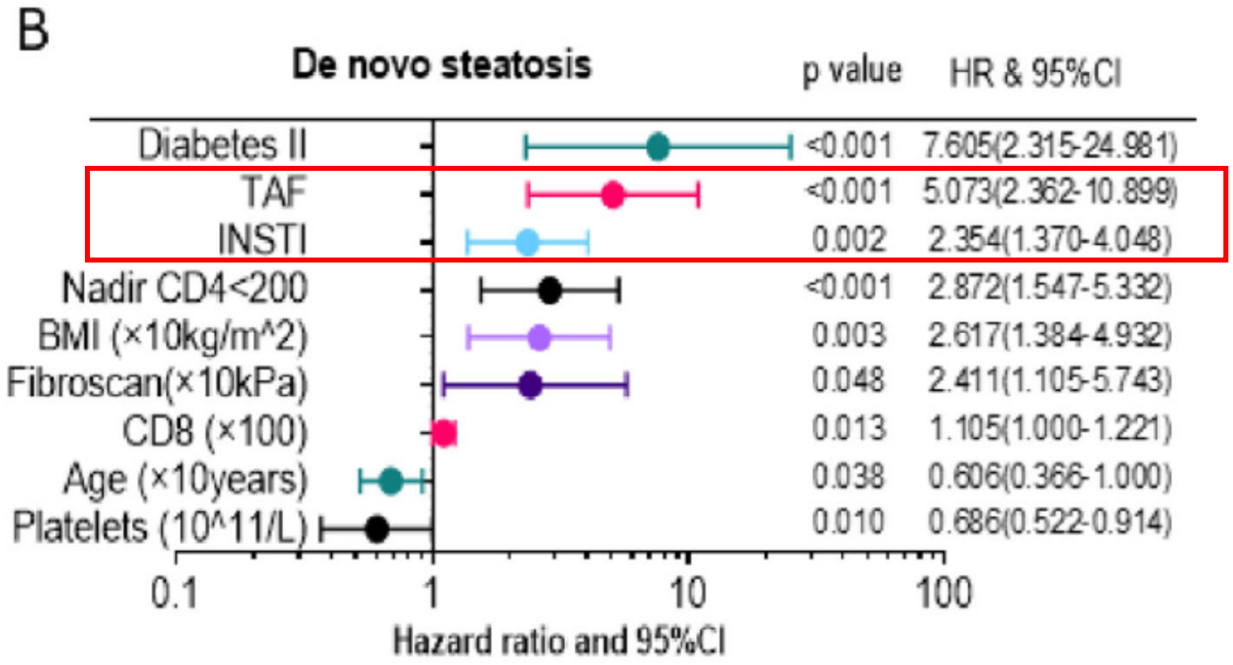


Bischoff. EClinicalMedicine 2021 Sept 5;40:101116

De-Novo Hepatic Steatosis with Weight Gain After ART Initiation

- Exposure to TAF and INSTIs associated with de-novo steatosis.





Bischoff. EClinicalMedicine 2021 Sept 5;40:101116

Management of Weight Gain on ART

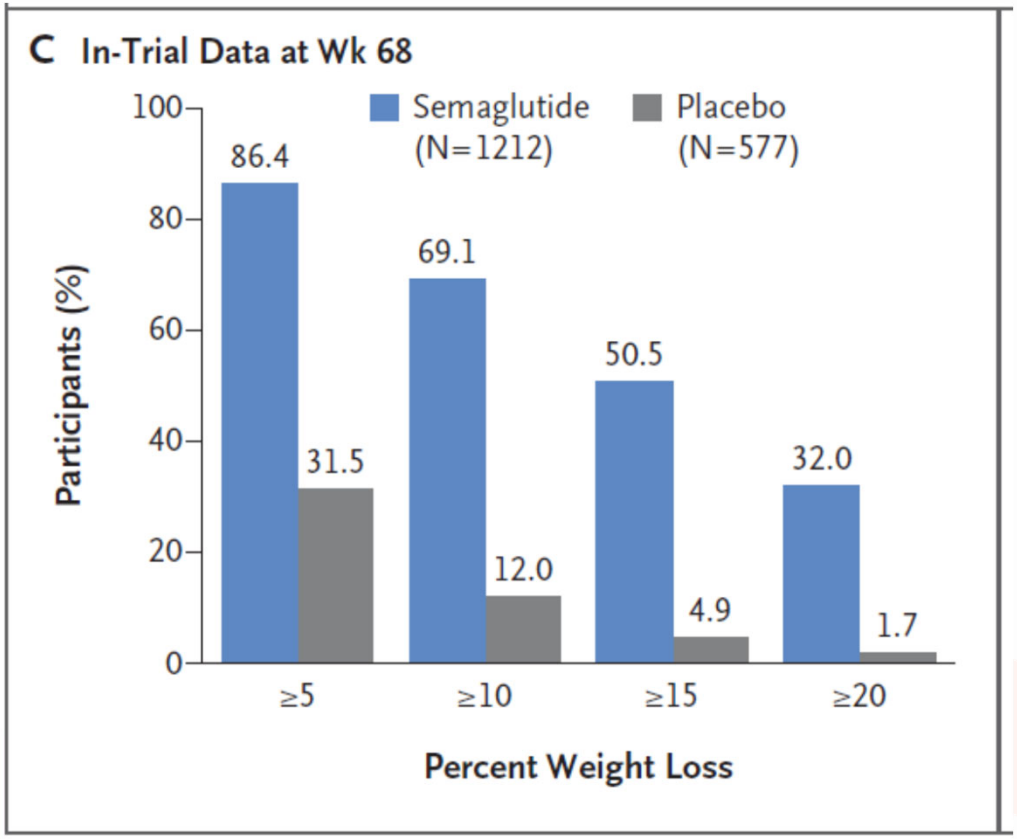
- Antiretroviral Switch
  - Reversal of weight gain with switch to non-INSTI or non-TAF regimen still uncertain.
- Weight Loss Medications
  - Interesting new data from GLP-1 analogues; Being explored in HIV
- Lifestyle Modification
  - Diet and exercise have been reported to work. Ancillary benefit in PLWH include prevention/mitigation of non-AIDS complications
  - DHHS: Counsel patient on lifestyle modification and dietary interventions and starting an exercise regimen, especially strength training.[1]

1. https://clinicalinfo.hiv.gov/en/guidelines; Accessed March 7th, 2022

Management of Weight Gain on ART

Once-weekly semaglutide 2.4 mg as an adjunct to lifestyle intervention

Also, participants who received semaglutide had a greater improvement with respect to cardiometabolic risk factors and a greater increase in participant-reported physical functioning from baseline than those who received placebo.



Wilding. N Engl J Med 2021;384:989-1002

Summary

- Accumulating data that INSTI- and TAF-based regimens are associated with greater weight gain than other regimens (also, PIs to some extent)
  - Increases in weight on DTG are higher in women, Blacks (and Hispanics?)
- Initial data on patterns and mechanism of weight gain: mostly fat, with INSTI. Need to evaluate effect on appetite, caloric intake, energy expenditure
- Metabolic Complications: Increased lipids with TAF; probably metabolic syndrome, insulin resistance and hepatic steatosis with TAF and INSTI
- In patients with significant weight gain: does changing to non-INSTI or non-TAF regimen help?