

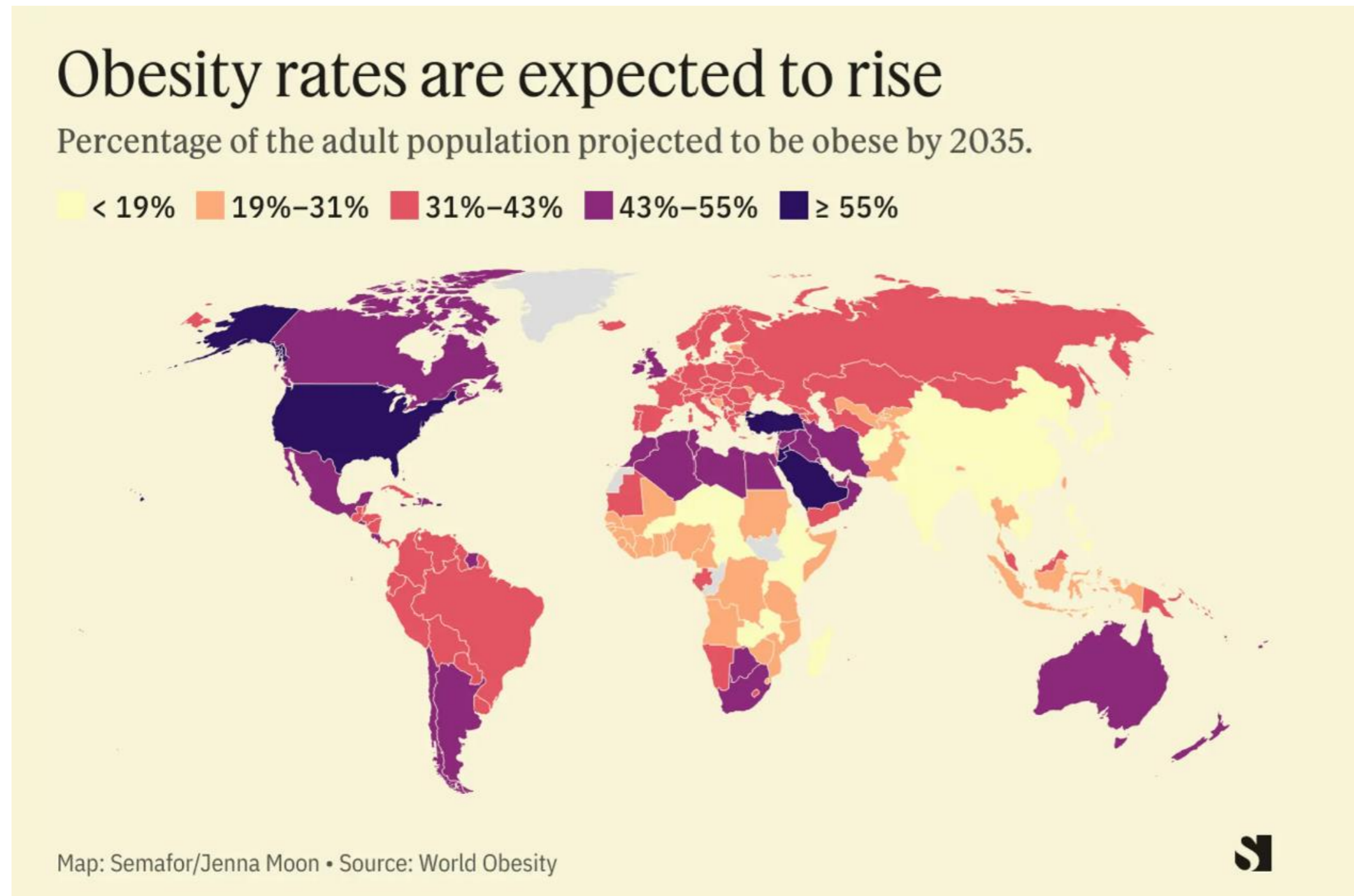
WEIGHT GAIN IN PLHIV

De Scheerder Marie-Angélique, BREACH 28/11/2024, Brussels

DISCLOSURES

- Invited speaker for Viiv, Gilead, Abbvie, GSK, Pfizer, MSD
- Grants from MSD, Viiv, Gilead
- Sponsoring from Pfizer, Viiv, Gilead

HOW BIG IS THE PROBLEM?



General population
Sciensano 2024:
49% overweight
18% obese

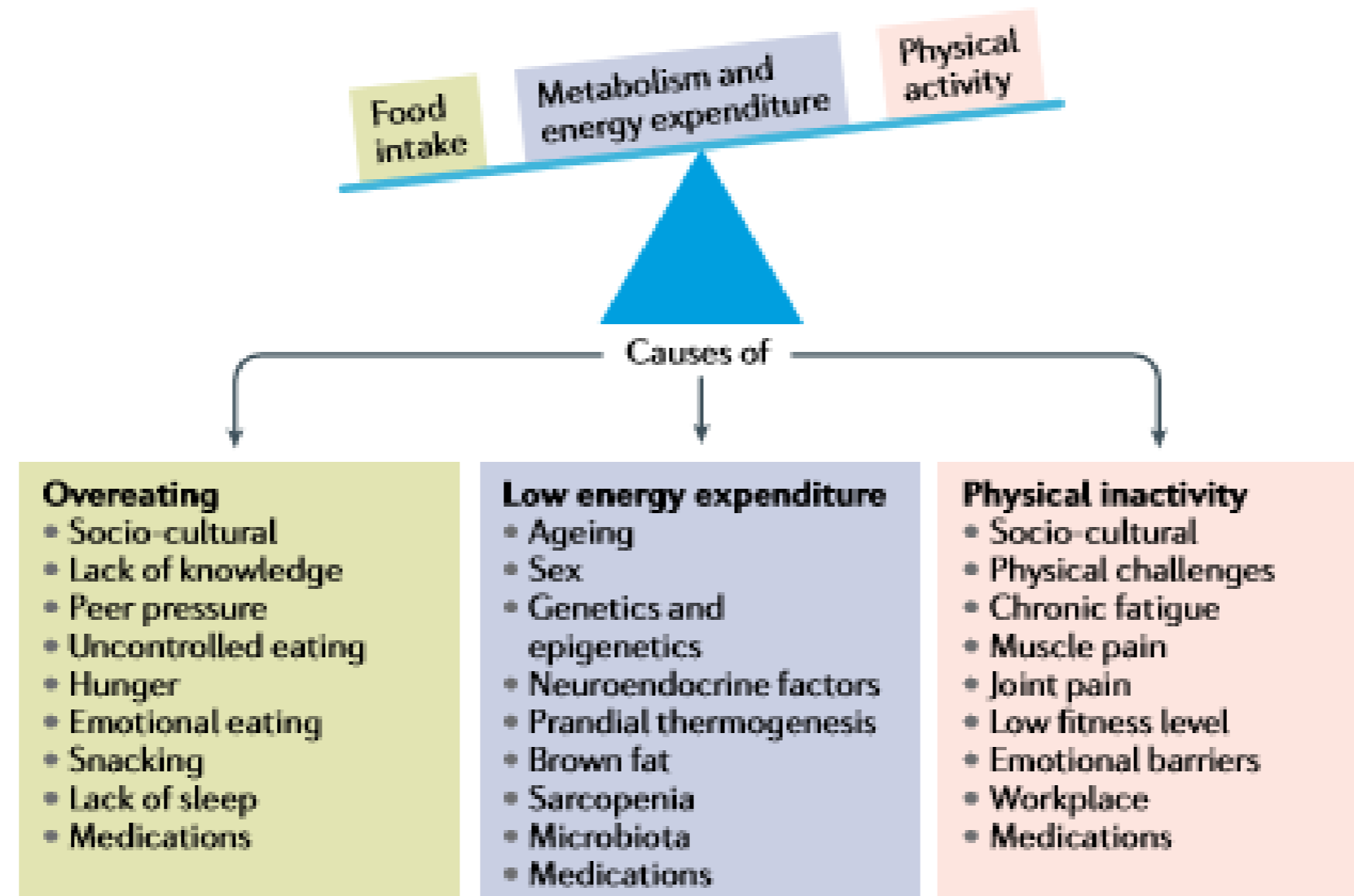
PLHIV
Swiss cohort 2016
39% overweight, 13% obese
Belgian data overweight 33%, 10% obese
S-A, Uganda 2022 23,2-18% obese

After 3 Y of ART: shift in BMI class

- nl to overweight: 22%
- overweight to obese in 18%

(Koethe et al 2016)

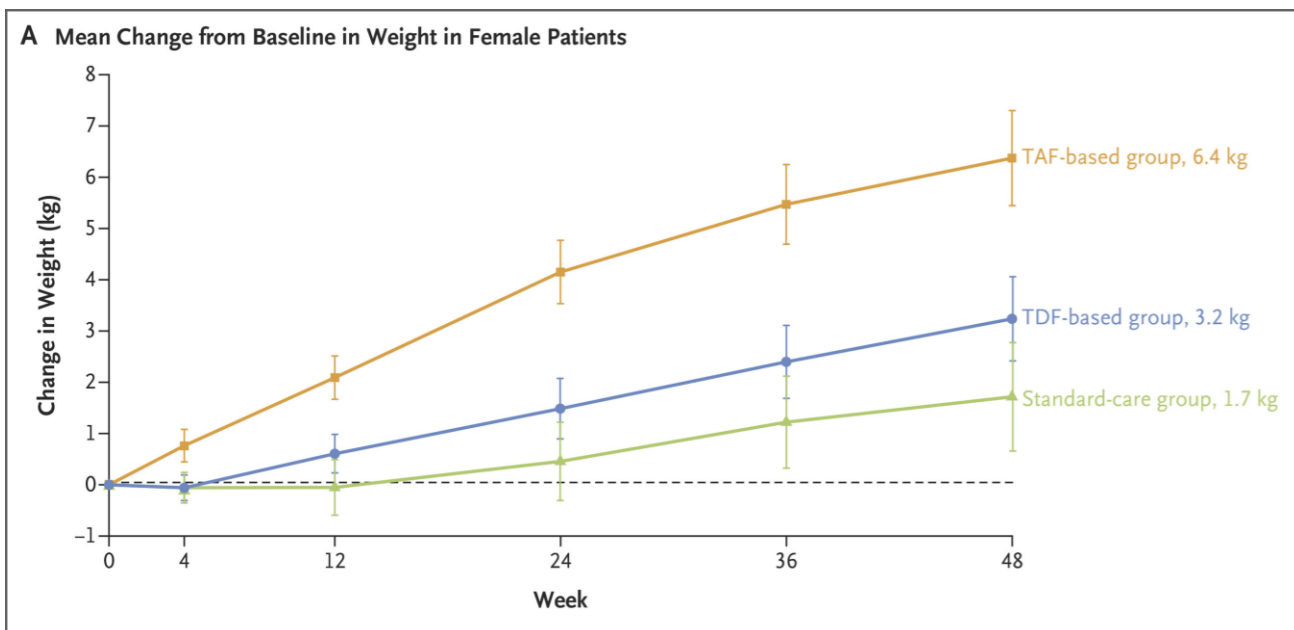
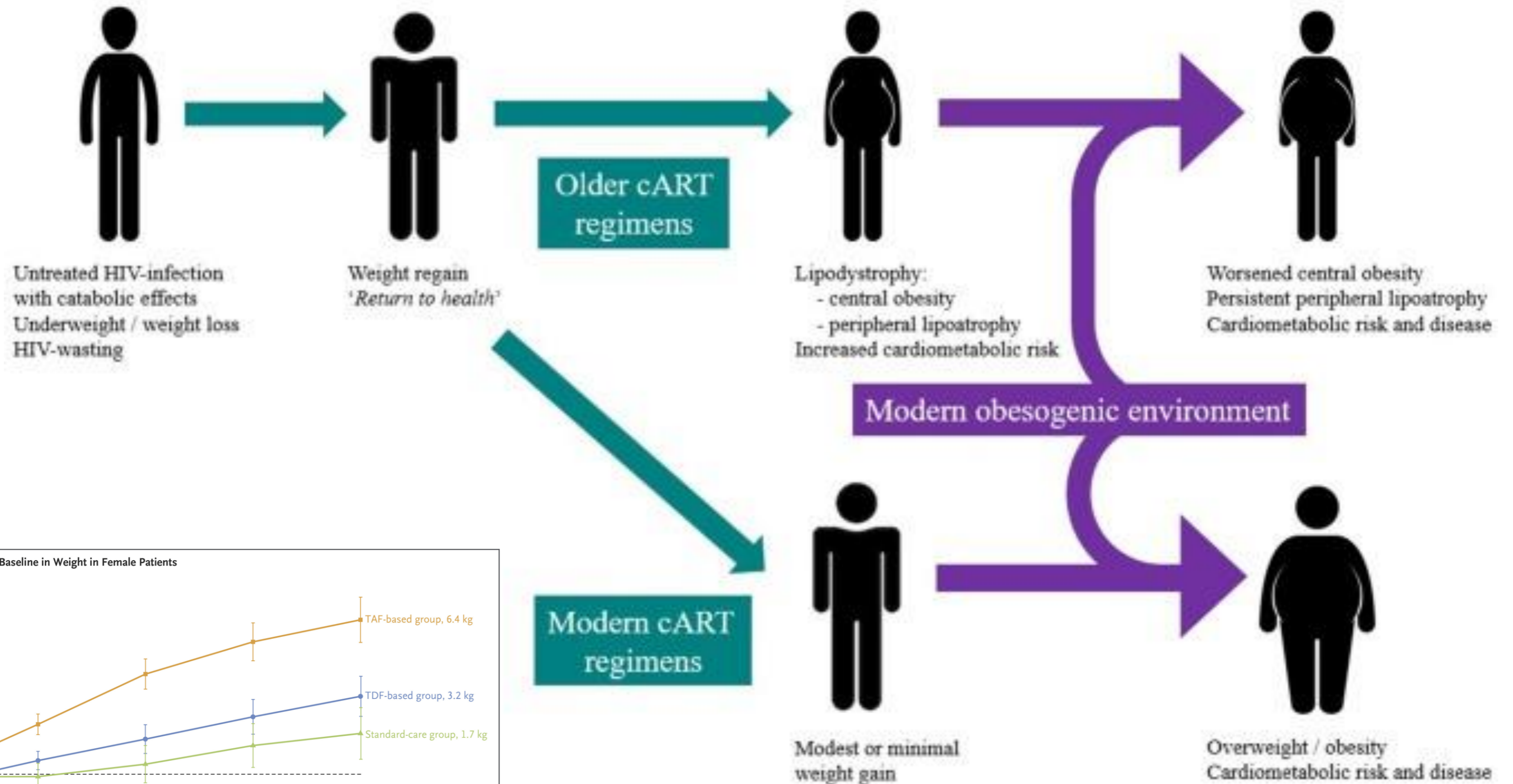
Obesity is complex and multifactorial



ROLE OF ART?

The Impact of Weight Gain During HIV Treatment on Risk of Pre-diabetes, Diabetes Mellitus, Cardiovascular Disease, and Mortality

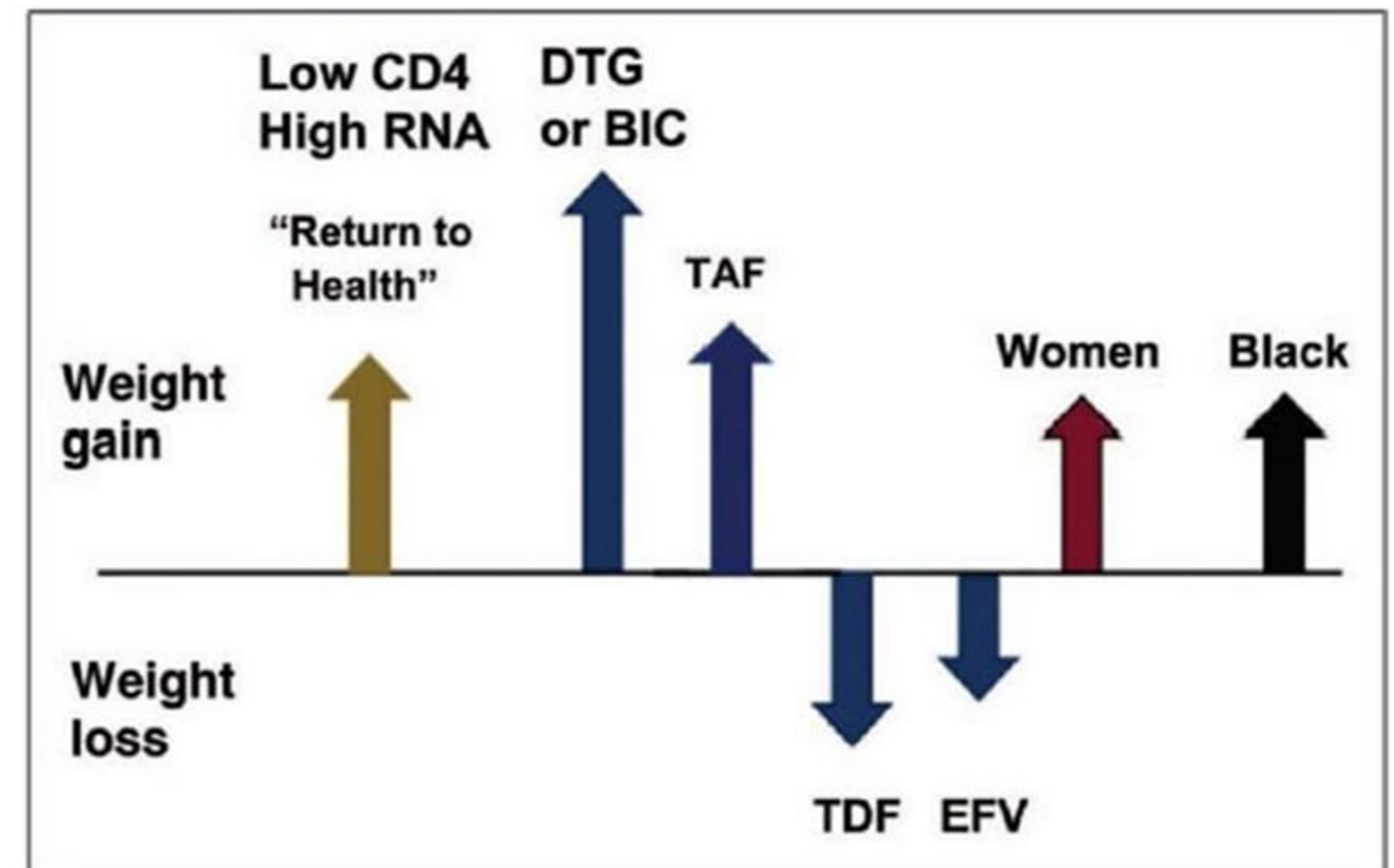
Shejil Kumar^{1,*} and Katherine Samaras^{2,3,4}



ADVANCE, NEJ, 2019

IS IT CLASS OR
DRUG RELATED?

ARE SOME PLHIV
MORE AT RISK



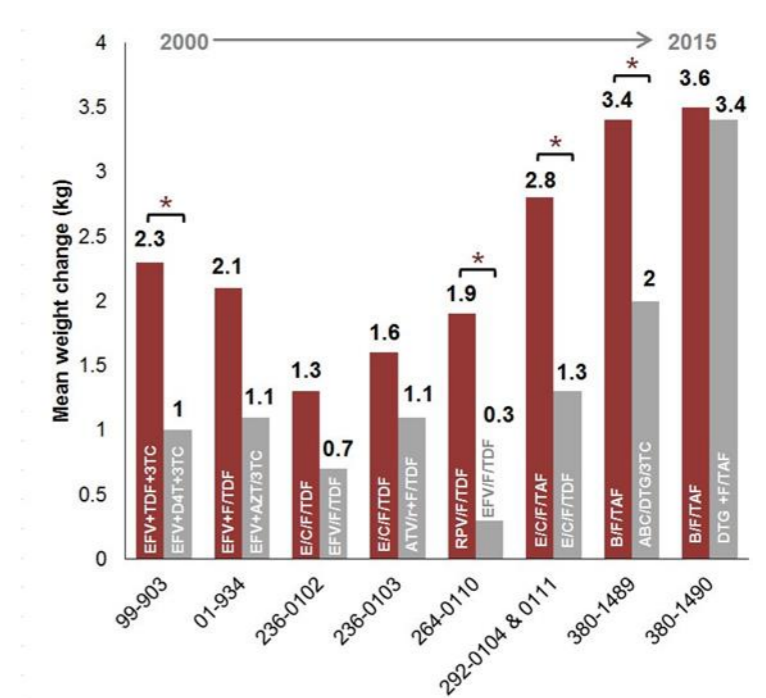
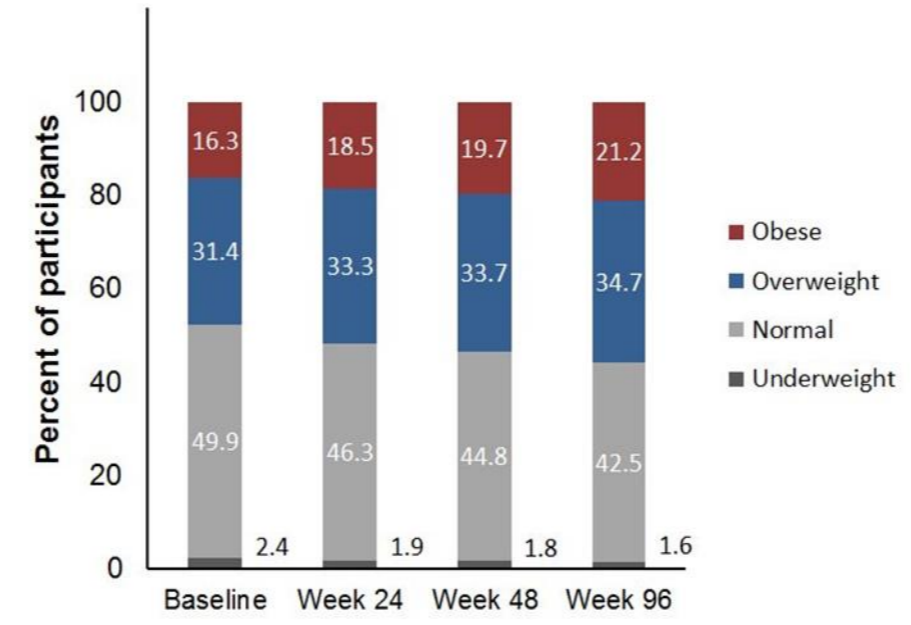
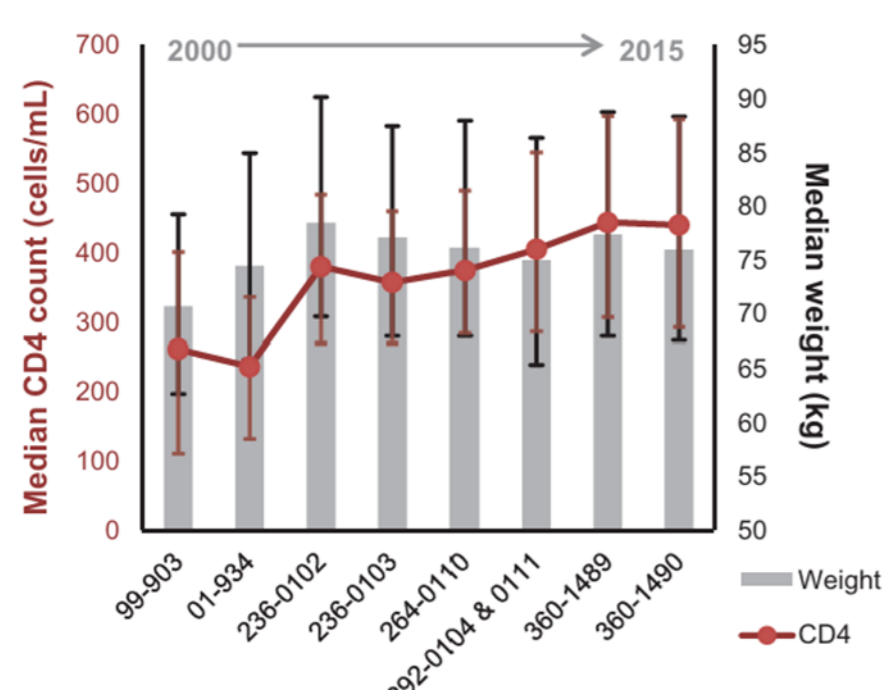
Nomathemba C Chandiwana, Francois Venter, Weight Gain After HIV Therapy Initiation: Pathophysiology and Implications, The Journal of Clinical Endocrinology & Metabolism, Volume 109, Issue 2, February 2024

NAIVE

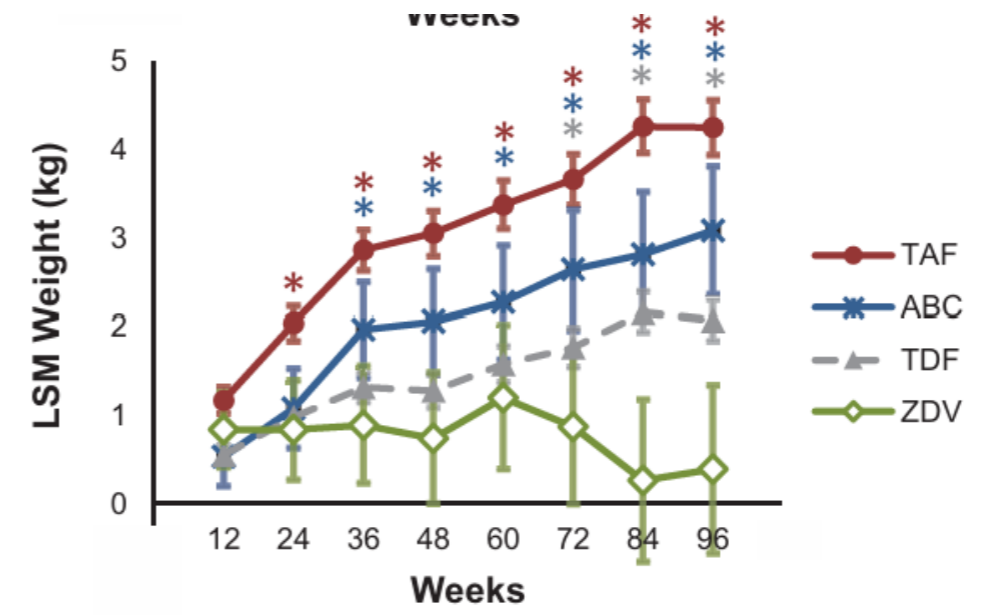
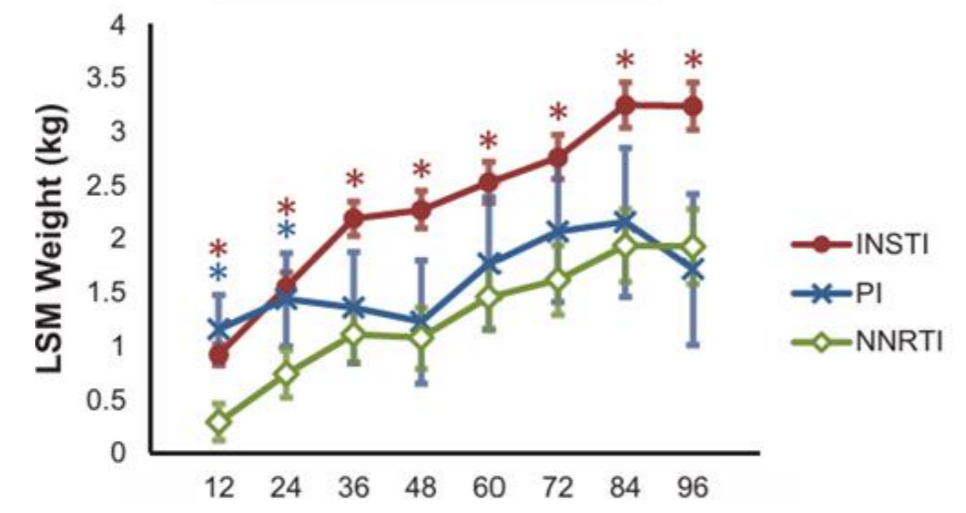
Weight Gain Following Initiation of Antiretroviral Therapy: Risk Factors in Randomized Comparative Clinical Trials

Paul E. Sax,¹ Kristine M. Erlandson,² Jordan E. Lake,³ Grace A. McComsey,⁴ Chloe Orkin,⁵ Stefan Esser,⁶ Todd T. Brown,⁷ Jürgen K. Rockstroh,⁸ Xuelian Wei,⁹ Christoph C. Carter,¹⁰ Lijie Zhong,⁹ Diana M. Brainard,⁹ Kathleen Melbourne,⁹ Moupali Das,⁹ Hans-Jürgen Stellbrink,¹⁰ Frank A. Post,¹¹ Laura Waters,¹² and John R. Koethe¹³

CID 2020



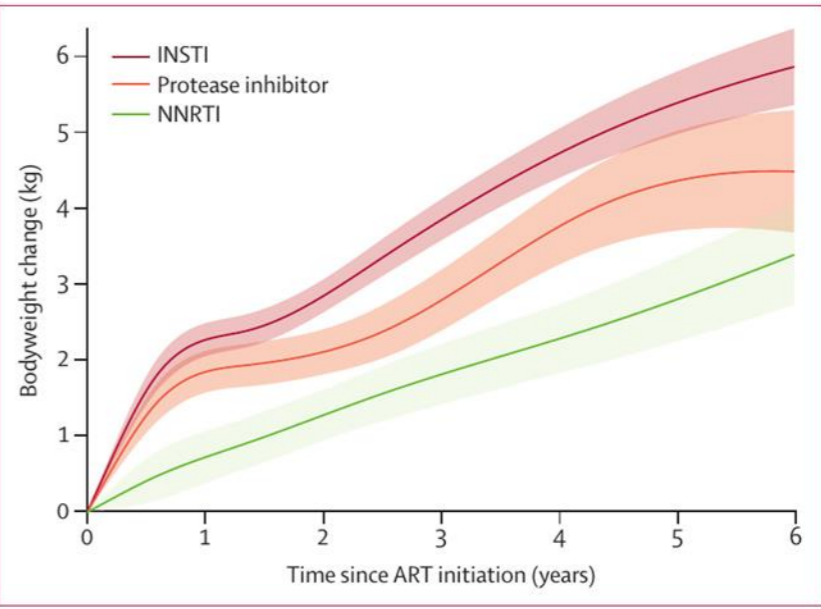
Weight Change



Changes in bodyweight after initiating antiretroviral therapy close to HIV-1 seroconversion: CASCADE collaboration, Pantazis N, et al. Lancet HIV

2024.11.e660-9
 Retrospective data from clinical records of **5698** participants (>16yrs) initiating ART **within 1 year of seroconversion**

- INSTI (n=2778)
- PI (n=1809)
- NNRTI (n=1111)



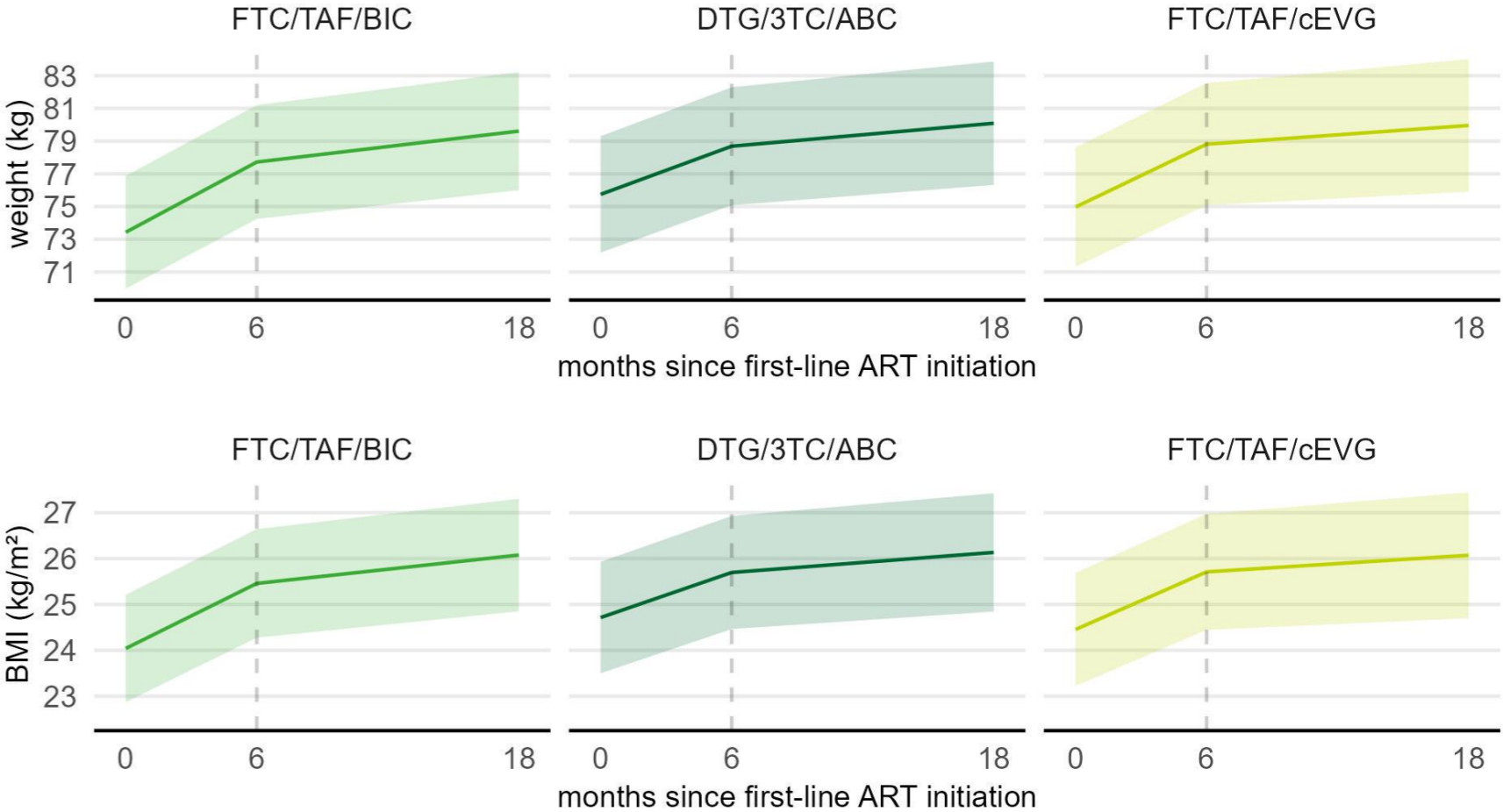
Estimated bodyweight changes after ART initiation by ART class

Dynamics of Weight Change After Initiation of Contemporaneous Antiretroviral Therapy in Treatment-Naive HIV-1 Infected Patients: Results From the Belgian HIV Cohort 2015–2021

Van Praet, Jens T. MD, PhD^{a,b}; Serrien, Ben PhD^c; Ausselet, Nathalie MD^d; Darcis, Gilles MD, PhD^e; Demeester, Rémy MD^f; De Munter, Paul MD, PhD^{g,h}; De Scheerder, Marie-Angélique MD, PhDⁱ; Goffard, Jean-Christophe MD^j; Libois, Agnès MD^k; Messiaen, Peter MD, PhD^{l,m}; Yombi, Jean Cyr MDⁿ; Van Beckhoven, Dominique MD^c; on behalf of the Belgian HIV Cohort Study Group

JAIDS 2023
 728 pat, 407-201-120

Adjusted weight- (top) and BMI- (bottom) changes in tr with HIV-1 from baseline to 18 months after initiation



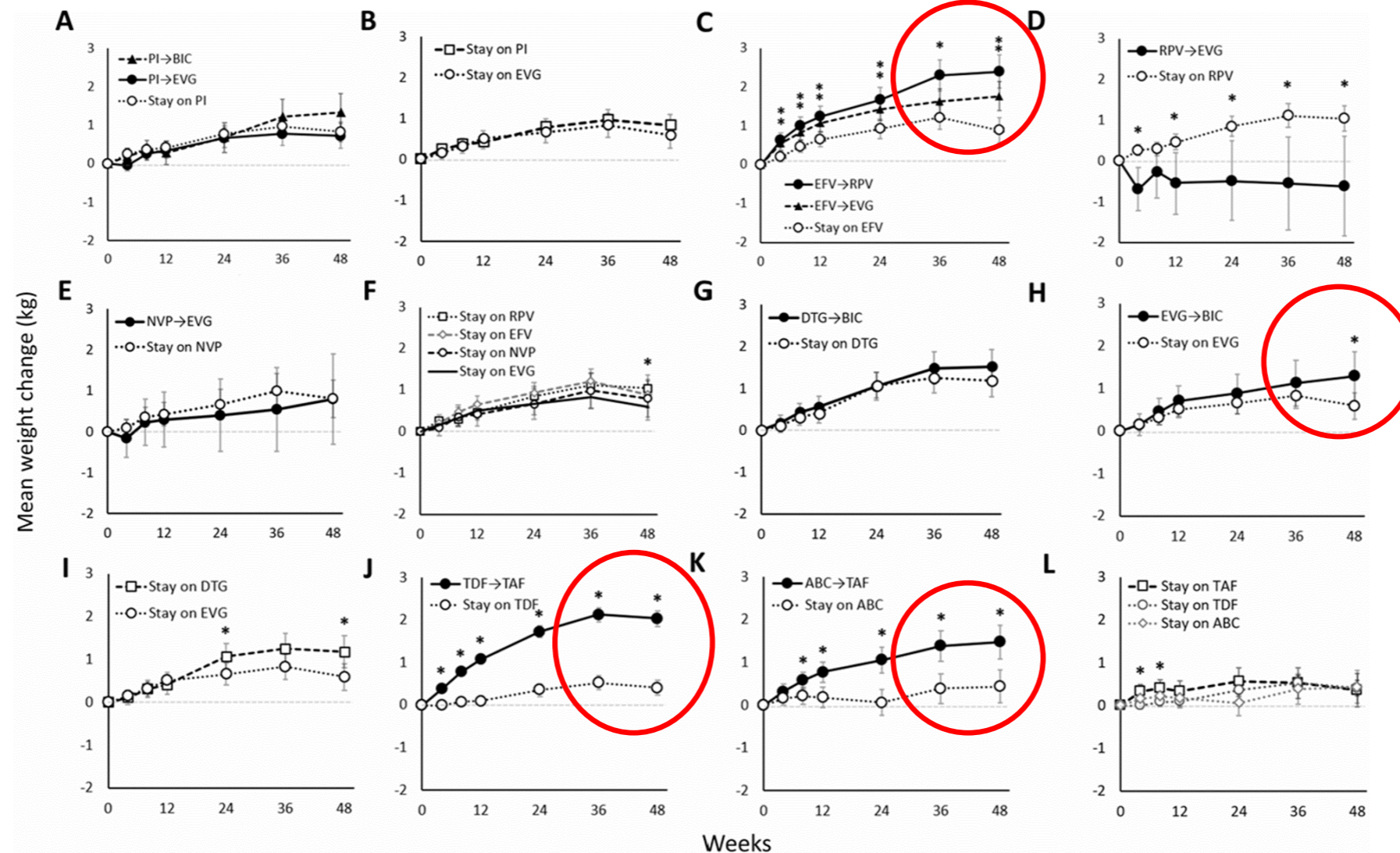
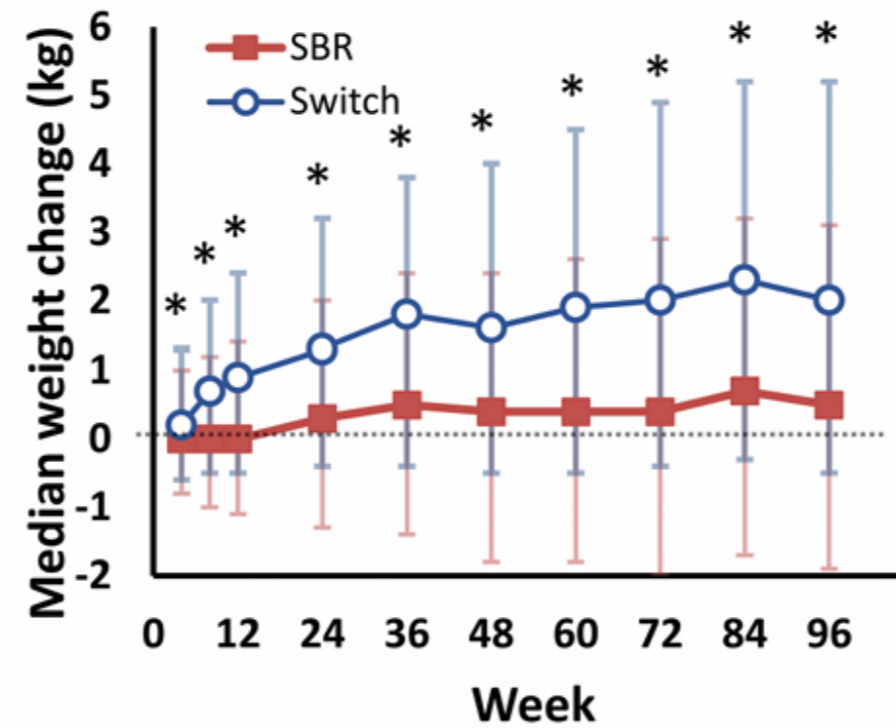
SWITCH

Weight Change Following Antiretroviral Therapy Switch in People With Viral Suppression: Pooled Data from Randomized Clinical Trials

Kristine M. Erlandson,¹ Christoph C. Carter,² Kathleen Melbourne,² Todd T. Brown,³ Cal Cohen,² Moupali Das,² Stefan Esser,⁴ Hailin Huang,² John R. Koethe,⁵ Hal Martin,² Grace A. McComsey,^{6,7} Chloe Orkin,⁸ Frank A. Post,⁹ Jürgen K. Rockstroh,¹⁰ Paul E. Sax,¹¹ Hans-Jürgen Stellbrink,¹² Laura Waters,¹³ Xuelian Wei,² and Jordan E. Lake¹⁴

CID 2021

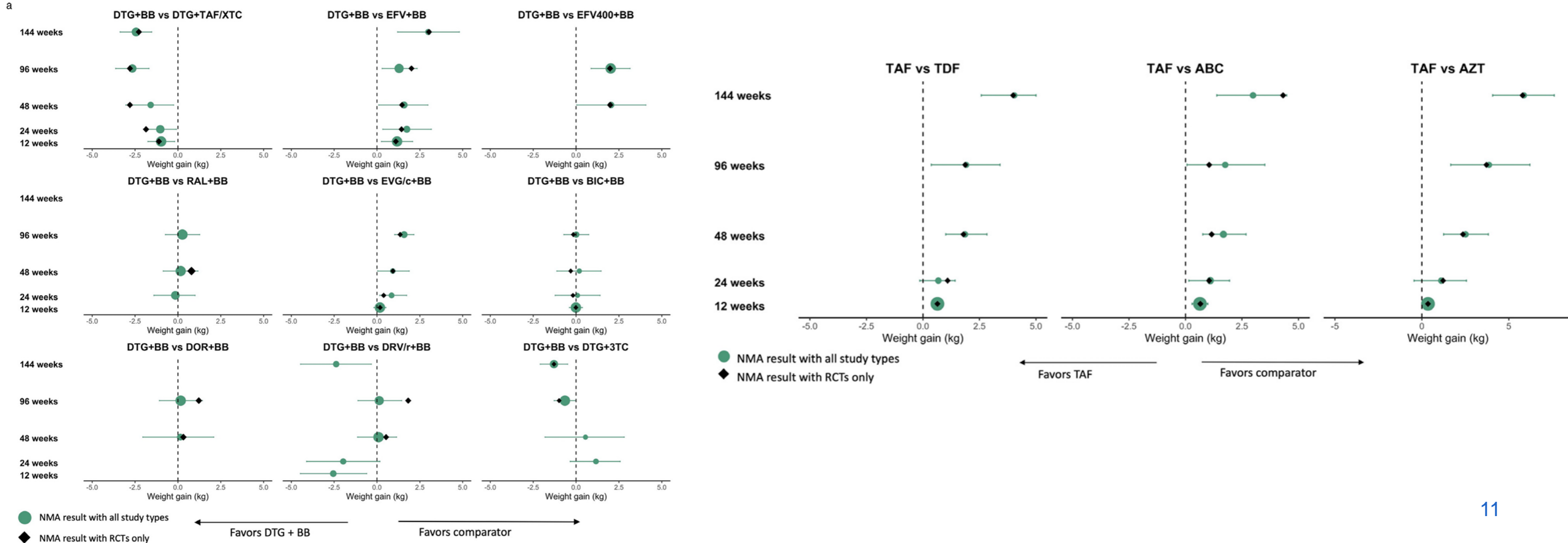
12 RCT switch trials; 4166 switched, 3150 stayed, 11456 person-years FU



Evidence synthesis evaluating body weight gain among people treating HIV with antiretroviral therapy - a systematic literature review and network meta-analysis

Steve Kanters,^{a,b,*} Françoise Renaud,^c Ajay Rangaraj,^c Kenneth Zhang,^b Eve Limbrick-Oldfield,^b Monica Hughes,^d Nathan Ford,^c and Marco Vitoria^c

DTG based regimens versus other ART regimens and TAF to other NRTI
 113 publications, 73 studies, 57124 pat: RCTs (50) and obs studies, 2011 to 2021

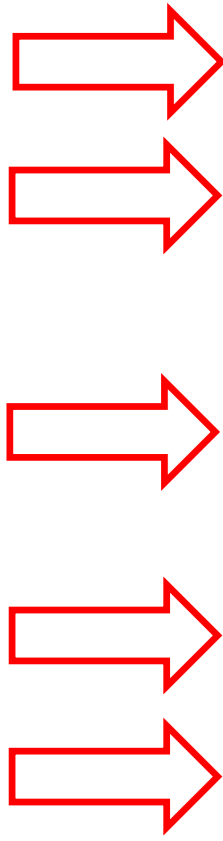
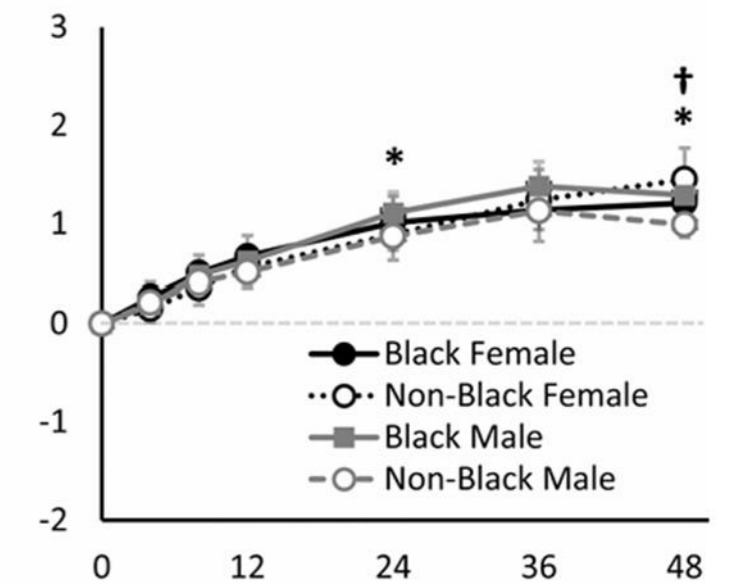
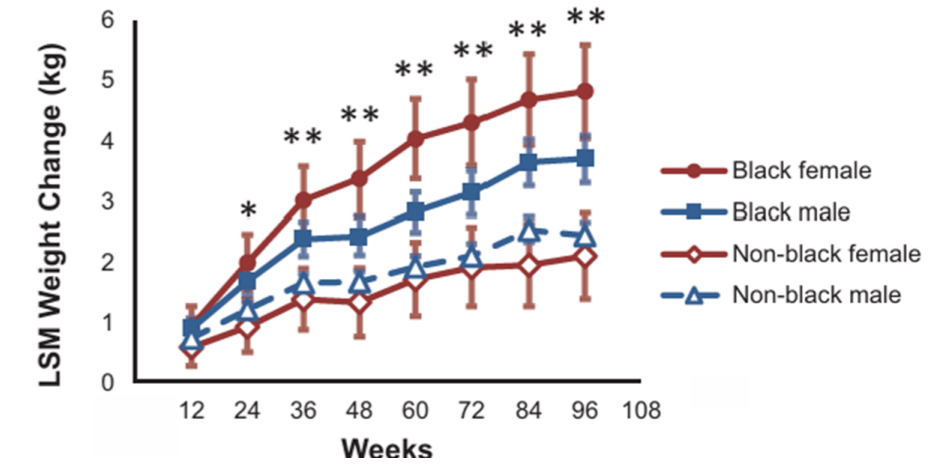


Overview of the prognostic factors (host and viral) analysis for weight change while on antiretroviral therapy

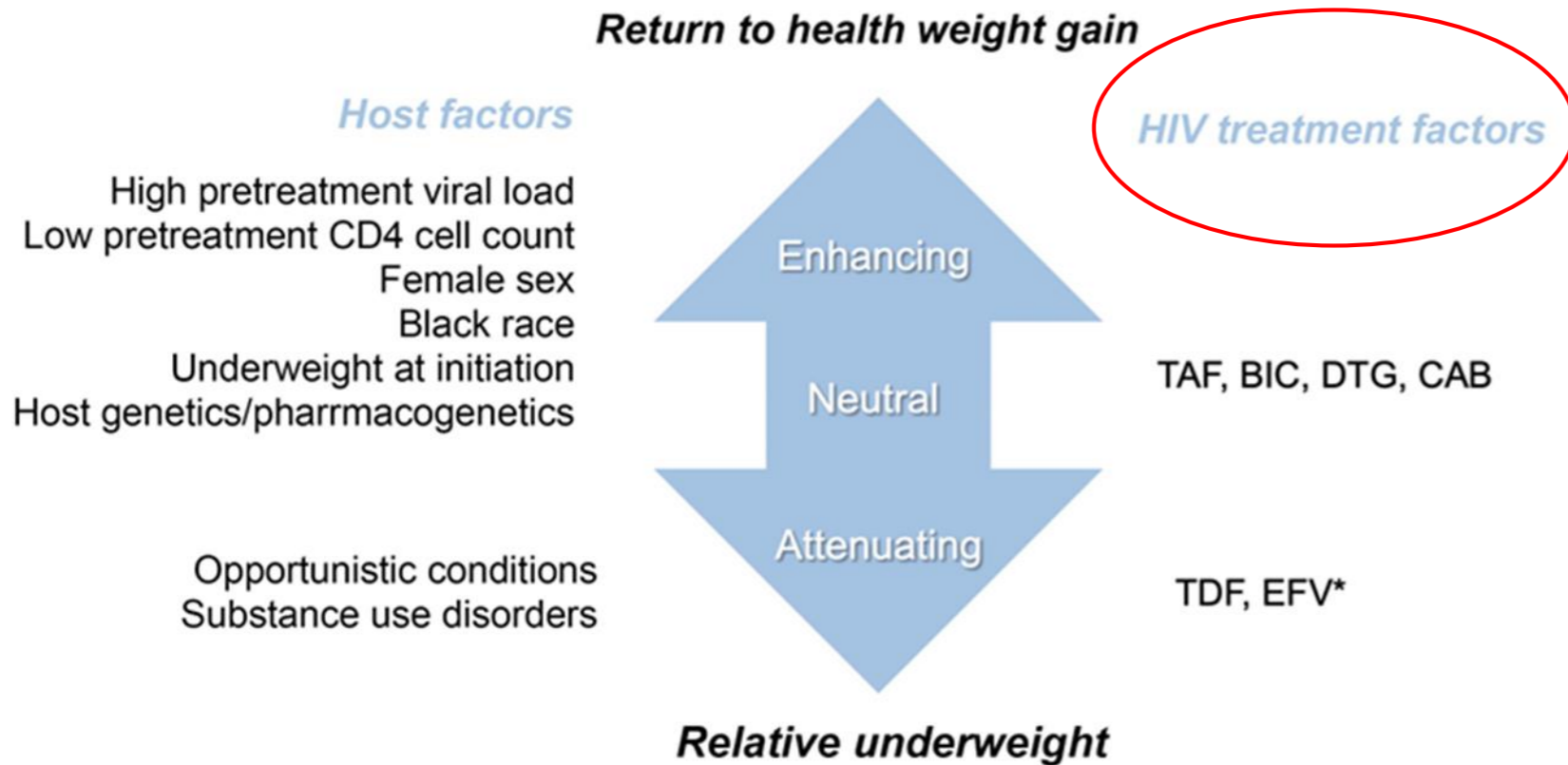
Baseline Characteristics	ACTG 5224	ACTG 5257	ADVANCE	AMPATH	Bekir 2013	Caiza 2020b	DRIVE-AHEAD	Gilead Sciences Trials	McComery 2018	McComery 2021	NA-ACCORD	NAMSAL	SCOLTA	RESPOND	Vanderbilt CCC	Wei 2023	Ernst 2021	Lamtrak 2021
Study location	US	US	ZA	KE	BE	IT	Global	US	--	--	US	CM	IT	Europe /AU	US	CN	US	PL
Female Sex (vs male)	↑	↑	↑	↑	□	↑	□	↑	□	□	↑	↑	↓	□	↑	□	↑	--
African origins (vs Other)	□	□	--	--	□	--	↑	↑	□	↑	□	--	--	↑	□	--	□	--
Older Age (vs young)	□	□	↑	↑	↑	↑	□	--	□	↓	↓	--	□	--	--	↑	□	↑
Lower Weight (vs higher weight)	--	--	--	--	--	--	□	--	↑	--	--	--	↑	--	--	--	--	--
Lower or Normal BMI (vs higher BMI)	□	□	↓	↑	--	↑	□	↓	↑	↑	--	--	--	↑	--	--	↑	□
Low CD4 count (vs high CD4)	↑	↑	↑	↑	--	↑	↑	↑	--	↑	↑	--	↑	--	--	↑	--	□
High HIV-1 RNA (vs low RNA)	↑	↑	↑	--	--	□	↑	↑	--	--	--	↑	--	--	--	--	--	--

↑ Significant positive factor ↑ Positive factor □ No effect ↓ Negative factor ↓ Significant negative factor -- Not reported

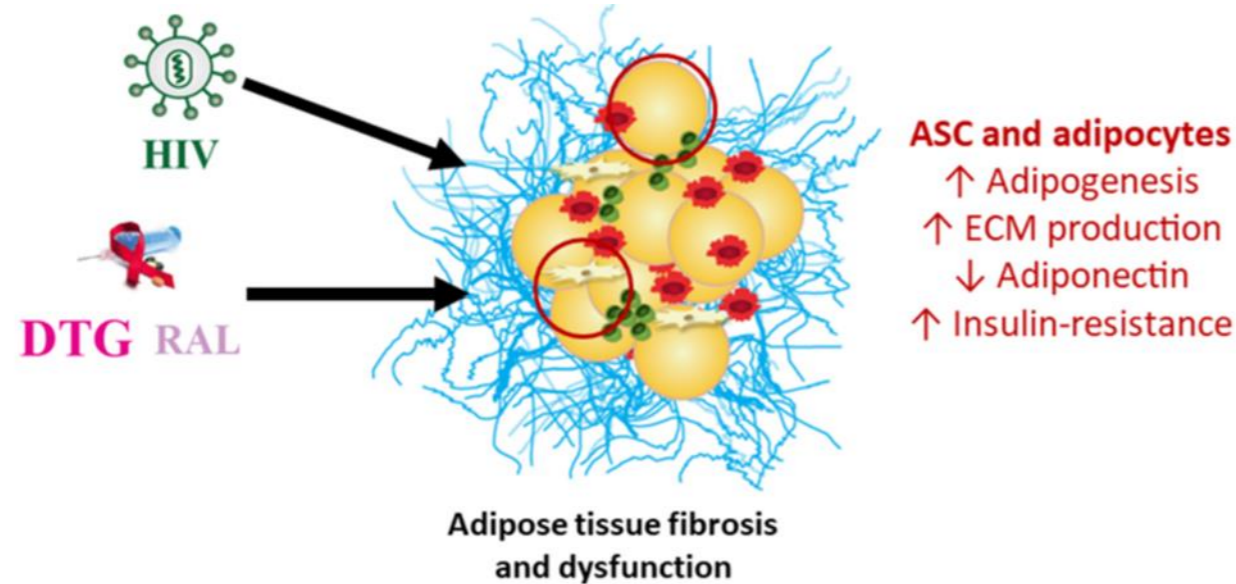
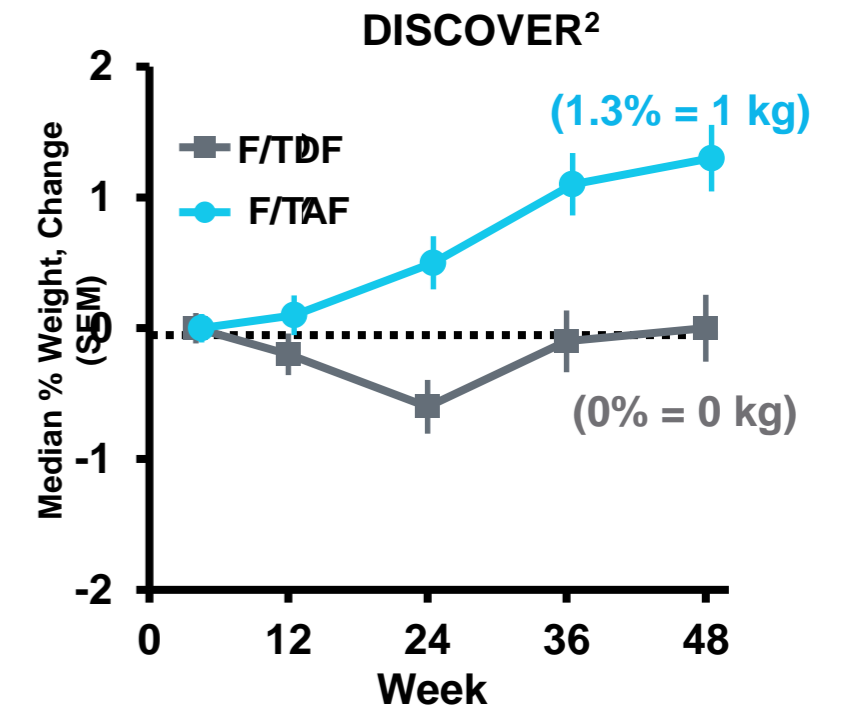
Naive versus switch



WHAT ARE THE MECHANISMS?



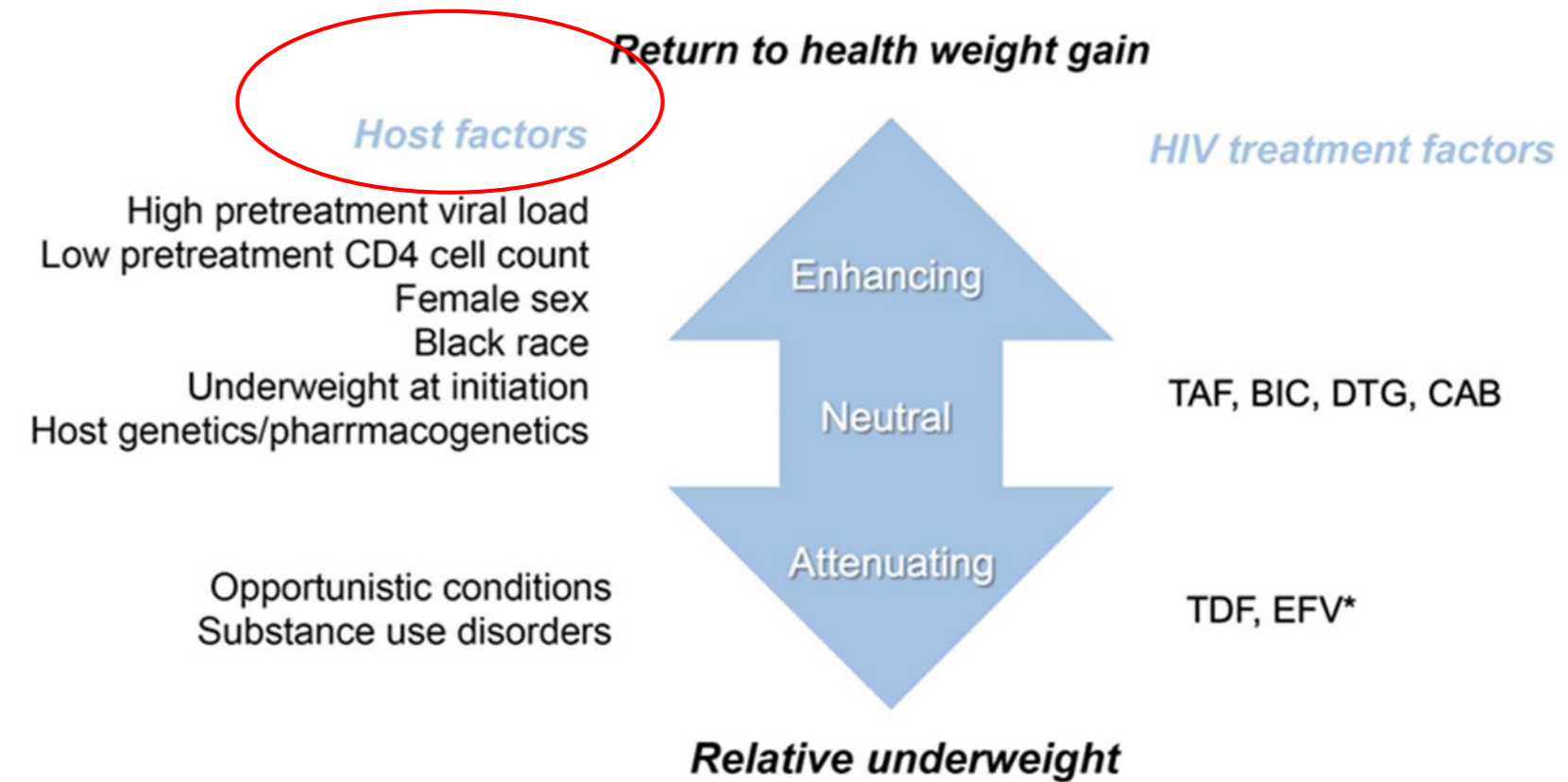
Better tolerability of modern ART
 Effect of EFZ side effects in slow metabolizers?
TAF versus TDF



2nd gen INSTI

- Effect on hunger and leptin levels, binding MC4R (in vitro)
- Mitochondrial dysfunction
- Effect on adipogenesis
- DMType 2 and insuline resistance, AHT
- Sleep disturbance, depression

- Stage of disease marked by CD4 nadir AND length of infection
- Gut lymphoid tissue ?
- Over-rebound effect
- Changes in adipocytes due to immune desregulation and gut alterations, leading to pro fibrotic changes and hypertrophy



You only see what you get:

Weight/BMI/DEXA - sarcopenia/gain-loss of lean mass versus accumulation of fat especially visceral fat

Weight gain in adolescents?

Sex-race-but also location, socioeconomic factors-physical activity, menopause, smoking status?

IS WEIGHT GAIN REVERSIBLE
AFTER SWITCHING OF
INSTI/TAF?



RUMBA W48

<https://doi.org/10.1093/infdis/jiae405>

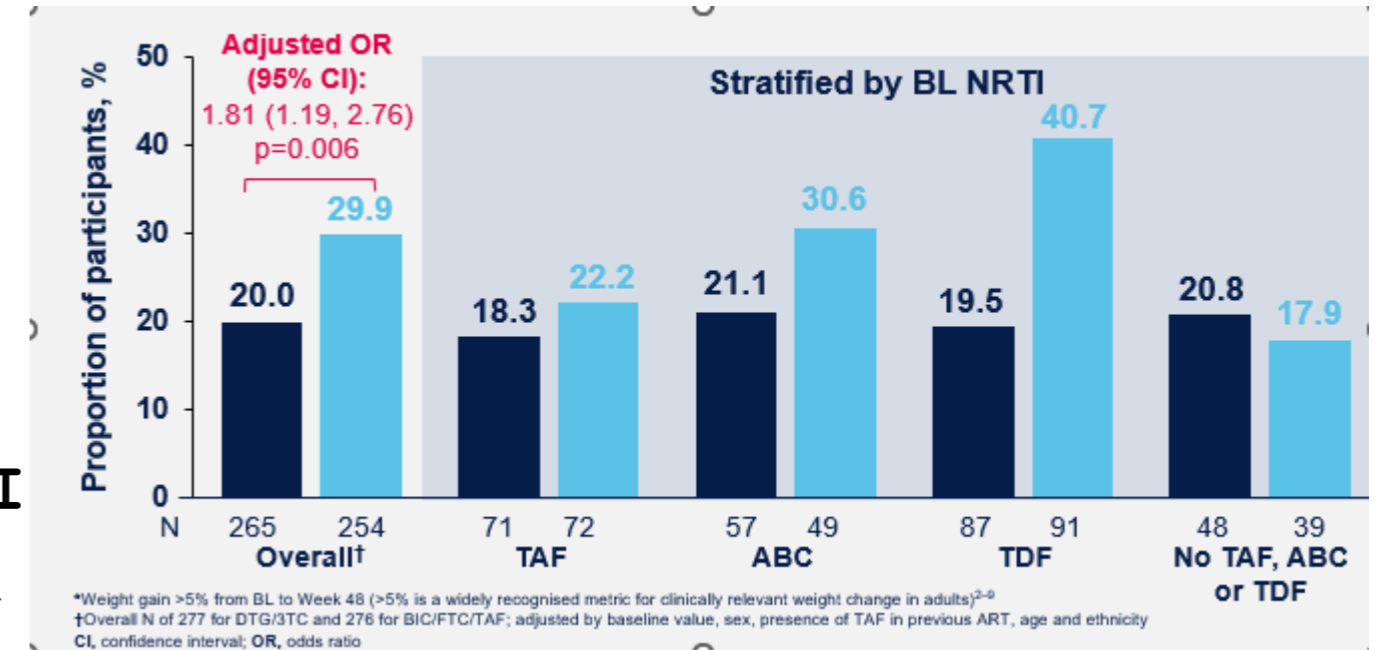


81 B/F/TAF
48 DTG/ABC/3TC

Versus

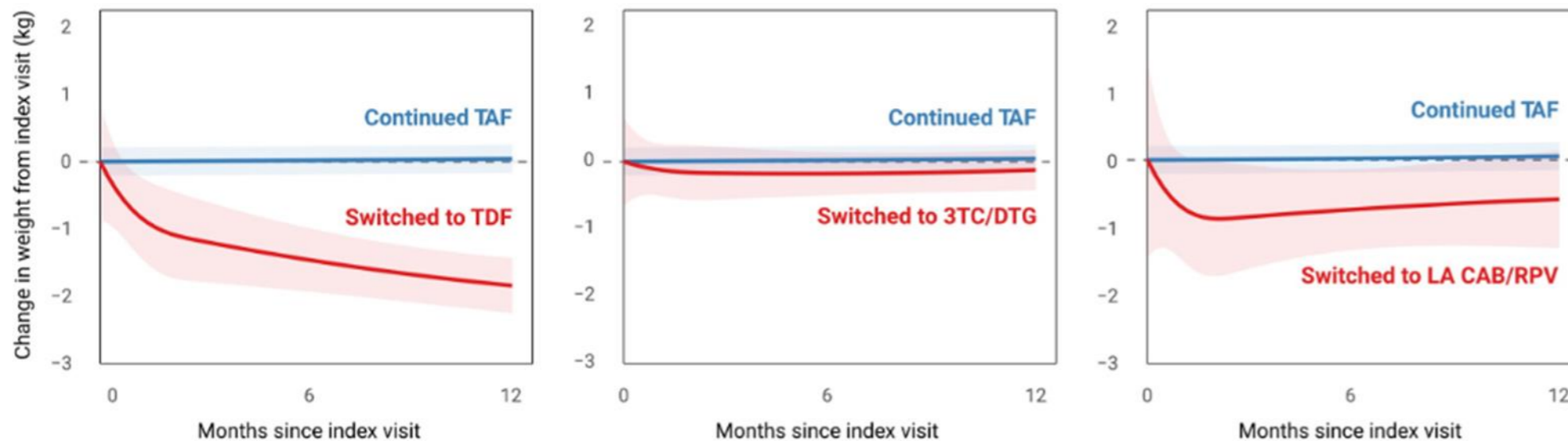
0% 2nd gen INSTI
28% TAF
35% TDF

PASO DOBLE W48 Proportion of participants with clinically relevant (>5%)* weight gain



Tango, 2021 TAF->3TC
DYAD, 2023

Damas et al. CID 2024: swiss observational cohort



Kaupinnen et al, 2022 ACTG A5391? Delite?
Characterise, 2022 INSTI/TAF-

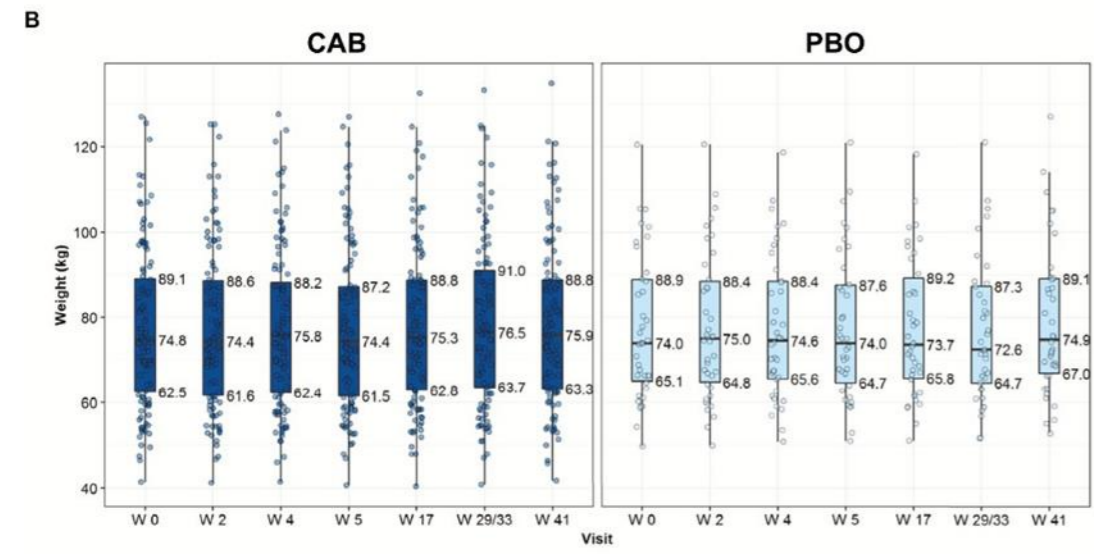
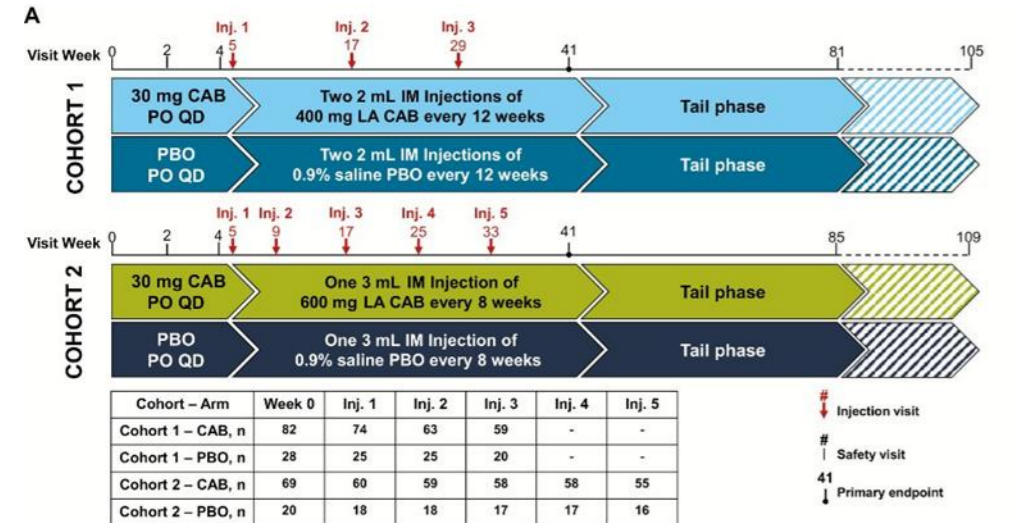
TAF->TDF

>DOR (TDF/FTC)
(CAR->DOR/ISL)

Cabotegravir Is Not Associated With Weight Gain in Human Immunodeficiency Virus–uninfected Individuals in HPTN 077

Raphael J Landovitz ✉, Sahar Z Zangeneh, Gordon Chau, Beatriz Grinsztejn, Joseph J Eron, Halima Dawood, Manya Magnus, Albert Y Liu, Ravindre Panchia, Mina C Hosseinipour ... Show more

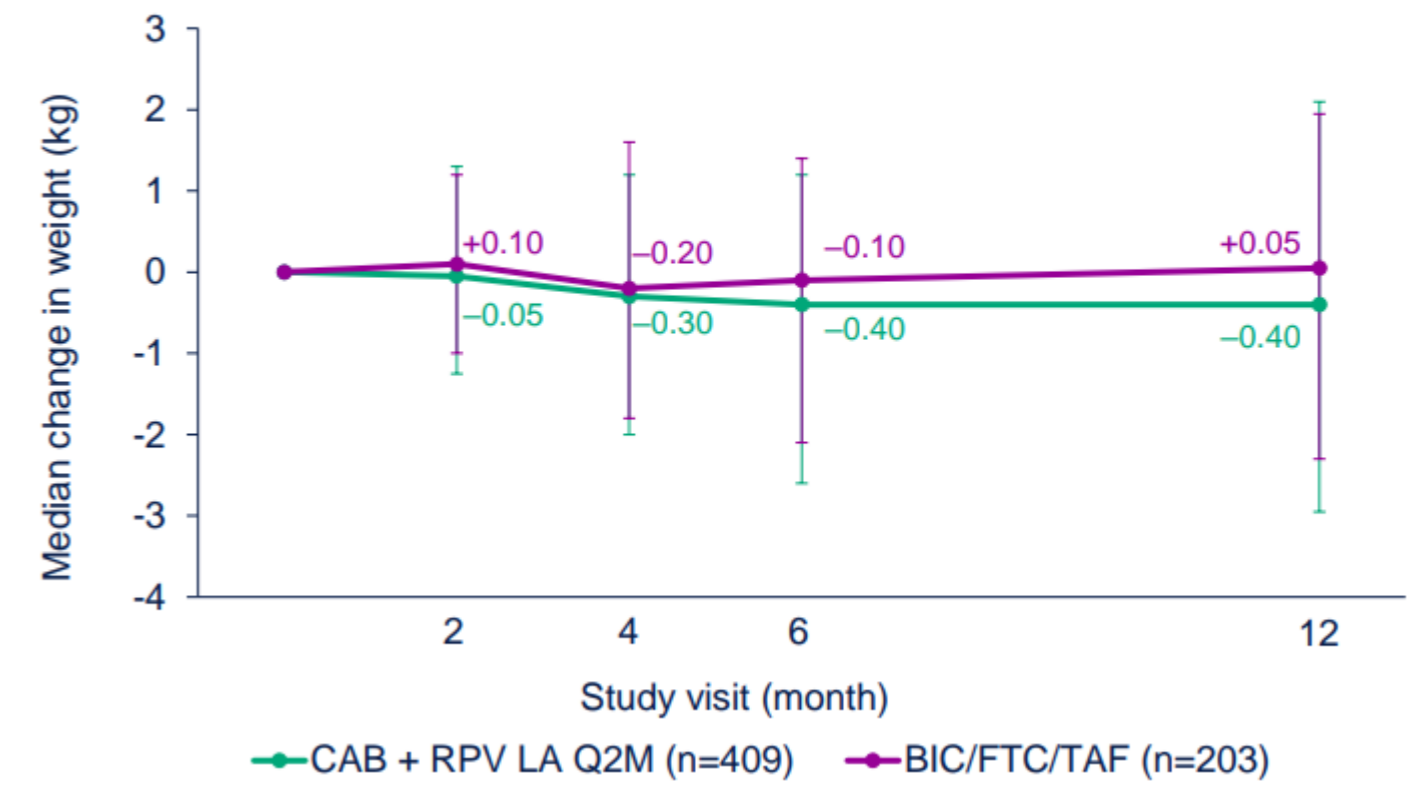
Clinical Infectious Diseases, Volume 70, Issue 2, 15 January 2020, Pages 319–322,



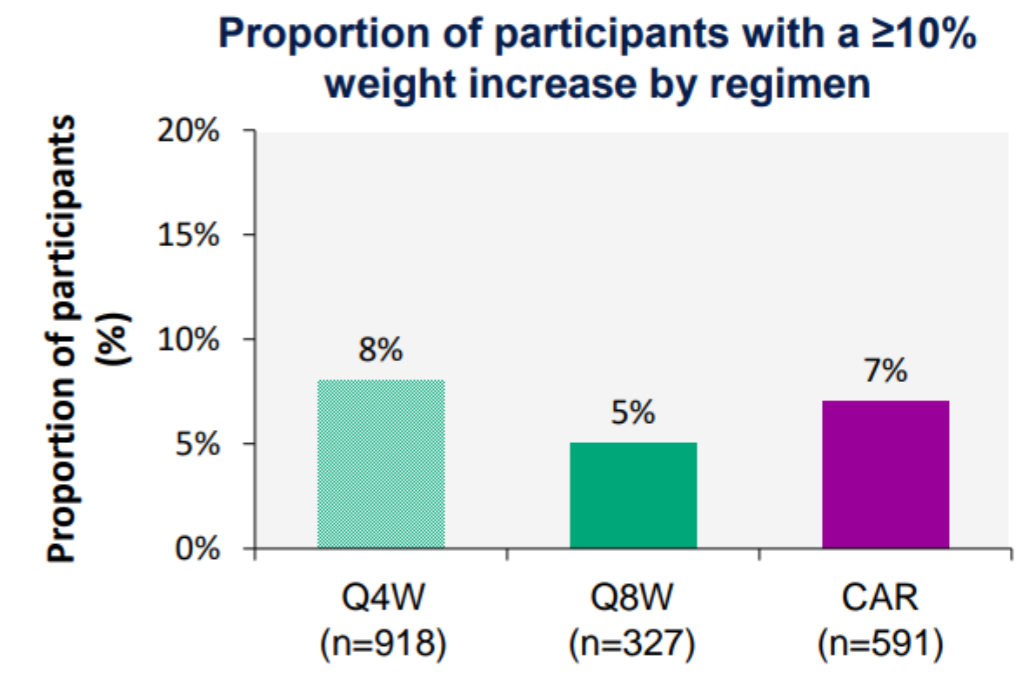
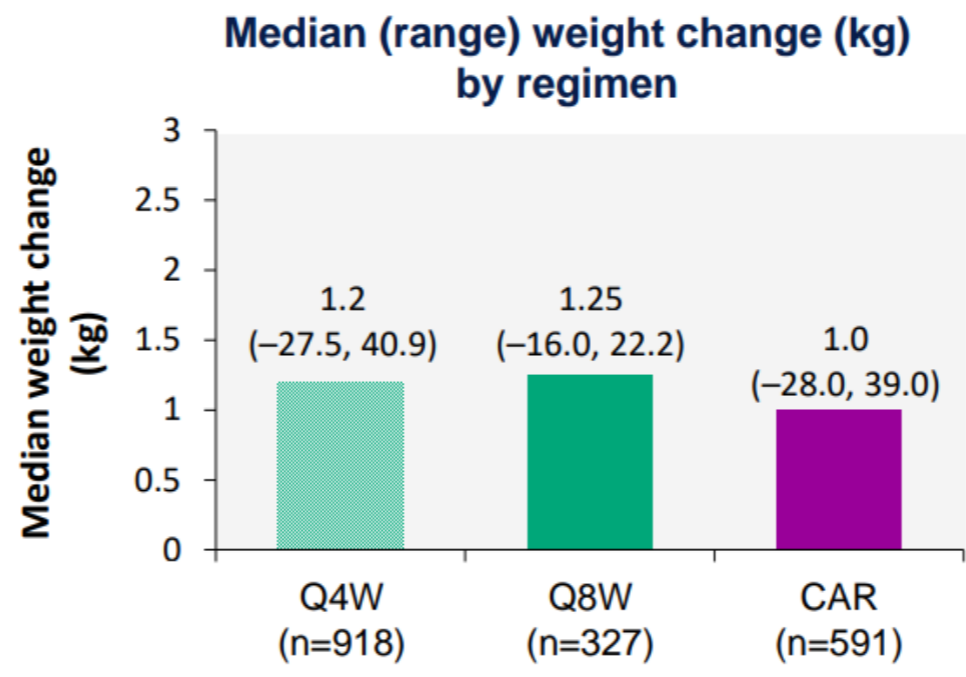
SOLAR

ATLAS, FLAIR

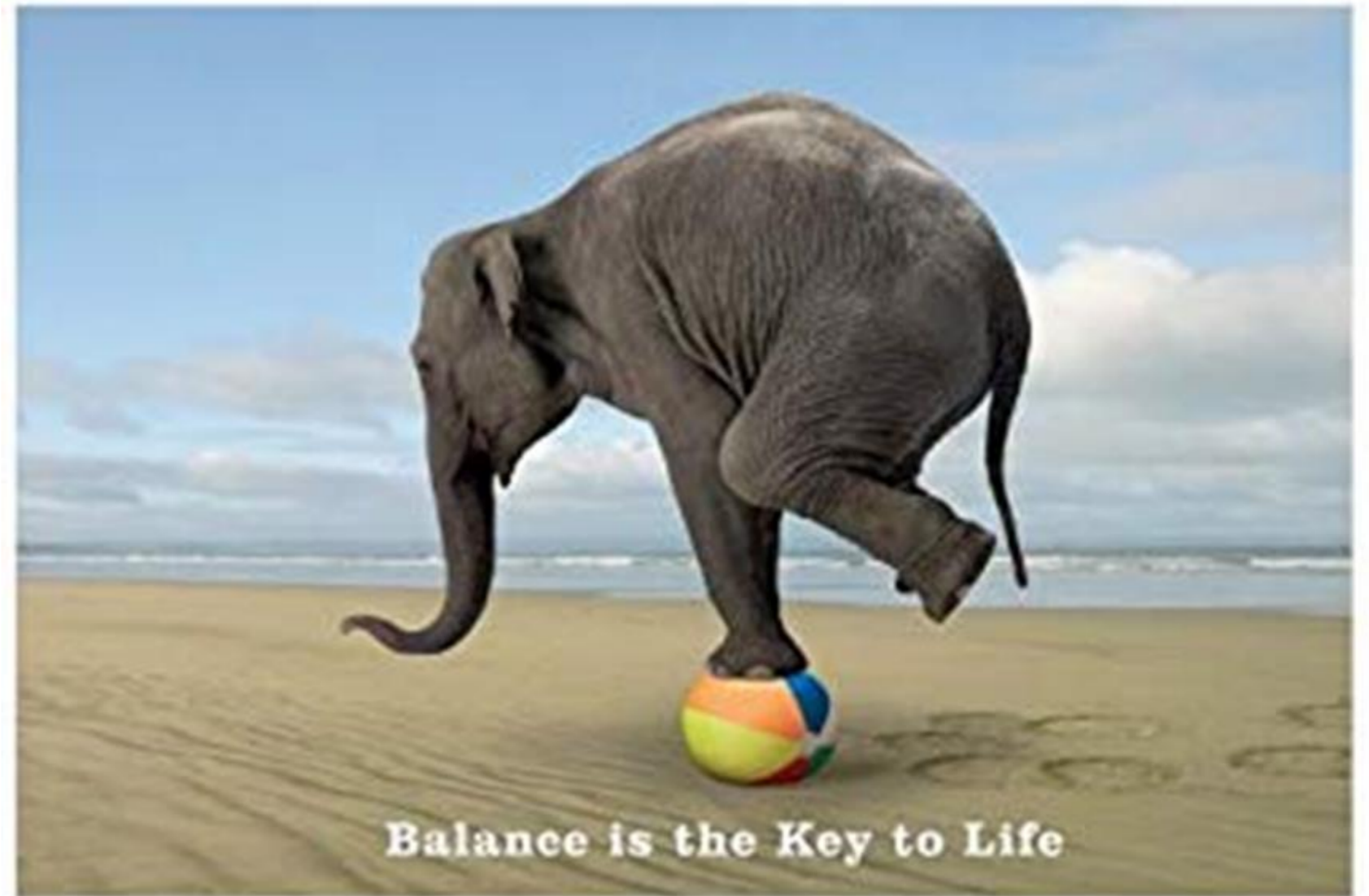
Median (IQR) Change in Weight Through Month 12†



Weight Change by Treatment Regimen From Baseline to Week 48



WHAT SHOULD WE DO ABOUT IT?



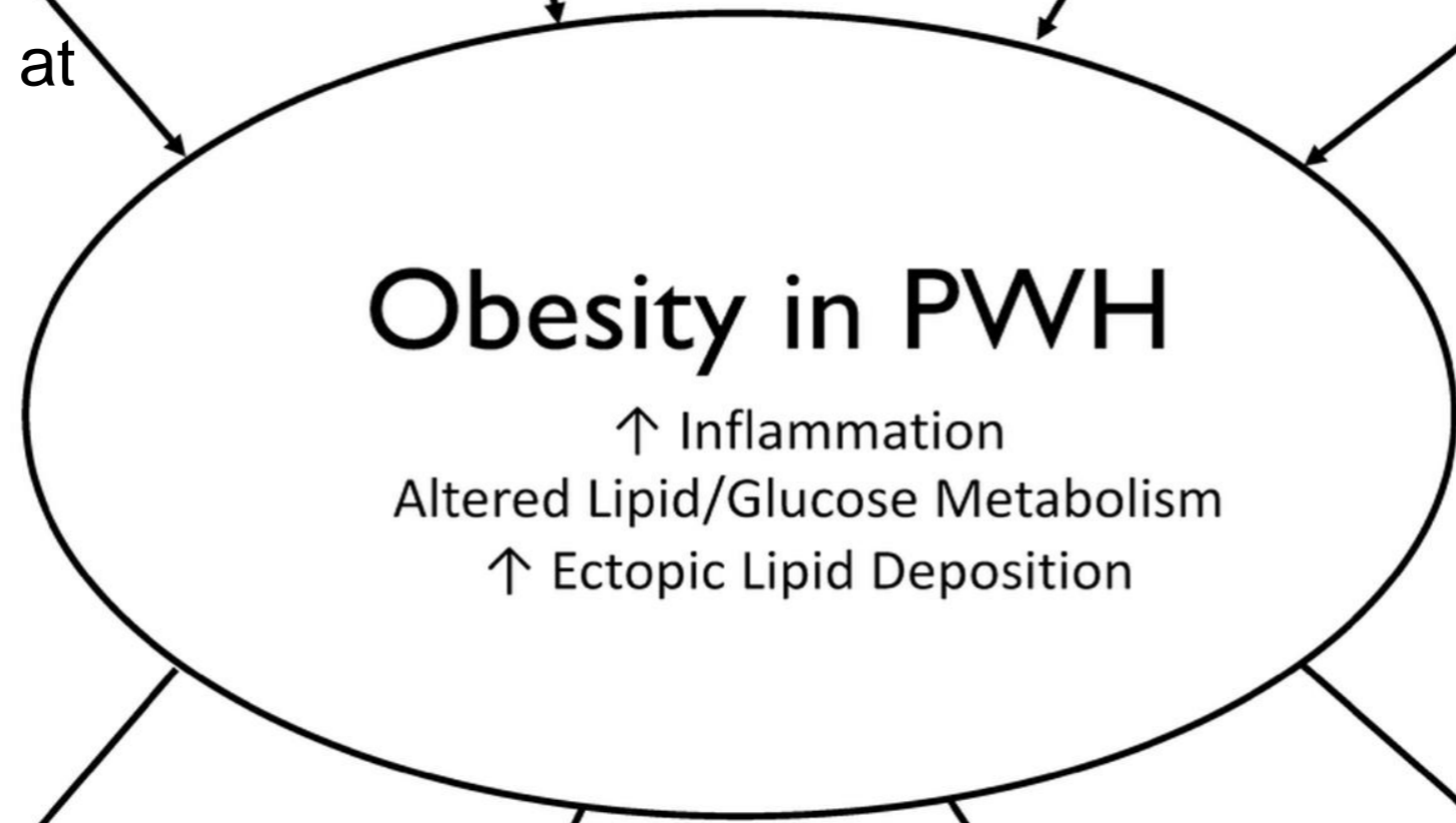
Sustained and early
ART for all PLHIV

Promote healthy lifestyle:
DIET and EXERCISE
SMOKING Cessation

Prevention-identify those at
risk

Antiretroviral Therapy Obesogenic Environment Shifting Demographics Aging Population

Less obesogenic ART in people at
risk as part of individualised
treatment approach?



Screen and treat
COMORBIDITIES such as
AHT/DM and hyperlipidemia

Diabetes Mellitus Neurocognitive Impairment Hepatic Disease Cardiovascular Disease

Treat obesity?

De Scheerder Marie-Angélique

GENERAL INTERNAL MEDICINE AND
INFECTIOUS DISEASES
GHENT UNIVERSITY HOSPITAL
GHENT UNIVERSITY

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