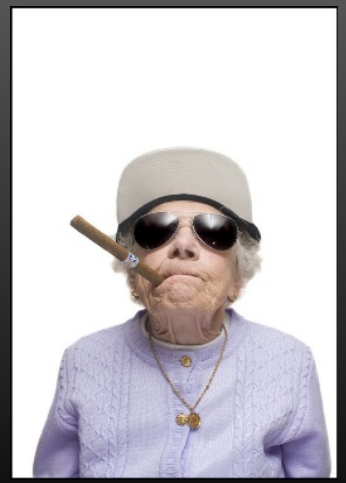
Weight gain and new antiretrovirals

2020

Professor Francois Venter
Ezintsha, University of the Witwatersrand

Thanks to Andrew Hill, ADVANCE study team



Disclosures: Francois Venter

Research Support: USAID; Unitaid; South African Medical Research Council; Bill and Melinda Gates Foundation; study drug donations from ViiV Healthcare and Gilead Sciences; study support Merk and ViiV

Speaker's Bureau: Merck, Gilead Sciences, AbbVie, Cipla, Johnson and Johnson, ViiV Healthcare, Mylan and Southern African HIV Clinicians Society

Board Member/Advisory Panel: Gilead Sciences, ViiV Healthcare, Merk, Mylan

Unitaid
Innovation in Global Health

PEPFAR

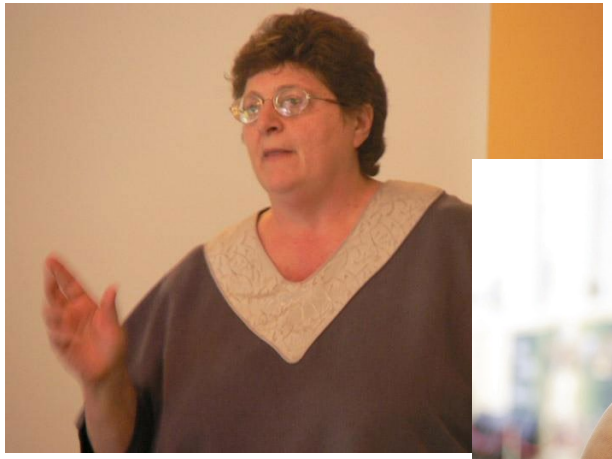
USAID
FROM THE AMERICAN PEOPLE

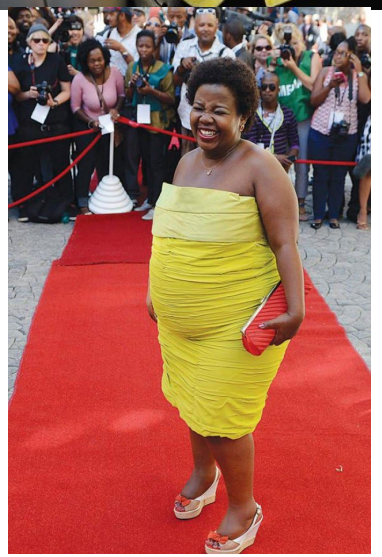
saMRC

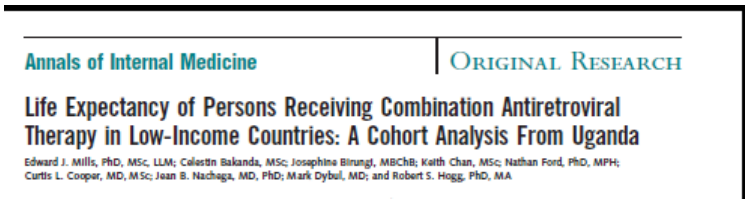
Ezintsha
INVESTIGATE INNOVATE ADVANCE

How on earth did we get here?

HIV-positive people are leading normal lives – which means they will gain weight if prone






Annals of Internal Medicine | ORIGINAL RESEARCH

Life Expectancy of Persons Receiving Combination Antiretroviral Therapy in Low-Income Countries: A Cohort Analysis From Uganda

Edward J. Mills, PhD, MSc, LLM; Celestin Bakanda, MSc; Josephine Birungi, MBChB; Keith Chan, MSc; Nathan Ford, PhD, MPH; Curtis L. Cooper, MD, MSc; Jean B. Nachega, MD, PhD; Mark Dybul, MD; and Robert S. Hogg, PhD, MA

- Uganda/ US/ UK – 'higher life expectancy that matched populations
- HIV positive people are going to get old


Annals of Internal Medicine | EDITORIAL

Life Expectancy in Africa: Back to the Future?

From 1950 to 1990, life expectancy in sub-Saharan Af- uals challenged global trade rules and regulations, ulti-

1. Expect a normal life expectancy:

May et al. AIDS 2014

- UK CHIC: 21 388 people started ART 2000-2010

	life expectancy		
CD4	Baseline	1 year ART	5 years ART
<200	**71**		**& VL>50 54**
200-349	**78**	**78**	
>350	**77**	**81**	**& VL<50 80**
General population	**78**		

10 | 16 August 2011 | Annals of Internal Medicine | Volume 155 • Number 4

Conclusion: If diagnosed, in care and on effective ART: life expectancy is normal

Great information to give to people newly diagnosed and encourage good adherence

Thanks: Julie Fox, Guys

First reports of weight gain with new regimens…

- Mid-2017
- Case report of someone switching INSTI due to weight gain

Weight gain reported with….

- Most modern drugs but worse with
  - Newer integrase inhibitors (not cabotegravir)
  - Tenofovir alafenamide (TAF)
  - Also rilpivirine
- Weight not reported in dolutegravir or bictegravir registration studies
- In context where >30 million people moving to dolutegravir across the world; and where TAF and bictegravir are extensively used in richer countries

Are new antiretroviral treatments increasing the risks of clinical obesity?

Andrew Hill[1]*, Laura Waters[2] and Anton Pozniak[3]

[1] Department of Translational Medicine, University of Liverpool, UK
[2] Central and North West London NHS Trust, Mortimer Market Centre, London, UK
[3] Chelsea and Westminster Hospital, London, UK; London School of Hygiene and Tropical Medicine, UK

Table 1. Effects of raltegravir, dolutegravir and bictegravir on body weight in randomised trials

Study [ref]	Design	Results
Raltegravir		
NEAT 001 [12] (naïve, *n*=126)	DRV/r+RAL DRV/r + TDF/FTC	DEXA sub-study: trunk fat 7.3% higher DRV/r/RAL *vs* TDF/FTC/RAL at week 96 (*P*=0.021)
ACTG 5260s [10,11] (naïve, *n*=126)	TDF/FTC/RAL TDF/FTC/DRV/r TDF/FTC/ATV/r	Higher risk of severe weight gain for RAL vs ATV/r
Dolutegravir		
NEAT 022 [13] (switch, *n*=415)	NRTIs + DTG NRTIs + PI/r	+1 kg increase in body weight to week 48 (*P*=0.002)
SPRING-1 [13] (naïve, *n*=204)	TDF/FTC/EFV TDF/FTC/DTG	Increases in body weight higher in DTG arms
Gilead 1490 [15] (naïve, *n*=645)	TAF/FTC/DTG TAF/FTC/BIC	+3.9 kg increase in body weight to week 96 +3.5 kg increase in body weight to week 96
MONODO [9] (naïve, *n*=8)	DTG monotherapy	+4.1 kg increase in body weight to week 24

ATV/r; atazanavir/ritonavir; BIC: bictegravir; DRV/r: darunavir/ritonavir; DTG: dolutegravir; FTC: emtricitabine; NRTI: nucleoside reverse transcriptase inhibitors; PI/r: ritonavir-boosted protease inhibitor; RAL: raltegravir; TAF: tenofovir AF; TDF: tenofovir DF.

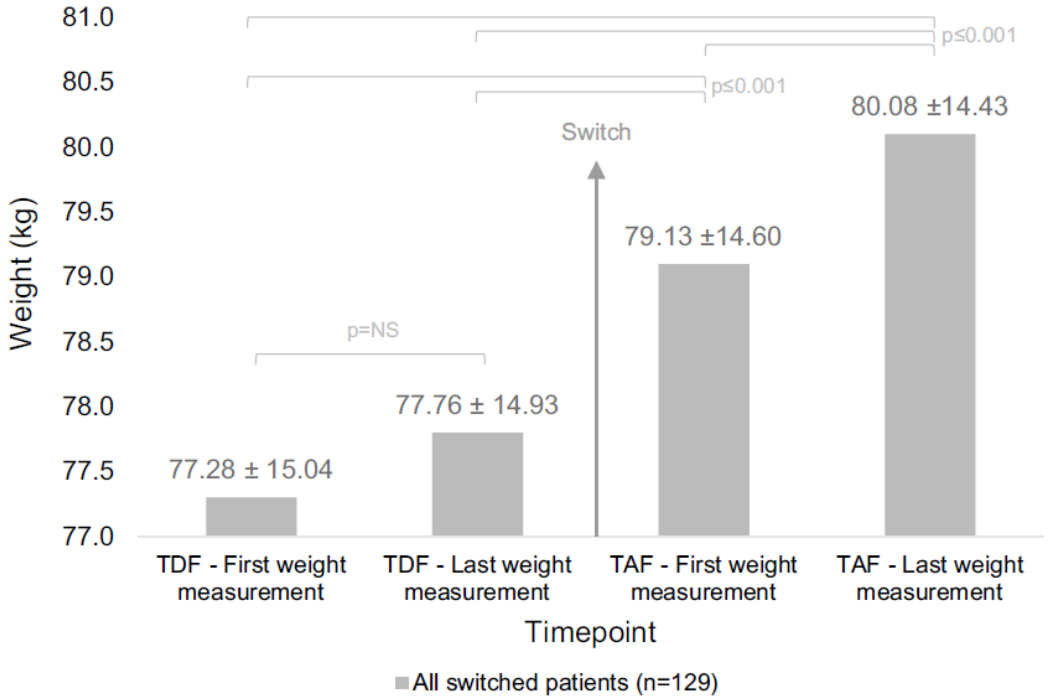
Use of TDF versus TAF or ABC – effects on body weight

DISCOVER trial (PrEP): +1kg on TAF/FTC, versus +0kg on TDF/FTC

STEAL trial (treatment): +1kg on ABC/3TC versus +0kg on TDF/FTC

AMBER trial (treatment): +1.8kg on TAF/FTC/DRV/c vs +0.8kg on TDF/FTC/DRV/c

Change in body weight after switch from TDF to TAF – German cohort study

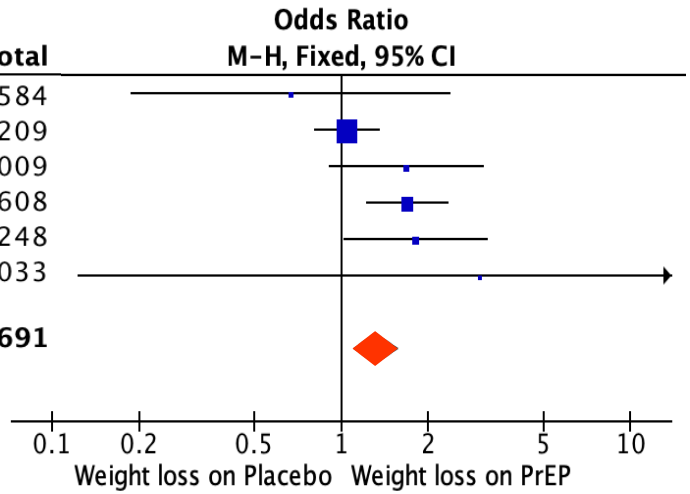


Only switch patients are shown, "TDF (TAF)—first/last weight measurement" denotes the first/last weight measured on TDF (TAF) treatment; results shown for weight in kg; *NS* not statistically significant

Gomez et al. Weight Gain switching TDF to TAF. Infection 2018

TDF as PrEP: weight loss >5%

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total
Partners (Daily TDF/FTC)	4	1579	6	1584
Bangkok Tenofovir Study	140	1204	135	1209
VOICE (Daily TDF/FTC)	28	1003	17	1009
TDF 2 (TDF/FTC)	113	611	72	608
iPREX (Daily TDF/FTC)	34	1251	19	1248
FEM-PrEP (Daily TDF/FTC)	1	1025	0	1033
Total (95% CI)		**6673**		**6691**
Total events	320		249	



Odds Ratio = 1.32 (1.11 to 1.58)

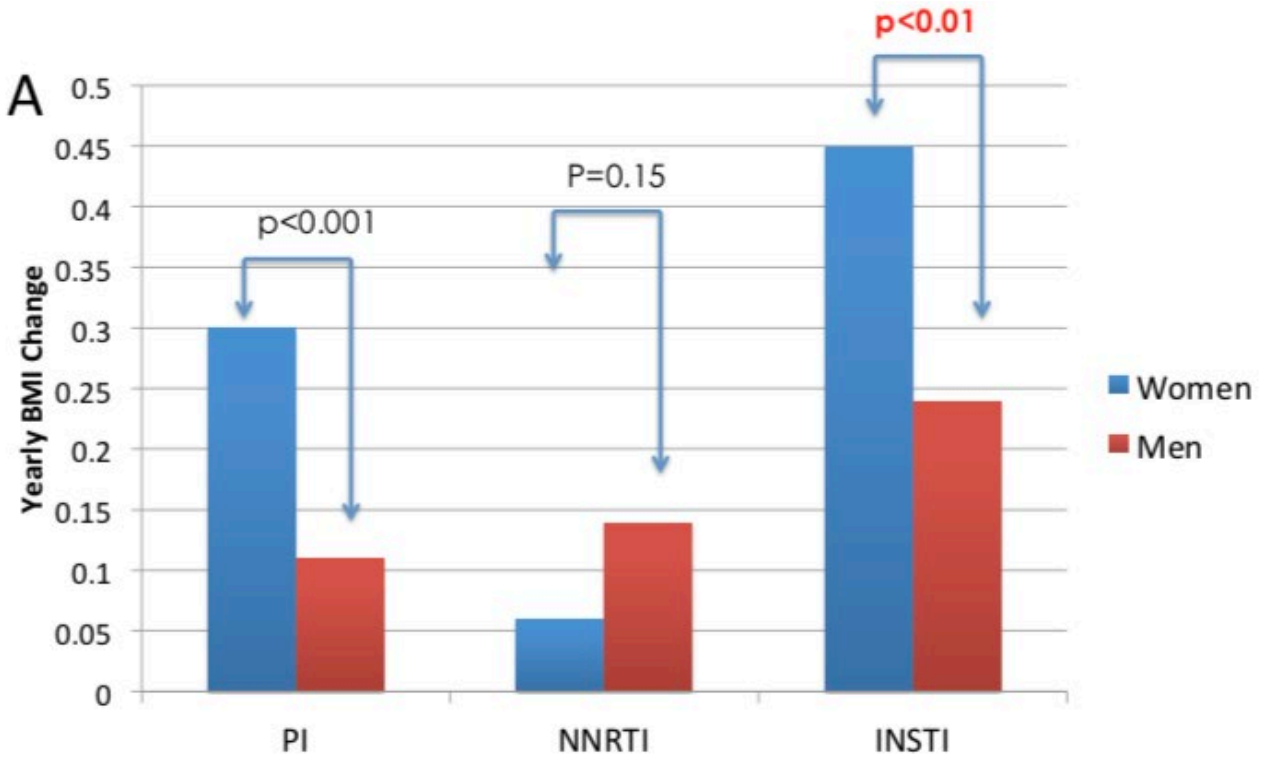
P = 0.002

Then came the INSTI's….

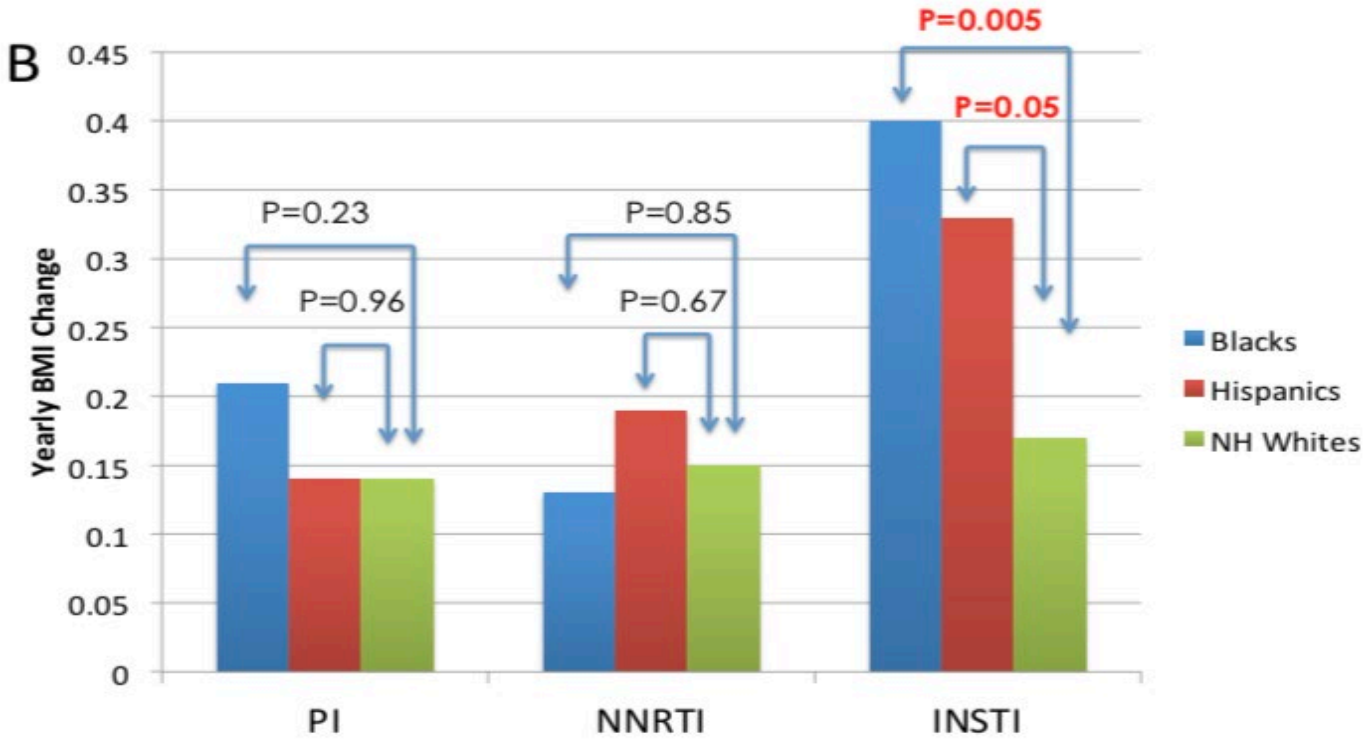
- Rapidly became standard of care
- 2 years later, at CROI – issue raised in themed discussion

Weight gain themed discussion : CROI 2019 http://www.croiwebcasts.org/s/2019croi/TD-08

Weight gain on INSTI – women gain 2x more than men (US cohort study)



Weight gain on INSTI – black people gain 2x more than whites (US cohort study)



Randomised trials – similar effects of DTG and BIC

Trial	Design	Outcomes
NEAT 022 (N=415, switch)	NRTIs + DTG NRTIs + PI/r	+1kg rise in body weight to Week 48 (p=0.002)
SPRING-1 N=204, naive	TDF/FTC/EFV TDF/FTC/DTG	rises in body weight higher in DTG arms
Gilead 1490	TAF/FTC/DTG	+3.9kg rise in body weight to Week 96
N=645, naïve	TAF/FTC/BIC	+3.5kg rise in body weight to Week 96
Gilead 1489	ABC/3TC/BIC	+2.4kg rise in body weight to Week 96
N=645, naïve	TAF/FTC/BIC	+3.6kg rise in body weight to Week 96
MONODO N=8, naïve	DTG mono	+4.1kg rise in body weight to Week 24

Clinical Infectious Diseases

MAJOR ARTICLE

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,[9] Lijie Zhong,[9] Diana M. Brainard,[9] Kathleen Melbourne,[9] Moupali Das,[9] Hans-Jürgen Stellbrink,[10] Frank A. Post,[11]

Table 5. Risk factors for significant (≥10%) weight gain in individuals initiating ART.

Variable	OR	95% CI	p value
CD4 (<200 vs. ≥200/μL)	4.36	3.6, 5.27	**<0.001**
HIV RNA (>100k vs. ≤100k c/mL)	1.98	1.65, 2.37	**<0.001**
BMI (normal vs. overweight	1.54	1.27, 1.87	**<0.001**
BMI (normal vs. obese)	1.66	1.29, 2.15	**<0.001**
Sex (female vs. male)	1.54	1.21, 1.96	**<0.001**
Race (black vs. non-black)	1.32	1.1, 1.59	**0.003**
Third agent (BIC/DTG vs. EFV)	1.82	1.24, 2.66	**0.002**
Third agent (EVG/c vs. EFV)	1.36	1.04, 1.78	**0.026**
Third agent (RPV vs. EFV)	1.51	1.03, 2.2	**0.035**
Third agent (ATV/r vs. EFV)	0.92	0.59, 1.45	0.73
NRTI (TAF vs. AZT)	1.75	1.04, 2.95	**0.034**
NRTI (TDF vs. AZT)	1.19	0.76, 1.87	0.44
NRTI (ABC vs. AZT)	0.93	0.47, 1.8	0.82
NRTI (TAF vs. ABC)	1.9	1.25, 2.88	**0.003**
NRTI (TDF vs. ABC)	1.29	0.79, 2.11	0.31
NRTI (TAF vs. TDF)	1.47	1.14, 1.9	**0.003**

Sax, CID, 2019

Clinical Infectious Diseases

MAJOR ARTICLE

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

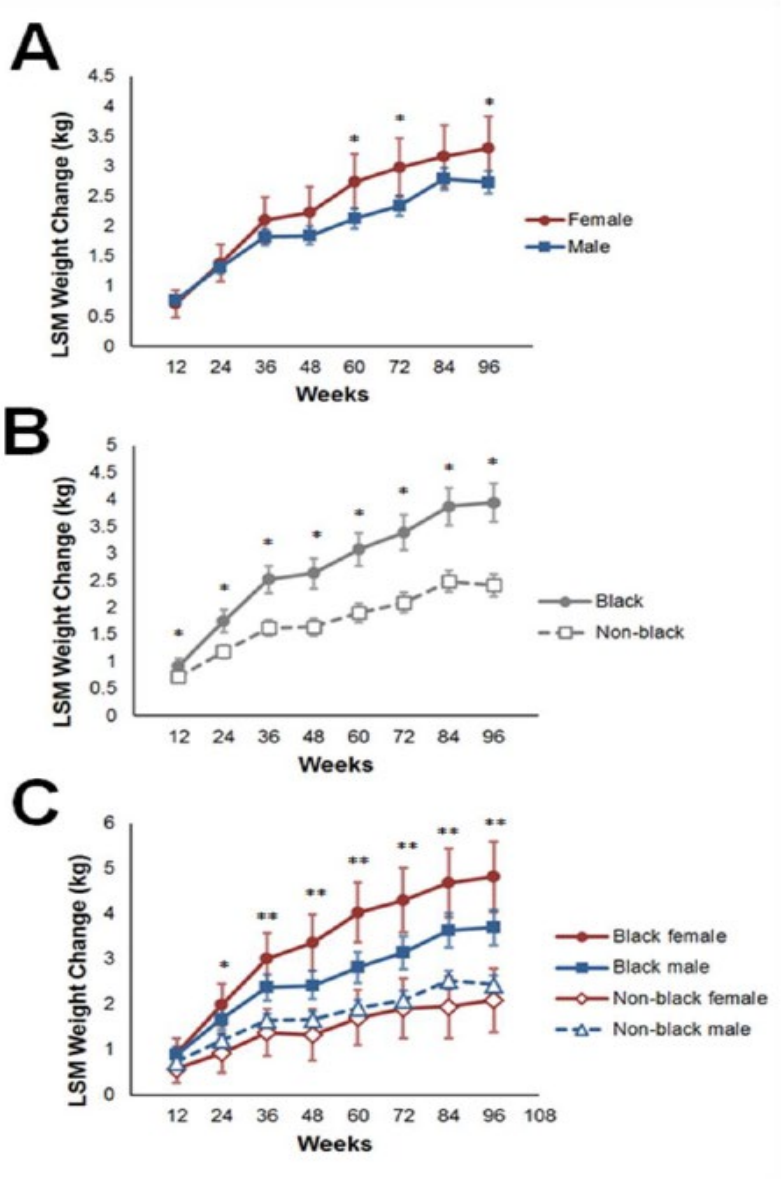
Paul E. Sax,[1] Kristine M. Erlandson,[2] Jordan E. Lake,[3] Grace A. McComsey,[4] Chloe Orkin,[5] Stefan Esser,[6] Todd T. Brown,[7] Jürgen K. Rockstroh,[8] Xuelian Wei,[9] Christoph C. Carter,[9] Lijie Zhong,[9] Diana M. Brainard,[9] Kathleen Melbourne,[9] Moupali Das,[9] Hans-Jürgen Stellbrink,[10]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

Table 5. Risk factors for significant (≥10%) weight gain in individuals initiating ART.

Variable	OR	95% CI	p value
CD4 (<200 vs. ≥200/μL)	4.36	3.6, 5.27	**<0.001**
HIV RNA (>100k vs. ≤100k c/mL)	1.98	1.65, 2.37	**<0.001**
BMI (normal vs. overweight	1.54	1.27, 1.87	**<0.001**
BMI (normal vs. obese)	1.66	1.29, 2.15	**<0.001**
Sex (female vs. male)	1.54	1.21, 1.96	**<0.001**
Race (black vs. non-black)	1.32	1.1, 1.59	**0.003**
Third agent (BIC/DTG vs. EFV)	1.82	1.24, 2.66	**0.002**
Third agent (EVG/c vs. EFV)	1.36	1.04, 1.78	**0.026**
Third agent (RPV vs. EFV)	1.51	1.03, 2.2	**0.035**
Third agent (ATV/r vs. EFV)	0.92	0.59, 1.45	0.73
NRTI (TAF vs. AZT)	1.75	1.04, 2.95	**0.034**
NRTI (TDF vs. AZT)	1.19	0.76, 1.87	0.44
NRTI (ABC vs. AZT)	0.93	0.47, 1.8	0.82
NRTI (TAF vs. ABC)	1.9	1.25, 2.88	**0.003**
NRTI (TDF vs. ABC)	1.29	0.79, 2.11	0.31
NRTI (TAF vs. TDF)	1.47	1.14, 1.9	**0.003**

Sax, CID, 2019

Figure 2



Sax, CID, 2019

OPERA: Longitudinal Prospective Cohort Analysis

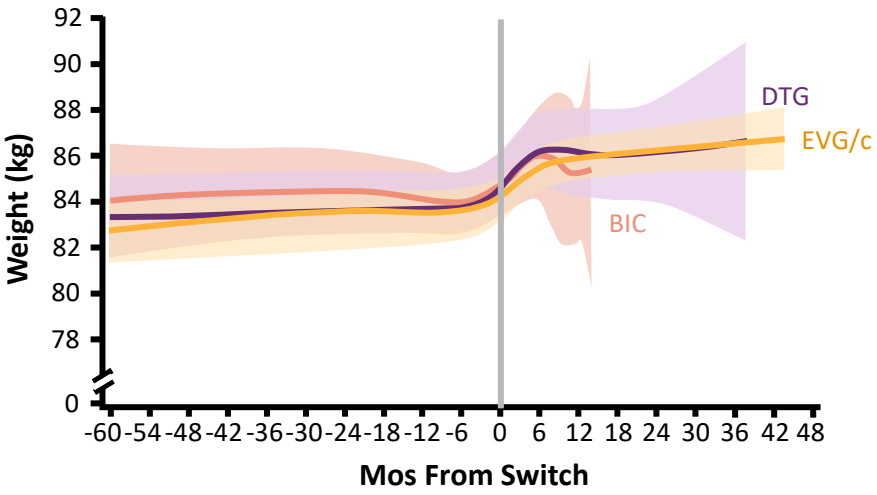
- Routine EHR data collected from ~ 8% of US PWH receiving care (> 115,000 individuals across 65 cities in 19 states and Puerto Rico)
- Current analysis restricted to adults receiving TDF-containing 3-drug ART at BL with ≥ 2 consecutive HIV-1 RNA < 200 copies/mL who switched TDF to TAF

Anchor Agent by Class, % (n)		Maintained Other ARVs (n = 5479)
INSTIs (n = 3281)	▪ Elvitegravir/cobicistat ▪ Dolutegravir ▪ Raltegravir	73 (2389) 20 (643) 8 (249)
NNRTIs (n = 1452)	▪ Rilpivirine ▪ Nevirapine ▪ Efavirenz ▪ Etravirine	85 (1238) 12 (176) 2 (26) 1 (12)
Boosted PIs (n = 746)	▪ Darunavir ▪ Atazanavir ▪ Lopinavir ▪ Fosamprenavir	68 (504) 28 (211) 3 (22) 1 (9)

Mallon. AIDS 2020. Abstr OAB0604.

Slide credit: clinicaloptions.com

OPERA: Weight Change With Switch From TDF to TAF While Also Switching to an INSTI

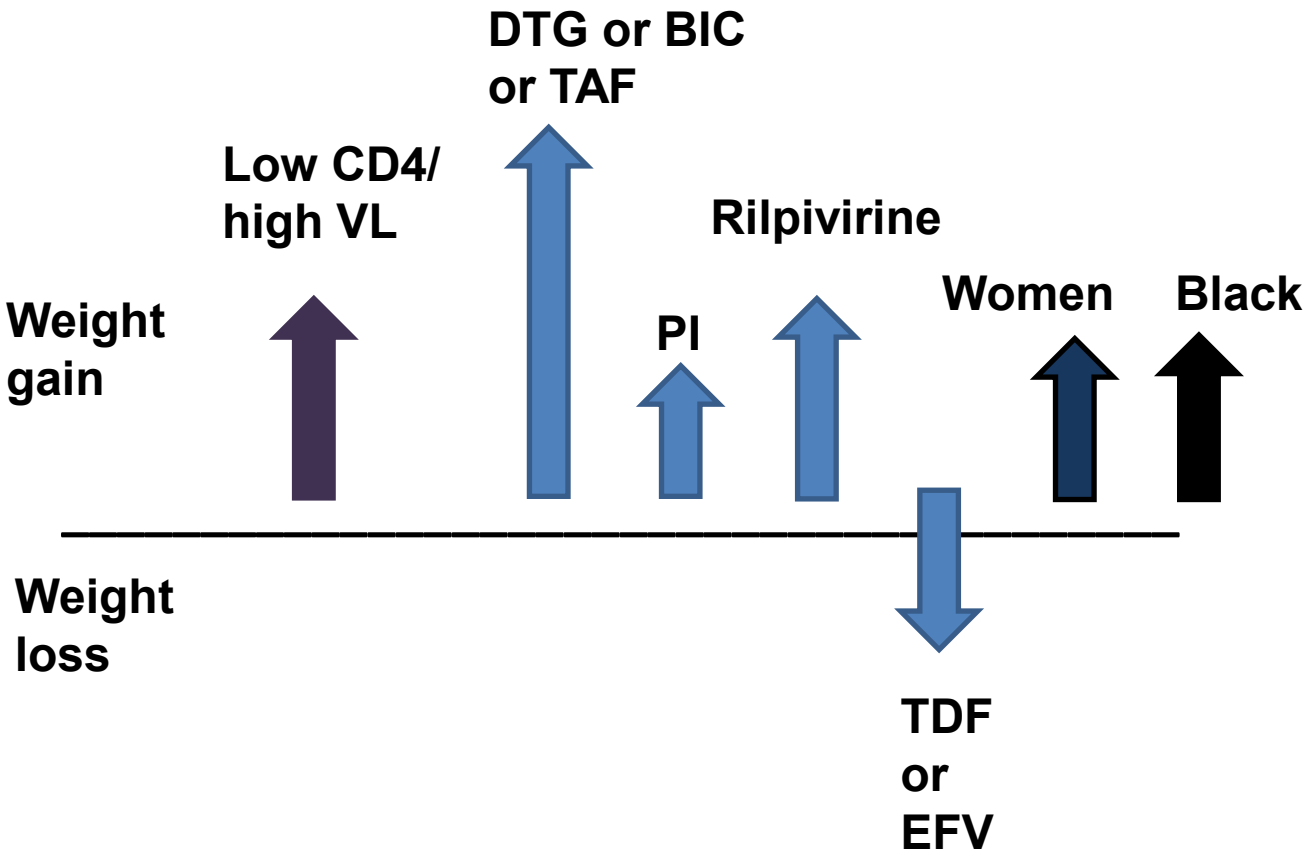


Estimated Weight Δ by Time From TDF to TAF Switch, kg/yr (95% CI)	EVG/c (n = 1120)	DTG (n = 174)	BIC (n = 129)
-60 to 0 mos	0.24 (0.04 to 0.43)	0.22 (-0.08 to 0.52)	0.01 (-0.38 to 0.39)
0 to 9 mos	2.55 (1.86 to 3.24)	3.09 (1.26 to 4.93)	4.47 (0.81 to 8.13)
9+ mos	0.26 (-0.10 to 0.61)	-0.23 (-1.62 to 1.16)	-9.97 (-23.79 to 3.85)

Mallon. AIDS 2020. Abstr OAB0604. Reproduced with permission.

Slide credit: clinicaloptions.com

Drivers of weight gain / loss



ORIGINAL RESEARCH
Journal of Virus Eradication 2020; 6: 70–73

Phase 3 trials of new antiretrovirals are not representative of the global HIV epidemic

Toby Pepperrell[1], Andrew Hill[2]*, Michelle Moorhouse[3], Polly Clayden[4], Kaitlyn McCann[5], Simiso Sokhela[3], Celicia Serenata[6], Willem Daniel Francois Venter[3]

[1]Faculty of Medicine, Imperial College London, UK
[2]Department of Translational Medicine, Liverpool University, Pharmacology, Liverpool, UK

- Most registration studies done in white males for almost all newer antiretrovirals

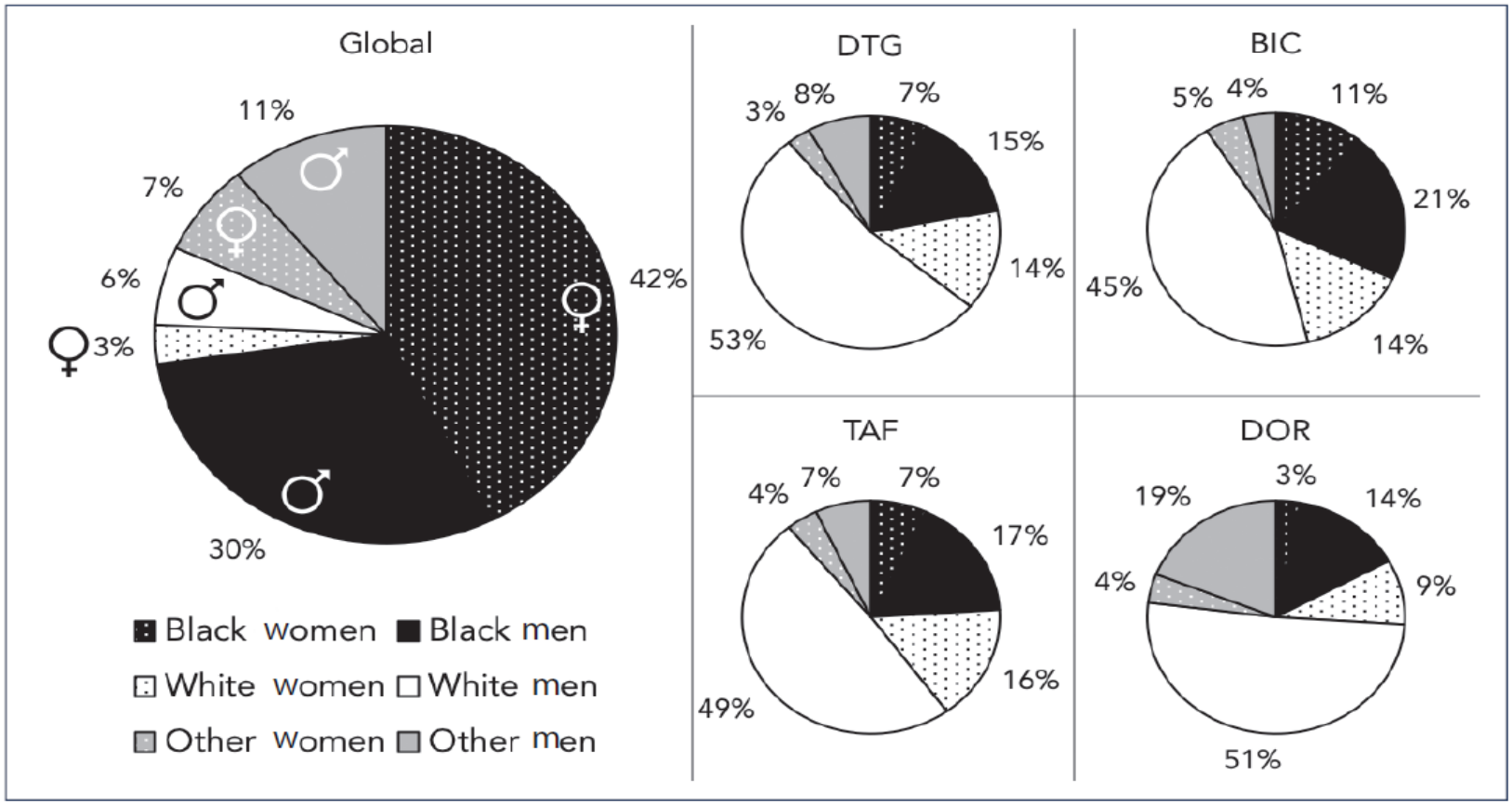
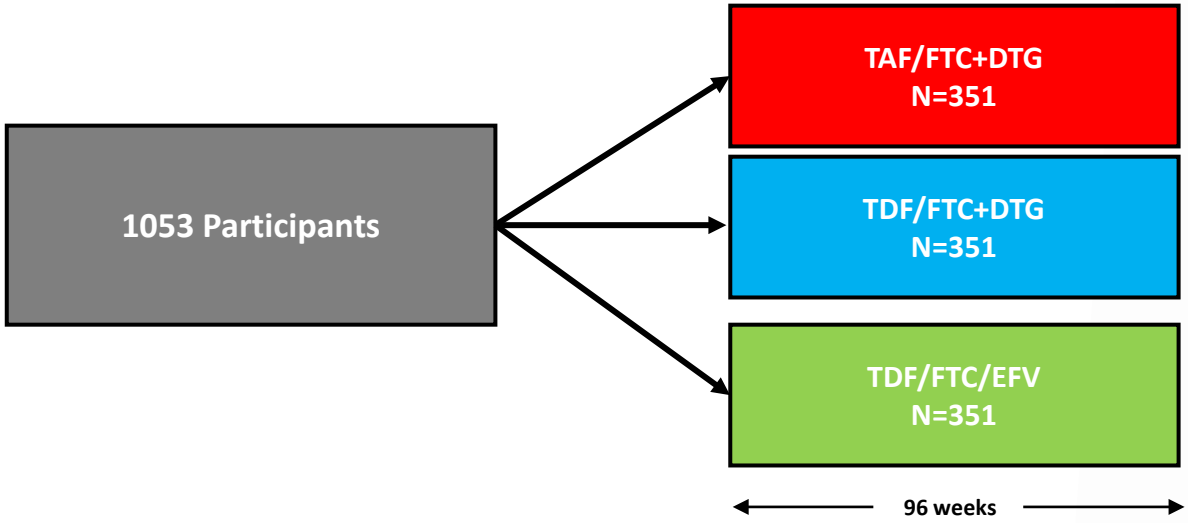
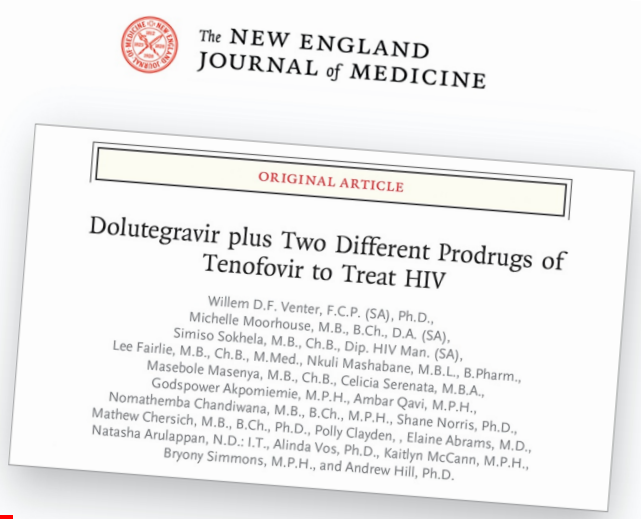


Figure 1. Estimated global demographics of PLWH *vs* RCT demographics. Percentages may be rounded up to make 100. Data are given as percentage. BIC: bictegravir; DOR: doravirine; DTG: dolutegravir; PLWH: people living with HIV; RCT: randomised controlled trial; TAF: tenofovir alafenamide.

ADVANCE: Study design

Inclusion criteria: treatment-naïve, HIV-1 RNA level ≥ 500 copies/mL, no TB or pregnancy, no baseline genotyping




The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dolutegravir plus Two Different Prodrugs of Tenofovir to Treat HIV

Willem D.F. Venter, F.C.P. (SA), Ph.D., Michelle Moorhouse, M.B., B.Ch., D.A. (SA), Simiso Sokhela, M.B., Ch.B., Dip. HIV Man. (SA), Lee Fairlie, M.B., Ch.B., M.Med., Nkuli Mashabane, M.B.L., B.Pharm., Masebole Masenya, M.B., Ch.B., Celicia Serenata, M.B.A., Godspower Akpomiemie, M.P.H., Ambar Qavi, M.P.H., Nomathemba Chandiwana, M.B., B.Ch., M.P.H., Shane Norris, Ph.D., Mathew Chersich, M.B., B.Ch., Ph.D., Polly Clayden, , Elaine Abrams, M.D., Natasha Arulappan, N.D.: I.T., Alinda Vos, Ph.D., Kaitlyn McCann, M.P.H., Bryony Simmons, M.P.H., and Andrew Hill, Ph.D.

Open-label, 96-week study in Johannesburg, South Africa – IN PRESS
Study visits at Baseline, Week 4, 12, 24, 36, 48, 60, 72, 84, and 96

And representative by race and gender and geography

Baseline characteristics (1/2)

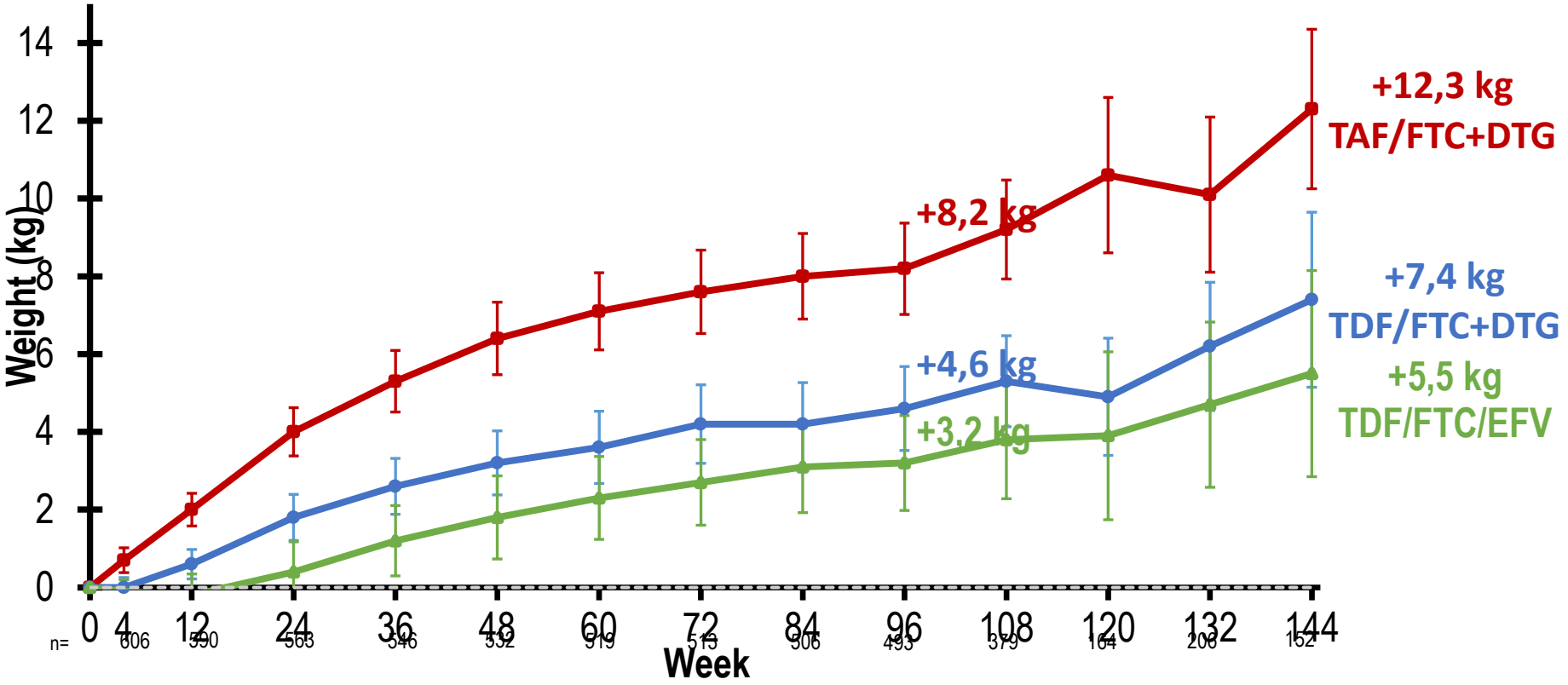
Characteristic	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
Age, mean (SD), years	33 ± 8	32 ± 8	32 ± 7
Female	61%	59%	57%
Black	99%	100%	100%
Baseline HIV-1 RNA			
≤100,000 copies/mL	78%	80%	77%
>100,000 copies/mL	22%	20%	23%
CD4+ cell count, mean (SD), cells/mm^3	349 ± 225	323 ± 234	337 ± 222

Weight was high even pre-ART!

Baseline characteristics (2/2)

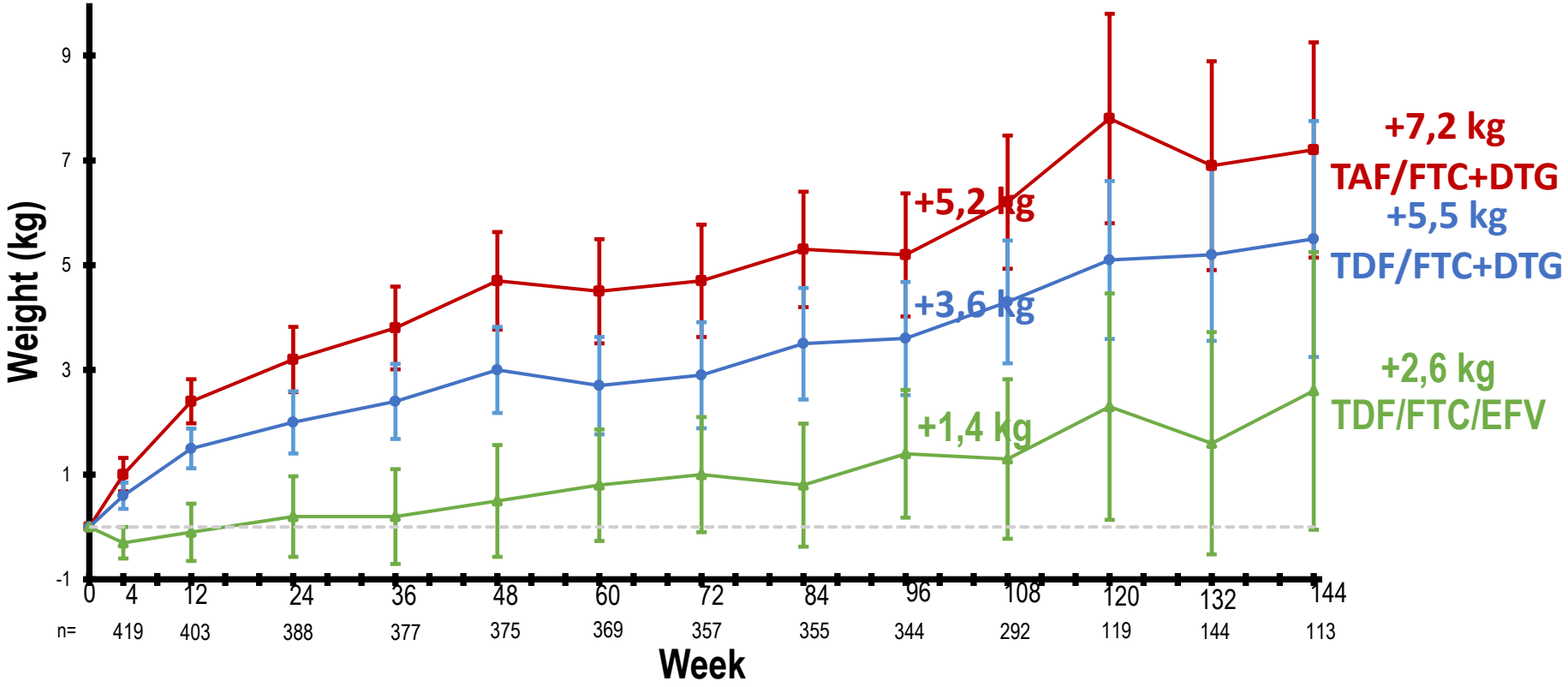
Characteristic	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
Weight, mean (kg)			
Male	67.9	67.1	67.3
Female	68.8	69.5	70.2
BMI, mean (kg/m^2)			
Male	21.7	21.6	21.8
Female	25.6	26.1	26.1
Categories of BMI, n (%)			
Underweight (< 18.5)	42 (12%)	35 (10%)	37 (11%)
Normal (18.5-25)	177 (51%)	190 (54%)	193 (55%)
Overweight (25-30)	96 (27%)	78 (22%)	77 (22%)
Obese (> 30)	35 (10%)	48 (14%)	44 (13%)

Mean change in weight (kg): women



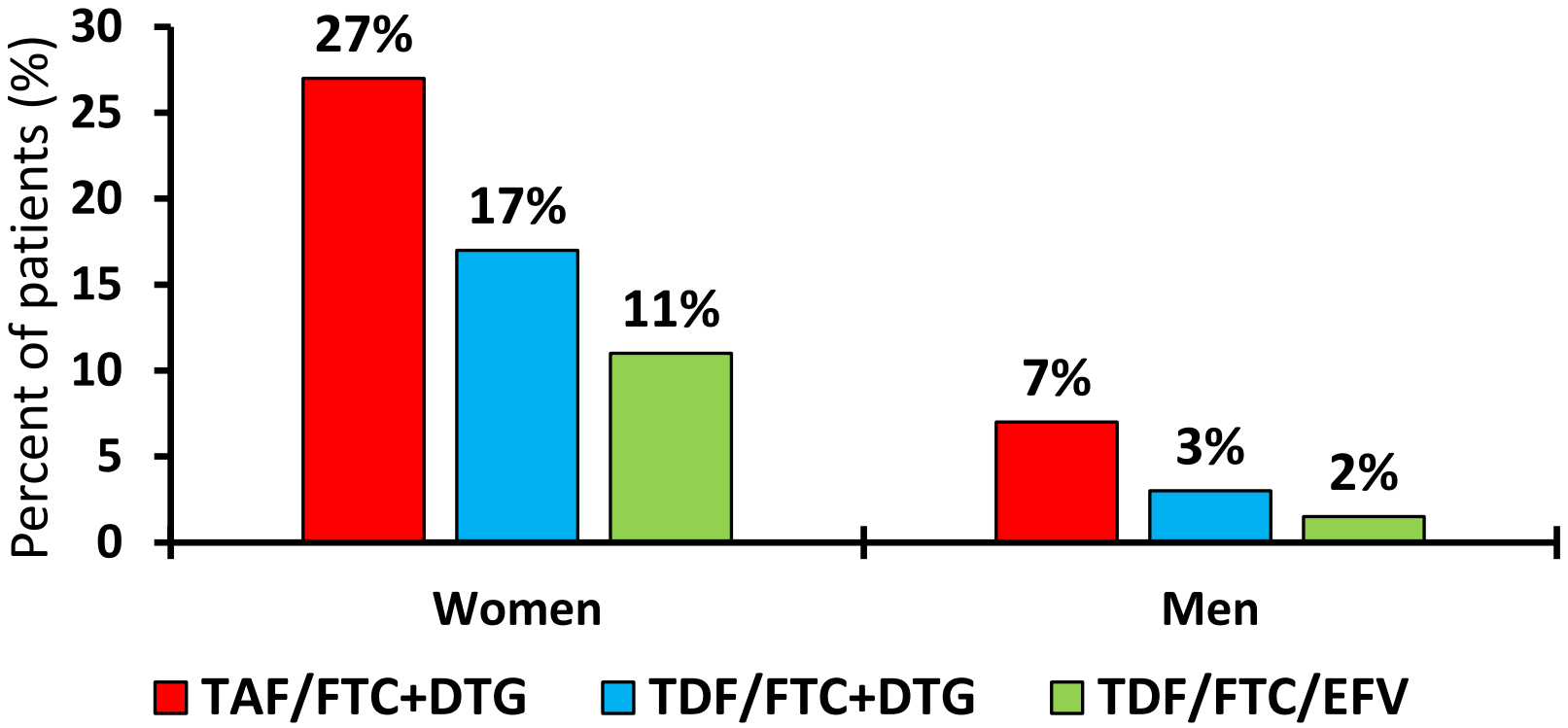
Note: data incomplete to week 144

Mean change in weight (kg): men

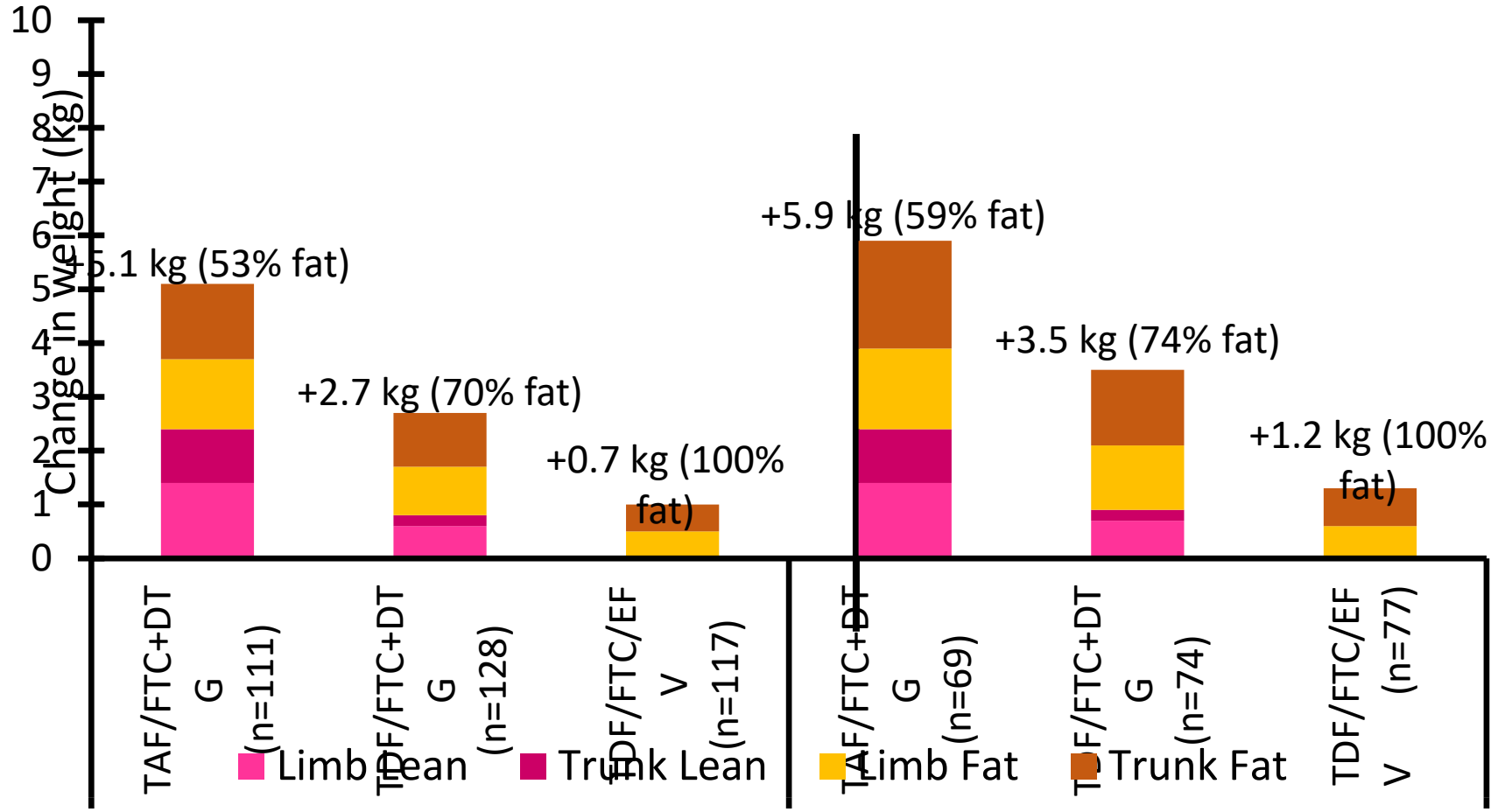


Note: data incomplete to week 144

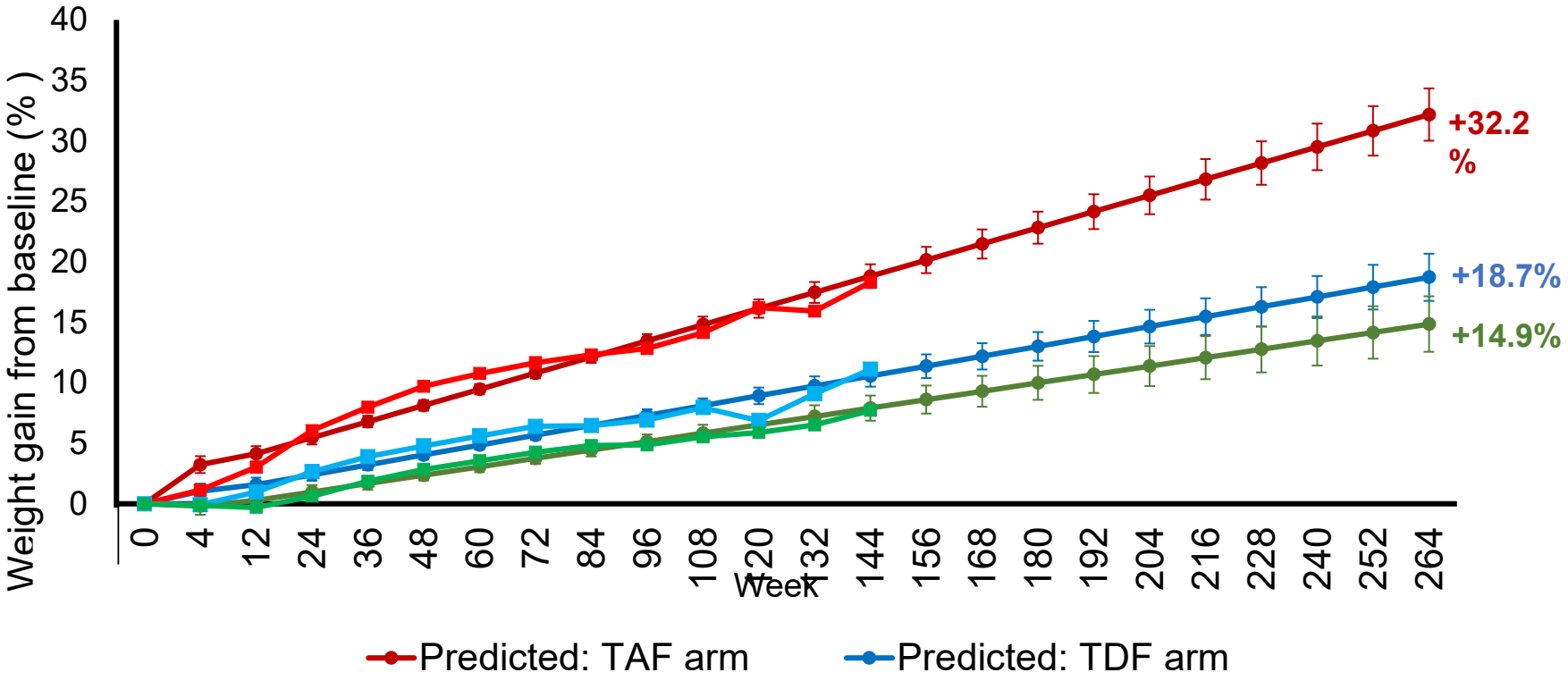
Treatment-Emergent Obesity at Week 96



Changes in DXA body composition: Men



Linear regression model: predicted mean percentage change in weight from baseline over 5 years in <u>females</u>

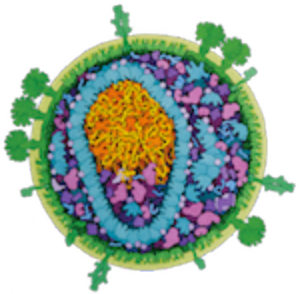


CYP2B6 Genotype and Weight Gain Differences Between Dolutegravir and Efavirenz

CID, in press

Rulan Griesel, Gary Maartens, Simiso Sokhela, Godspower Akpomiemie, Francois Venter, Michelle Moorhouse, Phumla Sinxadi

CROI
Conference on Retroviruses and Opportunistic Infections



CROI
Conference on Retroviruses and Opportunistic Infections

Predicted 10-year risks of diabetes and cardiovascular disease in the ADVANCE trial

Andrew Hill[1], Kaitlyn McCann[2], Ambar Qavi[2], Bryony Simmons[2] ,Victoria Pilkington[2], Michelle Moorhouse[3], Godspower Akopmiemie[3], , Simiso Sokhela[3], Celicia Serenata[3], Alinda Vos[4], Francois Venter[3]

[1] Liverpool University, Pharmacology, Liverpool, United Kingdom, [2] Imperial College London, Faculty of Medicine, London, United Kingdom
[3] Ezintsha, Wits Reproductive Health and HIV Institute, Johannesburg, South Africa; [4] University Medical Center Utrecht, Epidemiology, Utrecht, Netherlands

QDIABETES Equation Results: Females (Linear Predictions)

Treatment arm / 10 year diabetes risk	Median change from baseline to:				
	Baseline	Week 96 (Observed)	Year 3	Year 4	Year 5
TAF/FTC/DTG n = 120	0.30%	+1.20%	+1.40%	+2.00%	+2.50%
TDF/FTC/DTG n = 111	0.40%	+0.50%	+0.60%	+0.90%	+1.30%
TDF/FTC/EFV n = 116	0.30%	+0.80%	+1.00%	+1.30%	+1.50%

*TAF/FTC/DTG risk significantly higher than TDF/FTC/DTG at Week 96 (p=0.028); Year 3 (p= 0.025); Year 4 (p= 0.015); Year 5 (p= 0.014)

12 additional cases of diabetes in TAF vs TDF per 1000 females over 30 treated for 5 years

Conference on Retroviruses and Opportunistic Infections 2020

CHANGES IN BODY MASS INDEX AND THE RISK OF CARDIOVASCULAR DISEASE: THE D:A:D STUDY

Kathy Petoumenos, Locadiah Kuwanda, Lene Ryom, Amanda Mocroft, Peter Reiss, Stephane De Wit, Christian Pradier, Andrew Philips, Camilla I Hatleberg, Antonella d'Arminio Monforte, Rainer Weber, Caroline Sabin, Jens Lundgren, Matthew G Law

On behalf of the D:A:D Study group

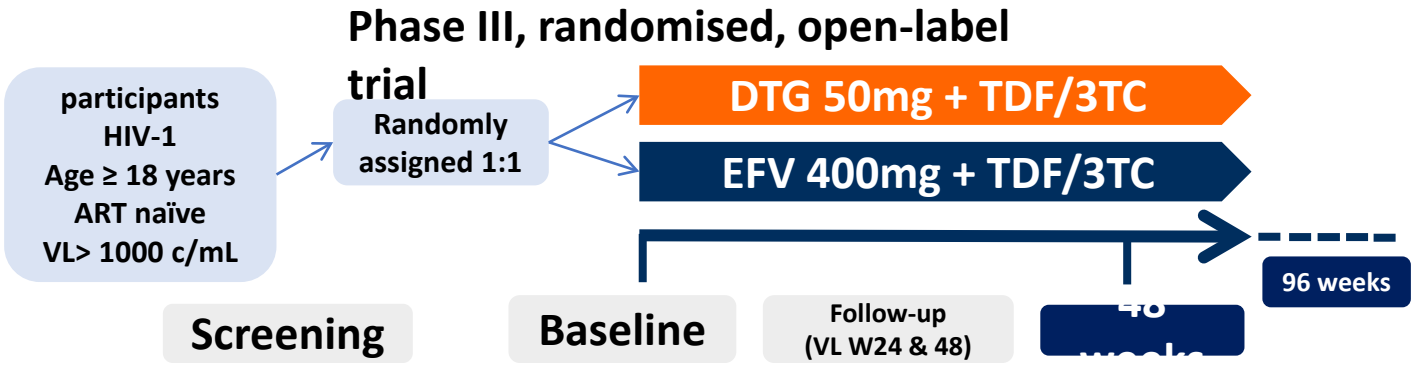
Kirby Institute

D:A:D

Conclusion

- Increases in BMI across all levels of baseline BMI were consistently associated with increased risk of DM
- Increases in BMI across all levels of baseline BMI were not associated with an increased risk of CVD
  - Some evidence of an increased risk of CVD with a decrease in BMI (especially at low baseline BMI)
- The extent to which these results apply to PLHIV with increased weight while receiving contemporary ART are uncertain
- Further analysis of weight change, INSTI/TAF and clinical events is needed

NAMSAL - Study design



3 study sites in Yaoundé, Cameroon

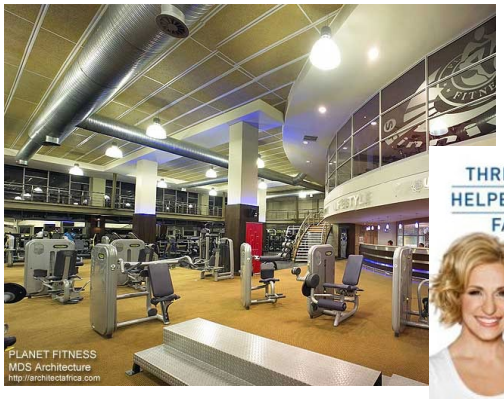
Namsal: body weight
Week 48 analysis

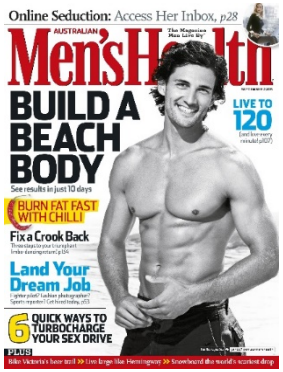
	TDF/3TC+DTG N=293	TDF/3TC+EFV N=278	p-value
Evolution W48-D0			
Weight gain (kg)	**+5.0kg**	**+3.0kg**	**<0.001**
Weight (% from DO)	+7.3%	+5.3%	0.001
Weight ≥ 10%	38%	29%	0.033
BMI	+1.7	+1.2	<0.001
Obesity incidence (BMI≥30)	**36 (12%)**	**15 (5%)**	**0.004**

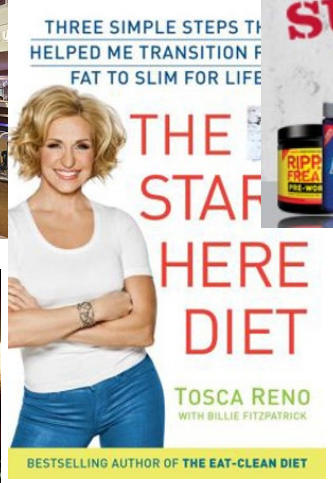
Lots of people stand to gain or lose from this being a side effect

- Pharmaceutical companies
- Governments, donors and budgets
- Researchers

People make a LOT of money from making you feel horrible about your body – implicated in everything from depression to anorexia







And we aren't really sure what is a "healthy diet"

HEALTH

A Call for a Low-Carb Diet

By ANAHAD O'CONNOR SEPT. 1, 20

THE LANCET

Search for in All Fields

Home | Journals | Content Collections | Multimedia | Conf

The Lancet, Volume 384, Issue 9953, Pages 1479 - 1480, 25 October 2014
doi:10.1016/S0140-6736(14)61413-6 Cite or Link Using DOI

Copyright © 2014 Elsevier Ltd All rights reserved.

Low carbohydrate diets: going against the grain

Jim Mann, Rachael McLean, Murray Skeaff, Lisa Te Morenga

Low carbohydrate high fat (LCHF) diets continue to attract media attention, despite a subst

PDF

Long–Term Effects of 4 Popular Die on Weight Loss and Cardiovascular Risk Factors: A Systematic Review of Randomized Controlled Trials

Circ Cardiovasc Qual Outcomes.
2014;CIRCOUTCOMES.113.000723published online before print November 11 2014,

THE LANCET Diabetes & Endocrinology

Search for All Fields GO

Home | Journals | Content Collections | Multimedia | Conferences | Information for

The Lancet Diabetes & Endocrinology, Early Online Publication, 16 October 2014
doi:10.1016/S2213-8587(14)70200-1 Cite or Link Using DOI
This article can be found in the following collections: Nutrition & Metabolism (Obesity, Nutrition & metabolism-other)

Copyright © 2014 Elsevier Ltd All rights reserved.

The effect of rate of weight loss on long-term weight management: a randomised controlled trial

Katrina Purcell BSc, Priya Sumithran PhD, Luke A Prendergast PhD, Celestine J Bouniu MBBS, Elizabeth Delbridge PhD, Prof Joseph Proietto PhD

Home » Low-Carb Diet » 23 Studies on Low-Carb and Low-Fat Diets – Time to Retire The Fad

23 Studies on Low-Carb and Low-Fat Diets – Time to Retire The Fad

October 15, 2013 | by Kris Gunnars | 104,408 views |

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 4, 2013 VOL. 368 NO. 14

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D.,

Weight is culturally sensitive…

- Different communities = different perceptions of what is healthy, desirable, sexy
- Stigma that skinny = HIV, TB, other illness
- Advertising and magazines – steadily skinnier models
- Self-perception is important (and flawed)

But obesity IS an issue…

"The associations of both overweight and obesity with higher all-cause mortality were broadly consistent in four continents."

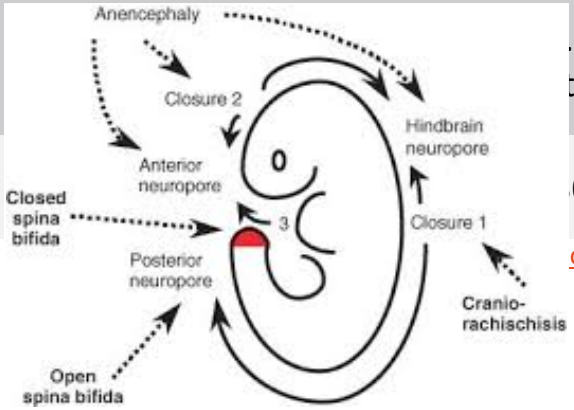
Being obese is linked to lots of issues

- Diabetes (glucose)
- Hypertension (blood pressure)
- Lipids (cholesterol, LDL ('bad cholesterol')
- Strokes
- Heart attacks
- Cancer
- Joint pain
- Mental health issues
- Poor COVID outcomes

"The associations of both overweight and obesity with higher all-cause mortality were broadly consistent in four continents."

Tsepamo Update: Prevalence of NTDs by ARV Exposure

Parameter	Conception			Pregnancy	HIV Negative (n = 119,630)
	DTG (n = 3591)	Non-DTG (n = 19,361)	EFV (n = 10,958)	DTG (n = 4581)	
Total NTDs per exposures, n/N	7/3591	21/19,361	8/10,958	2/4581	87/119,630
NTD prevalence, % (95% CI)					
▪ April 2019	0.30 (0.13-0.69)	0.10 (0.06-0.17)	0.04 (0.01-0.11)	0.03 (0.00-0.15)	0.08 (0.06-0.10)
▪ April 2020	0.19 (0.09-0.40)	0.11 (0.07-0.17)	0.07 (0.03-0.17)	0.04 (0.01-0.16)	0.07 (0.06-0.09)
Prevalence diff. with DTG conception, Apr 2020, % (95% CI)	Ref	0.09 (-0.03 to 0.30)			.12 to 32.0)
NTDs per exposures between April 2019 and April 2020, n/N	2/1908*	6/4569			0,258



Zash. AIDS 2020. Abstr OAXLB01.

options.com

*Includes 1 lumbosacral myelomeningocele (spina bifida) and 1 encephalocele.

Weight gain likely to have a much greater impact…

- On pregnancy outcomes than DTG teratogenicity!

AIDS 2020
23RD INTERNATIONAL AIDS CONFERENCE
6-10 JULY 2020

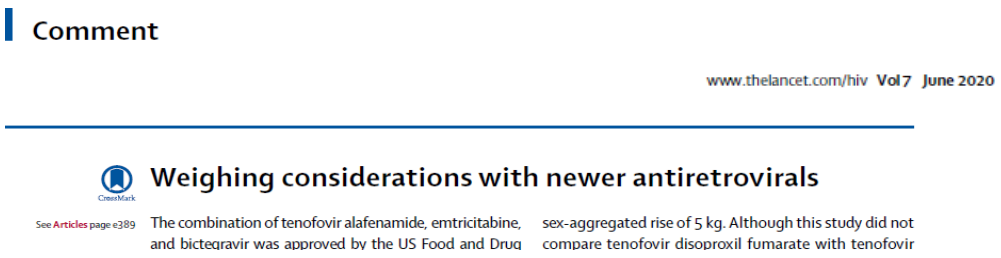
Predicting the risk of adverse pregnancy outcomes due to ART-induced weight gain

Sumbul Asif[1], Evangelina Baxevanidi[1], Andrew Hill[2], Celicia Serenata[3], WD Francois Venter[3], Lee Fairlie[3], Masebole Masenya[3], Nomathemba Chandiwana[3], Simiso Sokhela[3]

1. Imperial College London, Faculty of Medicine, London, United Kingdom, 2. Liverpool University, Department of Translational Medicine, Liverpool, United Kingdom, 3. Ezintsha, Wits RHI, University of the Witwatersrand, Johannesburg, South Africa

APO	Baseline	TAF/FTC+DTG	TDF/FTC+DTG	TDF/FTC/EFV
		96-weeks	96-weeks	96-weeks
Preterm delivery	70	73	71	70
Gestational Hypertension	28	39	34	29
Gestational diabetes mellitus	16	23	19	16
Pre-eclampsia	25	35	30	26
Postpartum haemorrhage	112	115	114	112
Caesarean section	213	232	224	215
Small-for-gestational-age infants	89	87	88	89
Large-for-gestational-age infants	134	154	145	137
Low birthweight infants	64	65	64	64
Macrosomia	31	37	34	31
Stillbirth	4	4	4	4
Neonatal death	2	2	2	2
Neural tube defect	0	0	0	0

Conclusions



Comment

www.thelancet.com/hiv Vol 7 June 2020

Weighing considerations with newer antiretrovirals

See Articles page e389

The combination of tenofovir alafenamide, emtricitabine, and bictegravir was approved by the US Food and Drug

sex-aggregated rise of 5 kg. Although this study did not compare tenofovir disoproxil fumarate with tenofovir

- Weight gain is real – definitely associated with DTG/BIC, and with TAF (and rilpivirine)
- DTG may not be as perfect as we hoped – but for most of the world – only efavirenz!
- No data on what to do if someone is gaining weight on either DTG or EFV (or anything else) – Orkin data on doravirine promising
- TAF unlikely to be recommended in Africa (?elsewhere)
- Major public health headache – swapping one epidemic for another – need new options

Thank you!

Ezintsha
INVESTIGATE INNOVATE ADVANCE