

# Switching to an integrase inhibitor containing antiretroviral regimen is not associated with above-average weight gain in middle-aged people living with HIV on long-term suppressive antiretroviral therapy, the AGE<sub>h</sub>IV cohort study



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on behalf of the



# Disclosures

- No financial disclosures

# Background

- **Recent studies: above-average weight gain among PWH initiating INSTI**
  - Predominantly in ART-naïve PWH → “return to health effect”?
  - ADVANCE trial\*:- Higher frequency of **clinically relevant** weight gains in DTG arms
    - Differential effect based on NRTI backbone and gender
    - Possible effect of African context?
  - Switch studies: smaller effect sizes (mean weight gain: 0-3kg)
- **AGE<sub>H</sub>IV cohort**
  - Since 2010 biennial standardized weight measurements
  - HIV-positive and –negative participants
  - ART history available from ATHENA cohort data / clinical data

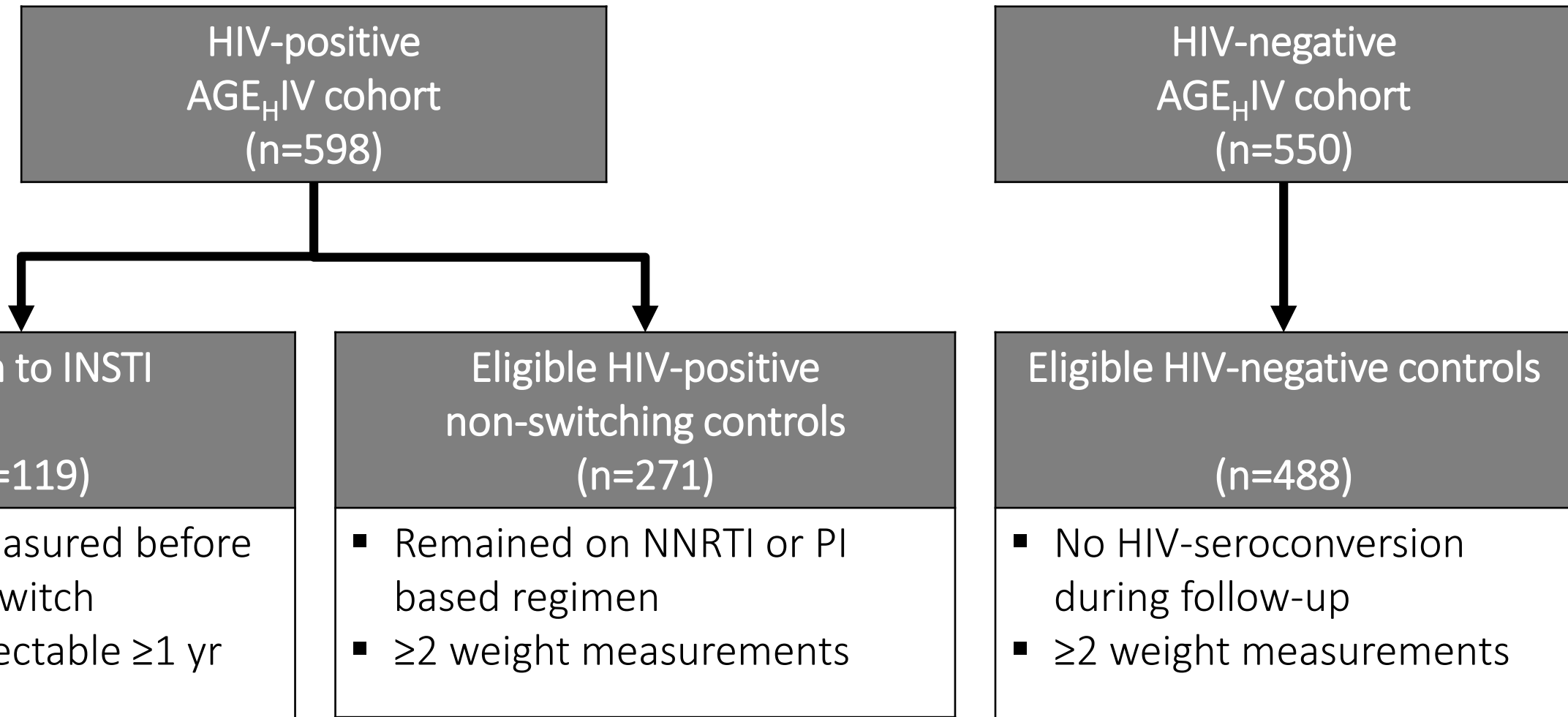
\*Hill IAS 2019 / Venter NEJM 2019

# Aim

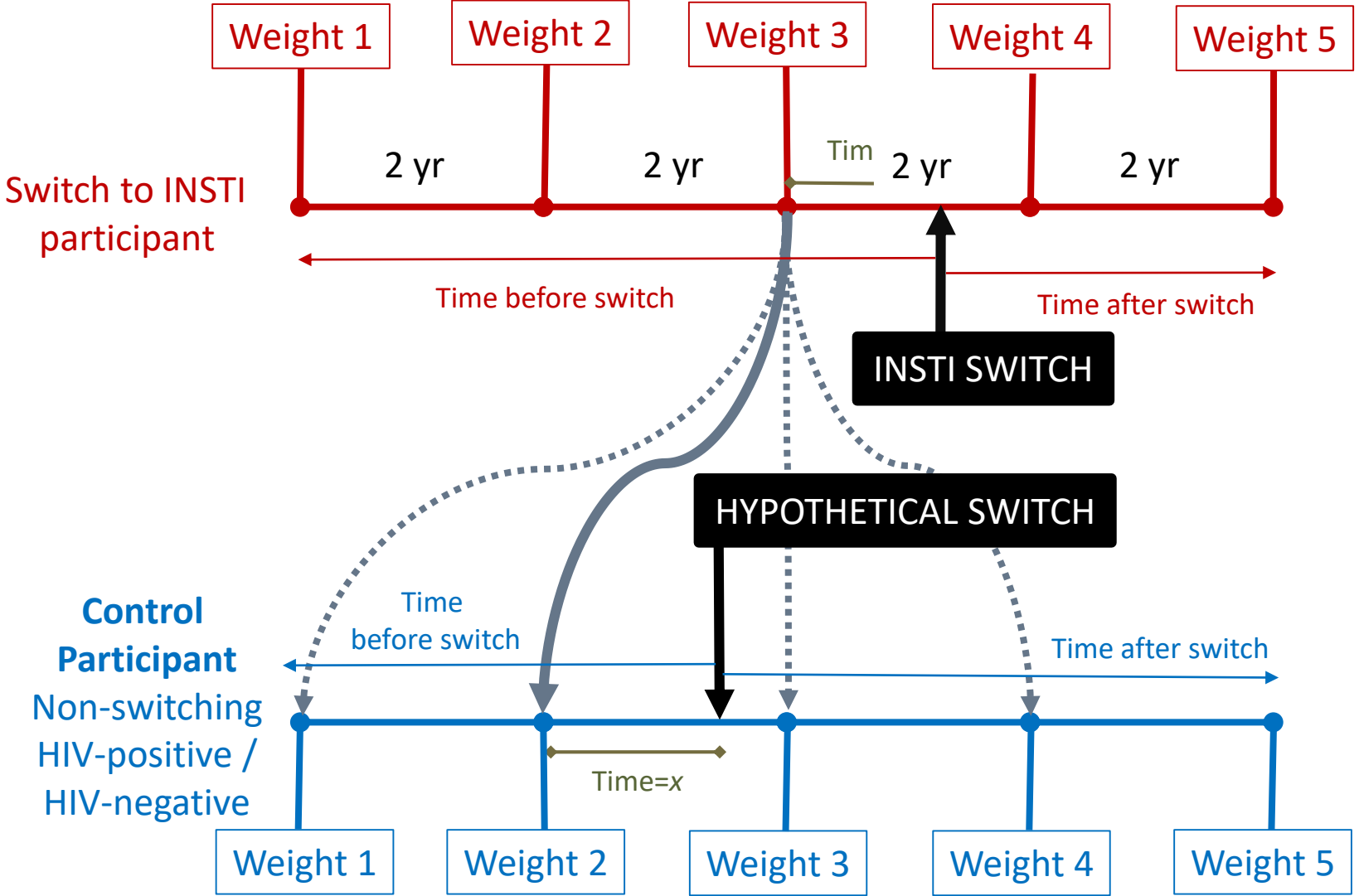
Evaluate mean and clinically relevant (>5% & >10%) weight gains after switch to INSTI in virally suppressed HIV-positive participants, compared to

- (1) HIV-positive virally suppressed non-switching participants
- (2) HIV-negative participants

# Methods – participant selection



# Methods - Propensity score matching



1:2:2 time-updated propensity score match base on

- Age
- BMI
- Sex
- Ethnicity

# Results - Study group description

	Switch to INSTI (n=119)	HIV-positive non-switching (n=238)	HIV-negative (n=238)
Age* (yr)	55 (51, 61)	54 (51, 61)	53 (50, 59)
BMI* (kg/m <sup>2</sup> )	24 (22, 26)	24 (22, 27)	24 (23, 26)
Male	104 (87%)	216 (91%)	201 (84%)
White	106 (89%)	212 (89%)	220 (92%)
MSM	90 (78%)	117 (78%)	164 (70%)
Last CD4 count* (cells/mm <sup>3</sup> )	640 (490, 790)	630 (490, 840)	850 (650, 1070)
CD4 nadir (cells/mm <sup>3</sup> )	190 (75, 270)	170 (90, 240)	N/A
Time since HIV diagnosis* (yr)	14 (8, 19)	14 (9, 19)	N/A
Time since ART initiation* (yr)	12 (7, 17)	12 (8, 16)	N/A

\*at visit prior to switch or hypothetical switch. Values are median (IQR) / N (%)

# Results – Switch to INSTI group description

Type of INSTI initiated	N (%)
dolutegravir	63 (53%)
elvitegravir	41 (34%)
raltegravir	15 (13%)

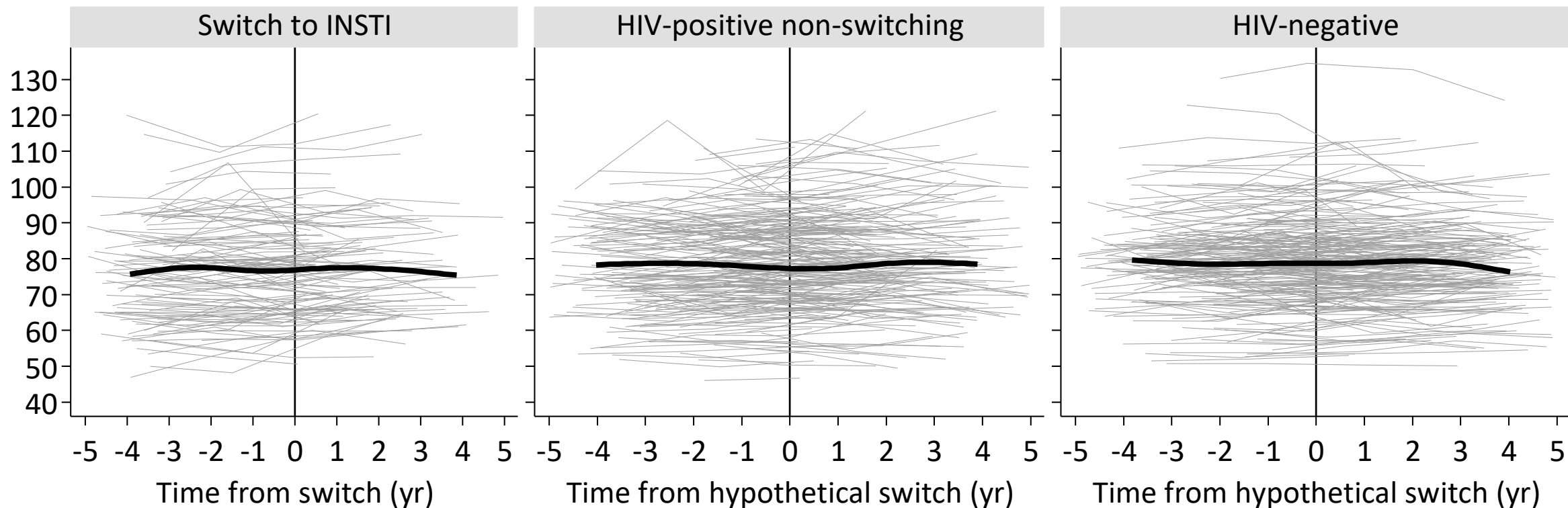
Reasons for switch to INSTI	N (%)
Simplification of regimen	41 (34%)
Neuro-/psychological side-effects from previous regimen	25 (21%)
Somatic side-effects from previous regimen	31 (26%)
Interaction of co-medication with previous regimen	8 (7%)
Unknown	14 (12%)

		NRTI use after switch to INSTI						
		ABC/3TC	TDF	TDF/FTC	3TC	3TC/AZT	TAF/FTC*	no NRTI
NRTI use before switch to INSTI	ABC/3TC	20 (17%)	...	...	1 (1%)	...	3 (3%)	1 (1%)
	ABC/3TC/AZT	3 (3%)	...	1 (1%)	...	...	...	1 (1%)
	TDF	...	1 (1%)	...	...	...	...	...
	TDF/ABC/3TC	...	1 (1%)	...	...	...	...	...
	TDF/FTC	<b>13 (11%)</b>	...	38 (32%)	3 (3%)	...	<b>21 (18%)</b>	3 (3%)
	TDF/3TC	2 (2%)	...	1 (1%)	...	...	...	...
	3TC/AZT	1 (1%)	...	...	1 (1%)	1 (1%)	1 (1%)	1 (1%)
	no NRTI	...	...	...	...	...	...	1 (1%)

\*Never combined with DTG



# Results – Individual weight trajectories



Median (IQR) follow-up  
time post-switch (yr)

→  
1.9  
(0.9, 2.9)

→  
2.0  
(1.0, 4.1)

→  
3.2  
(1.8, 4.6)

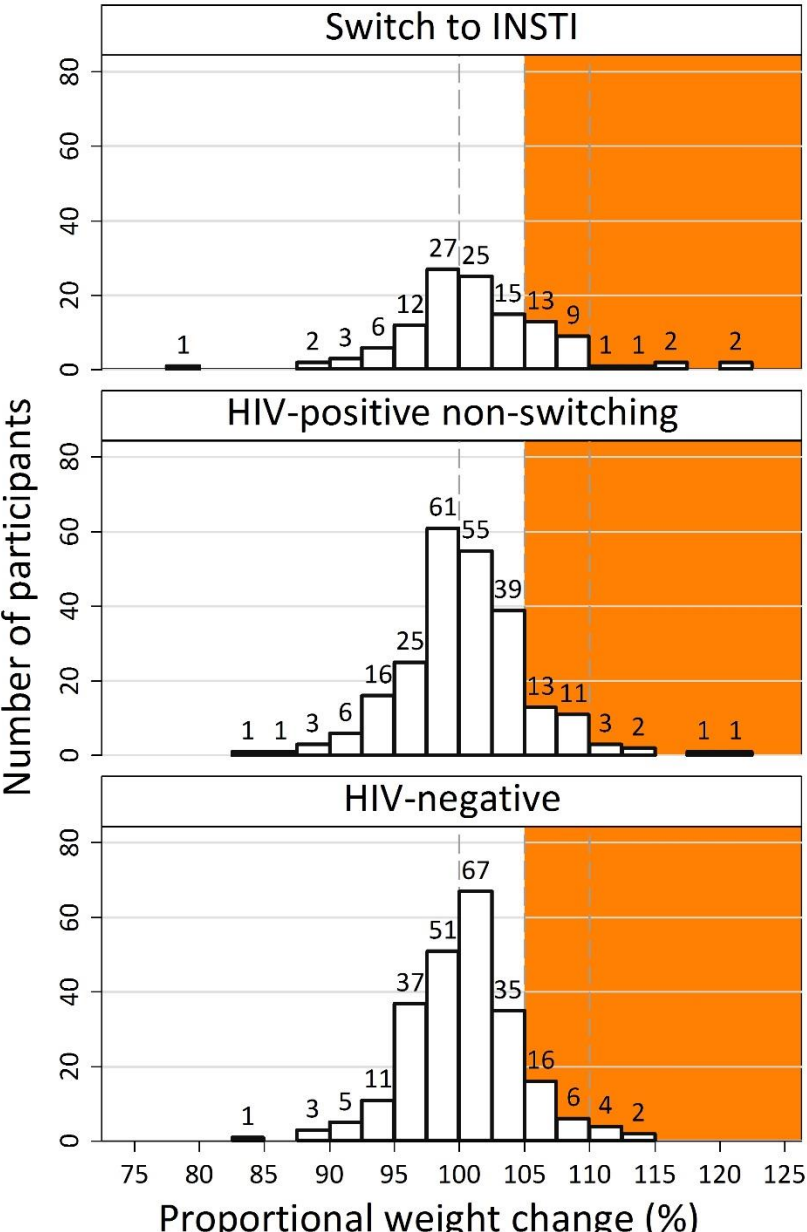
Black lines represent median splines

# Results – Mean weight changes before and after switch

	N	Mean annual change in body weight during follow-up periods				Difference in yearly change before and after switch / hypothetical switch	
		Before switch / hypothetical switch		After switch / hypothetical switch		hypothetical switch	
		kg/year	95% CI	kg/year	95% CI	Δ kg/year	95% CI
Switch to INSTI	119	0.11	-0.11, 0.33	0.17	-0.22, 0.55	0.06	-0.36, 0.48
HIV-positive non-switching	238	0.14	-0.06, 0.33	0.22	0.02, 0.42	0.08	-0.19, 0.34
HIV-negative	238	0.08	-0.12, 0.29	0.18	0.00, 0.36	0.09	-0.16, 0.35
Between group comparison	N	Δ kg/year	95% CI	Δ kg/year	95% CI		
Switch to INSTI vs.	119	Ref		Ref			
HIV-positive non-switching	238	0.03	-0.27, 0.32	0.05	-0.39, 0.49		
HIV-negative	238	-0.02	-0.33, 0.28	0.01	-0.41, 0.44		

Values calculated using a linear mixed-effects model

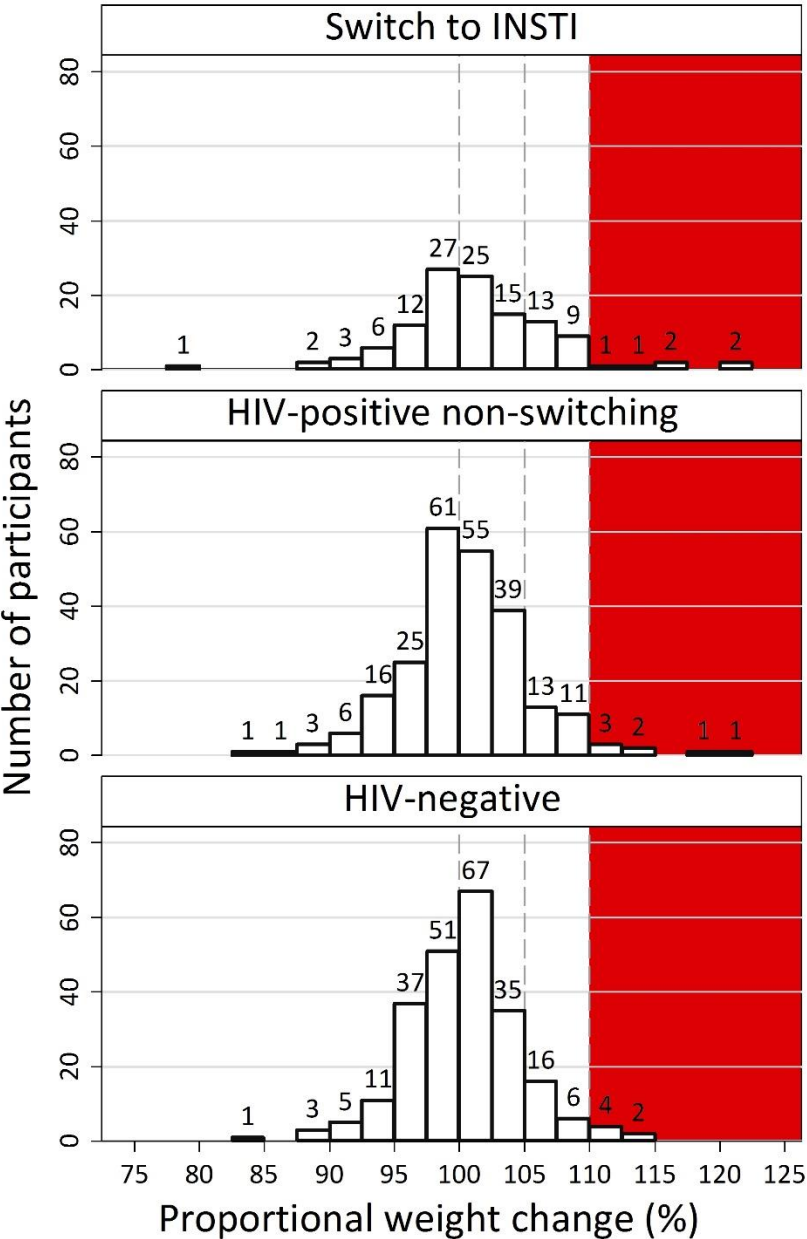
# Results – Frequency of clinically relevant weight gain



	Switch to INSTI	HIV-positive non-switching	HIV-negative
Time (yr) switch → weight after switch	0.9 (0.4-1.5)	1.0 (0.5-1.6)	0.8 (0.4-1.5)
<b>&gt;5% weight gain</b>	28 (24%)	31 (13%)	28 (12%)
<i>P</i> difference with switch to INSTI		.012*	.004*
<b>&gt;10% weight gain</b>	6 (5%)	7 (3%)	6 (3%)
<i>P</i> difference with switch to INSTI		.3*	.2*

\*  $\chi^2$  test

# Results – Frequency of clinically relevant weight gain



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Time (yr) switch → weight after switch	0.9 (0.4-1.5)	1.0 (0.5-1.6)	0.8 (0.4-1.5)
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>10% weight gain	6 (5%)	7 (3%)	6 (3%)
<i>P</i> difference with switch to INSTI		.3*	.2*

\*  $\chi^2$  test

# Results – Characteristics of INSTI-switching participants by weight gain

	≤5% weight gain	5-10% weight gain	>10% weight gain	<i>P</i> 5-10% vs ≤5% weight gain*	<i>P</i> >10% vs ≤5% weight gain*
<b>N</b>	91	22	6		
<b>Gender &amp; Ethnicity</b>					
Non-black male	78 (86%)	16 (73%)	3 (50%)	.3	<b>&lt;.001</b>
Non-black female	7 (8%)	3 (14%)	0 (0%)		
Black male	4 (4%)	3 (14%)	0 (0%)		
Black female	2 (2%)	0 (0%)	<b>3 (50%)</b>		
<b>Type of INSTI</b>					
Dolutegravir	45 (49%)	14 (64%)	4 (67%)	.4	.6
Elvitegravir	34 (37%)	5 (23%)	2 (33%)		
Raltegravir	12 (13%)	3 (14%)	0 (0%)		
<b>Regimen prior to switch</b>					
PI based	38 (42%)	13 (59%)	3 (50%)	.3	.9
NNRTI based	45 (49%)	9 (41%)	3 (50%)		
Both NNRTI/PI	5 (5%)	0 (0%)	0 (0%)		
No NNRTI/PI	3 (3%)	0 (0%)	0 (0%)		
<b>TAF after switch</b>	19 (21%)	4 (18%)	2 (33%)	.8	.5

\*  $\chi^2$ -test

# Discussion

## Conclusions

- No difference in mean weight gain among AGEhIV participants switching to INSTI compared to non-switching HIV-positive and HIV-negative participants.
- Clinically relevant weight gain (>5%) relatively more frequent after switch to INSTI
- >10% weight gain after switch to INSTI more frequent in black women

## Limitations

- Limited number of black and female participants
- Limited number of participants switching to TAF + DTG
- Limited number of weight measurements after switch

## Future studies

- Focus on those at risk for clinically relevant weight gain in the context of INSTI
- Identify underlying mechanisms

# AGE<sub>H</sub>IV Cohort Study Group

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## Financial support:

The Netherlands Organisation for Health Research and Development (ZonMW) grant nr. 300020007 & Stichting AIDS Fonds grant nr. 2009063

Additional unrestricted scientific grants from:

Gilead Sciences

ViiV Healthcare

Merck & Co

Janssen Pharmaceutica N.V.

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**And many thanks to all study participants!**