

Weight Gain After Initiating ART Close to HIV Seroconversion: Is There a 'Return to Health' Effect?

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BACKGROUND

- Excessive weight gain has been reported from studies of people living with HIV-1 on effective antiretroviral therapy (ART).
- Findings from seroprevalent cohorts suggest greater weight gain with Integrase Strand Transfer Inhibitors (INSTIs) and tenofovir alafenamide (TAF). However, it has been proposed that this is explained by a 'return to health' effect in people who have been living with uncontrolled HIV for a period of time.
- Objective:** to investigate weight trends and associated factors among individuals initiating ART within one year of HIV-1 seroconversion (SC).

METHODS

- Clinical data and laboratory results were collected from individuals with well estimated dates of HIV-1 seroconversion (HIV-1 test window ≤12 months or laboratory evidence of SC) in the multinational CASCADE study (<https://www.cascadestudy.net>).
- Inclusion:** stable (≥30 days) use of INSTI, non-nucleoside reverse transcriptase inhibitors (NNRTI) or protease inhibitor (PI) regimen initiated as first-line therapy ≥2007 within 12 months of SC; availability of baseline CD4 cell count, HIV-RNA, height and weight measurements and ≥1 weight measurement during follow-up.
- Follow-up censored at the first switch to a different ART class.
- Statistical analysis:** piecewise (1st slope 0-6 months, 2nd slope 6 months onwards) linear mixed models of weight changes relative to baseline.

RESULTS

- Of 5698 eligible individuals, 2778 (48.8%), 1809 (31.7%) and 1111 (19.5%) initiated INSTI, PI and NNRTI regimens, respectively. 79% (n=4,519) were men who had sex with men (MSM), and 4,347 (76%) originated from Europe or North America. Median (IQR) age at SC was 34 (27, 43) years and was similar across all ART classes. Median (IQR) time to ART initiation was 4.0 (1.9, 6.3) months; baseline CD4 and HIV RNA were 459 (328, 620) cells/μL, and 4.9 (4.3, 5.5) log10 copies/mL, respectively. Median (IQR) time of last weight measurement was at 1.9 (0.7, 4.0) years.
- Dolutegravir was the most prescribed INSTI (1167/2778, 42%), followed by elvitegravir (EVG, n=728, 26%), bicitgravir (BIC, n=558, 20%), and raltegravir (RTG, n=325, 12%). TAF was prescribed for 987 participants, mostly in combination with INSTIs (n=878), and BIC in particular (n=558).

- People treated with ART soon after HIV-1 seroconversion gain weight regardless of HIV drug or class prescribed
- However, weight gain continues to be highest for those on INSTIs and/or TAF suggesting that the greater weight gain seen among those on these regimens is unlikely to reflect a 'return to health' effect, but is more likely to reflect a direct effect of the drugs themselves

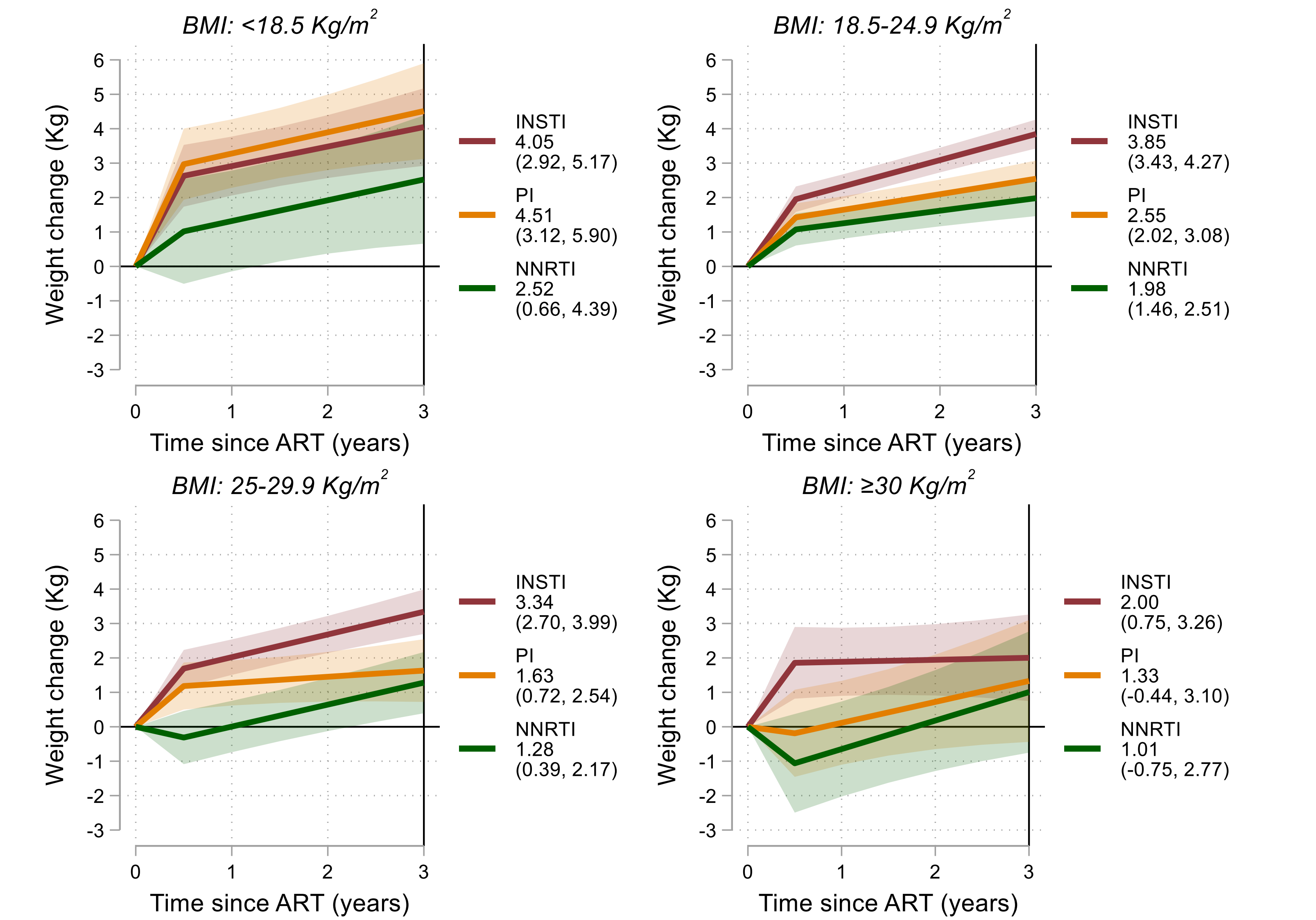
- Estimated weight gains over time by ART and baseline BMI are shown in the Table (without further adjustments) and Figure (adjusted; see legend).
- 53.4% (51.4, 55.4), 46.3% (43.4, 49.2) and 40.4% (37.7, 43.3) of those with BMI 18.5-24.9 kg/m² are estimated to gain >5% of their baseline weight after 3 years of treatment on INSTI, PI and NNRTI regimens, respectively.
- The corresponding percentages estimated to gain >10% of their baseline weight are 31.3% (29.5, 33.1), 25.3% (23.0, 27.7) and 20.8% (18.8, 22.9).

Table. Estimated weight change by ART class and baseline BMI category. TAF and TAF+INSTI denote the subset on regimens including irrespective of main drug, and those on TAF with an INSTI, respectively.

Baseline BMI (kg/m ²) Category	Estimated weight change (kg)	INSTI	PI	NNRTI	TAF	TAF+INSTI
<18.5	At 6 months	2.50 (1.63, 3.37)	3.03 (2.02, 4.04)	0.88 (-0.64, 2.39)	3.26 (1.75, 4.77)	3.28 (1.69, 4.88)
	At 3 years	4.22 (3.14, 5.30)	5.02 (3.67, 6.38)	2.74 (0.89, 4.60)	4.94 (2.31, 7.56)	4.78 (2.09, 7.47)
18.5-24.9	At 6 months	1.89 (1.60, 2.19)	1.55 (1.20, 1.90)	0.90 (0.48, 1.31)	2.23 (1.79, 2.68)	2.39 (1.91, 2.87)
	At 3 years	3.95 (3.65, 4.25)	2.87 (2.44, 3.31)	1.98 (1.54, 2.41)	4.61 (3.96, 5.27)	4.76 (4.05, 5.46)
25-29.9	At 6 months	1.78 (1.30, 2.26)	1.63 (1.00, 2.27)	-0.18 (-0.92, 0.55)	3.50 (2.67, 4.33)	3.75 (2.84, 4.66)
	At 3 years	3.43 (2.87, 3.99)	2.18 (1.33, 3.03)	1.46 (0.63, 2.29)	5.10 (3.78, 6.42)	4.98 (3.49, 6.47)
≥30	At 6 months	2.02 (1.01, 3.04)	0.36 (-0.88, 1.60)	-0.97 (-2.39, 0.44)	4.66 (2.73, 6.58)	4.56 (2.39, 6.73)
	At 3 years	2.25 (1.04, 3.46)	2.32 (0.58, 4.06)	1.04 (-0.70, 2.77)	3.99 (1.13, 6.85)	2.17 (-1.07, 5.41)

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Figure. Estimated weight changes after ART initiation by ART class and baseline BMI. Shaded areas represent 95% CIs. Estimates shown for MSM, aged 30-39 at SC, from Europe/N. America, with average height, baseline CD4 cell count and HIV-RNA



- Regimens with BIC and TAF were associated with the highest weight increases in individuals with initial BMI <30 kg/m² followed by EVG/TAF in those with 18.5-24.9 kg/m² BMI and RTG/tenofovir disoproxil fumarate (TDF) in those with initial BMI of 25-29.9 kg/m². In all BMI classes, elvitegravir was associated with faster weight gains when combined with TAF rather than with TDF.
- Significantly higher weight gains were observed on heterosexually infected women and individuals originating from Sub-Saharan Africa.

CONCLUSIONS

- INSTIs (especially BIC and EVG) combined with TAF were associated with the fastest increases in weight.
- As ART was initiated very close to seroconversion, the greater increases in those on these regimens is likely to reflect a direct effect of the drugs rather than a 'return to health' phenomenon.

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