

Effects of integrase strand transfer inhibitors (INSTIs) on body mass index and blood pressure in children living with HIV

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Background

INSTIs: first line treatment for Children Living with HIV (CLWH) (1)

Benefits of INSTIs (2)

- Less drug interactions
- Efficacy against multi-drug resistant strains

INSTIs associated with increased weight gain in adults (3)

Children living with perinatally acquired HIV (CLWPH) at risk of:

- Pro-inflammatory state (4)
- Accelerated aging (5)
- Metabolic syndrome (6)
- Lipodystrophy (6)

Methods

Sub-study of the EPIC4 study

Data collected between 2015-2019

Inclusion criteria:

- 0-19 years of age
- Living with perinatally acquired HIV
- Undergoing treatment in Canada

Spline regression analysis to assess change in BMI percentile relative to baseline

Chi-square test to assess change in BP category relative to baseline

Results

Group demographics

- Median age = 13 years (0.4-18.5)
- 53% female
- BMI
 - 75% normal
 - 20% overweight or obese
 - 5% underweight

Sample size

- INSTI (n=113)
 - DTG 29%
 - RAL 38%
 - EVG 33%
- Control (n=84)

HIV outcomes after 2 years

- INSTI: median CD4 772 cells/uL; detectable VL 11.5%
- Non-INSTI: median CD4 780 cells/uL; detectable VL 17.8%

Results

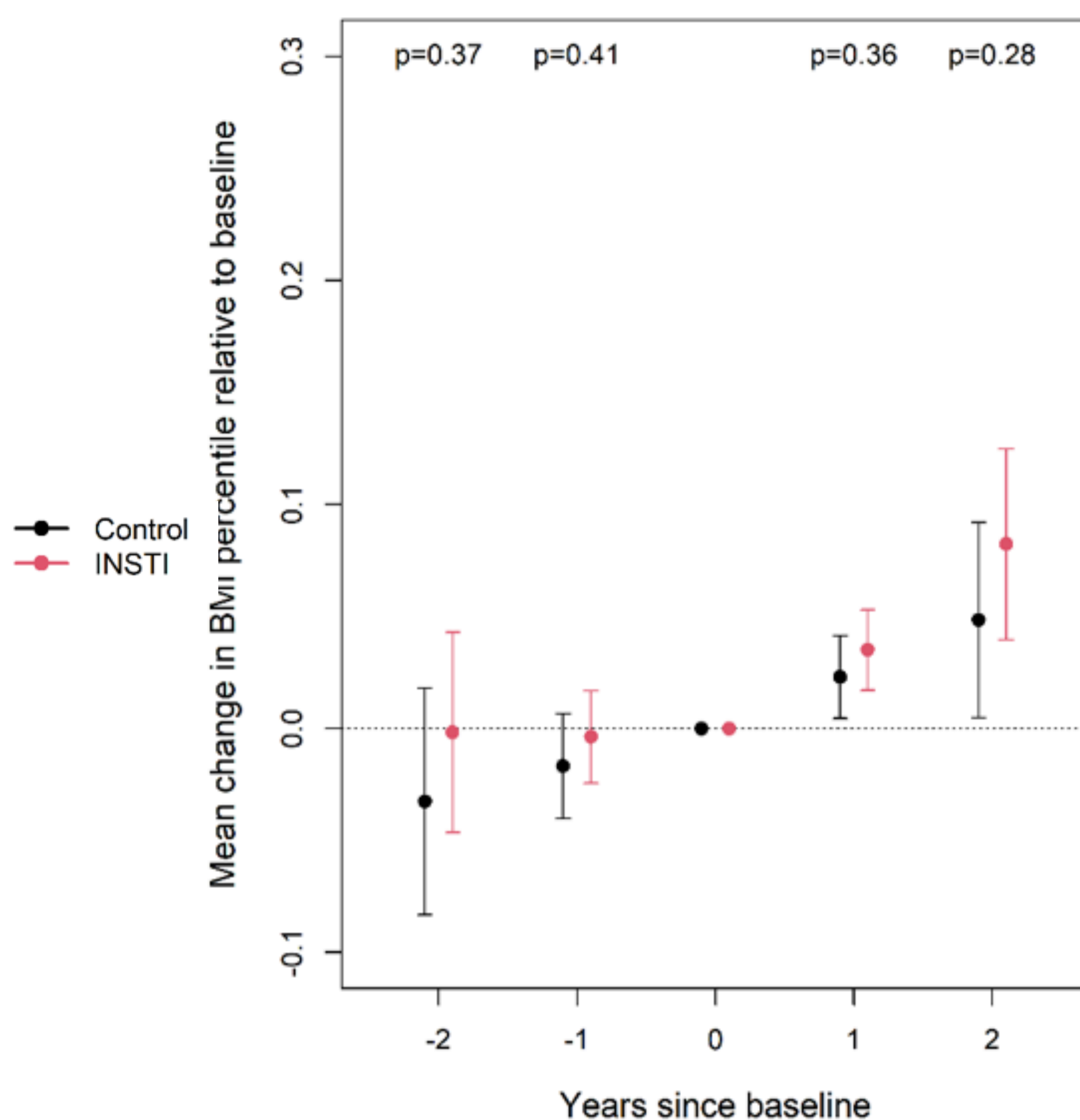


Fig 1. Mean change in BMI percentile relative to baseline comparing CLWPH taking INSTI containing regimens to non-INSTI containing regimens.

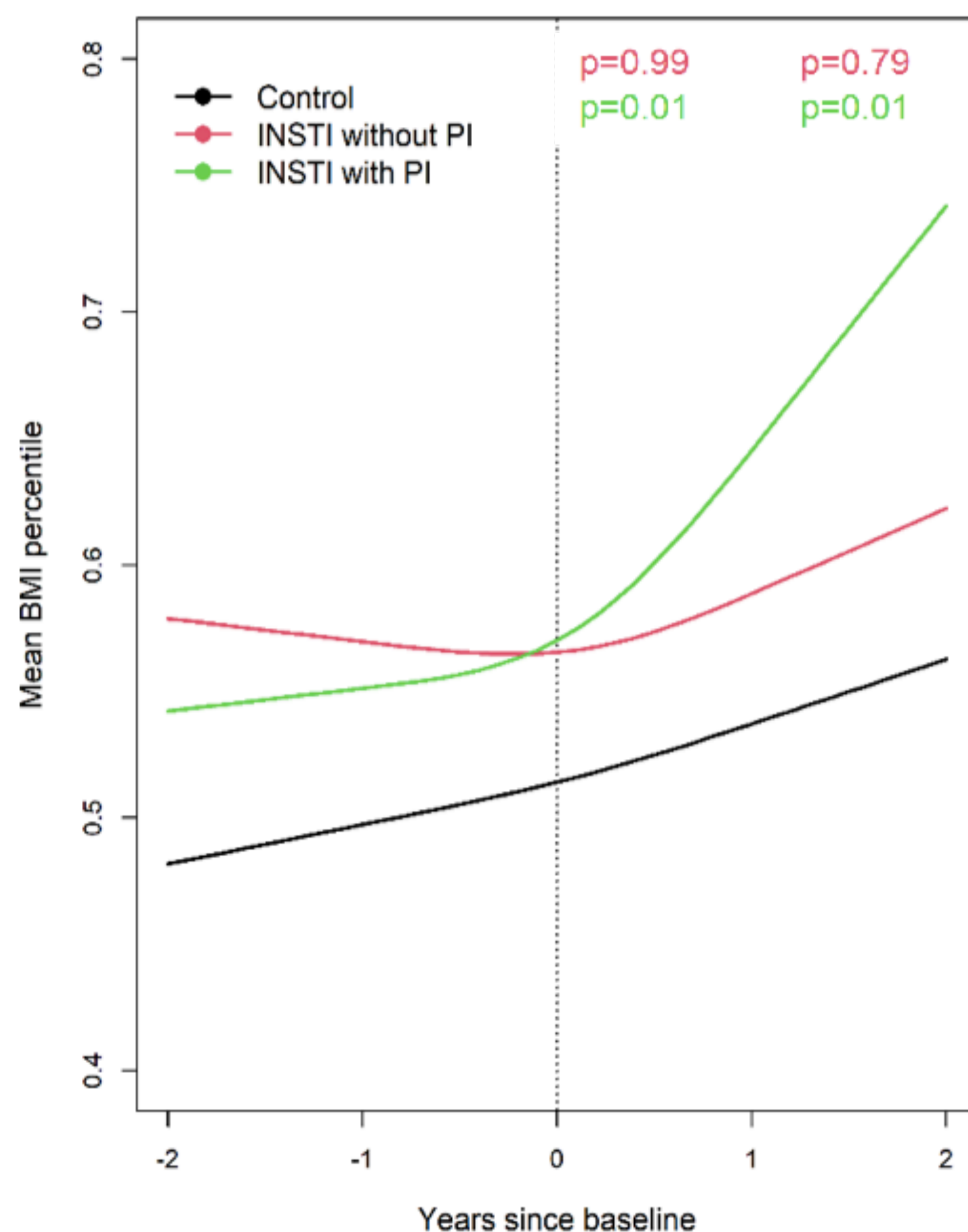


Fig 2. Mean change in BMI percentile relative to baseline comparing CLWPH taking INSTI + PI containing regimens to those taking INSTI without PI containing regimens.

Table 1. Change in BP category comparing CLWPH taking INSTI containing regimens to non-INSTI containing regimens.

	Control	INSTI	P
BP category/stage - baseline, n (%)			0.292
Normal/elevated	47 (82.5)	50 (74.6)	
Stage 1/2 HTN	10 (17.5)	17 (25.4)	
BP category/stage - year 1, n (%)			0.256
Normal/elevated	49 (76.6)	53 (67.9)	
Stage 1/2 HTN	15 (23.4)	25 (32.1)	
BP category/stage - year 2, n (%)			0.965
Normal/elevated	42 (76.4)	38 (76.0)	
Stage 1/2 HTN	13 (23.6)	12 (24.0)	
Worse BP category - year 1 (%)	10/55 (18.2)	16/57 (28.1)	0.215
Worse BP category - year 2 (%)	14/42 (33.3)	5/31 (16.1)	0.098

Conclusions

INSTI use is not statistically significantly associated with an increase in BMI percentile or BP category in CLWPH

Combination INSTI and PI regimens are associated with an increase in BMI percentile in CLWPH compared to INSTI regimens not containing PIs

Discussion

Limitations:

- Medication adherence: viral load as surrogate
- Sexual maturity: age and sex matched
- Fat distribution
- Confounding medications

Further research is required to assess the impact of protease inhibitors (PIs) alone on weight gain, versus the combination of INSTIs and PIs together.

Bibliography

- (1) Kanfers S, Jansen J, Zoratti M, Forrest J, Humphries B, Campbell J. Web Annex B. Systematic literature review and network meta-analysis assessing first-line antiretroviral treatments In: Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidelines. Supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2018.
- (2) Rathbun RC, Lockhart SM, Miller MM, Liedtke MD. Dolutegravir, a second generation integrase inhibitor for the treatment of HIV-1 infection. *Ann Pharmacother.* 2014;48:395-403.
- (3) Menard, A, et al. Dolutegravir and weight gain: an unexpected bothering side effect? *AIDS.* 2017;31:1499-1502.
- (4) Fastenackels S, Sauce D, Vigouroux C et al. HIV-mediated immune aging in young adults infected perinatally or during childhood. *AIDS.* 2019;33:1705-1710.
- (5) Horvath S, Stein DJ, Phillips N et al. Perinatally acquired HIV infection accelerates epigenetic aging in South African adolescents. *AIDS.* 2018;32:1465-1474.
- (6) Barlow-Mosha L, Eckard AR, McComsey GA and Musoke PM. Metabolic complications and treatment of perinatally HIV-infected children and adolescents. *Journal of the International AIDS Society.* 2013;16:18600.

