

Myrthe L. Verburgh^{1,2,3}, Ferdinand W.N.M. Wit^{1,2,4}, Anders Boyd^{4,5}, Peter Reiss^{1,2,3,6} and Marc van der Valk^{1,2,4}; for the ATHENA HIV observational cohort study

1 Amsterdam UMC location University of Amsterdam, Infectious Diseases, Amsterdam, The Netherlands; 2 Amsterdam Institute for Infection and Immunity, Amsterdam, The Netherlands; 3 Amsterdam Institute for Global Health and Development, Amsterdam, The Netherlands; 4 HIV Monitoring Foundation, Amsterdam, The Netherlands; 5 Public Health Service of Amsterdam, Infectious Diseases, Amsterdam, The Netherlands; 6 Amsterdam UMC location University of Amsterdam, Global Health, Amsterdam, The Netherlands

BACKGROUND

- Data on reversibility of TAF- and/or INSTI-associated weight gain (WG) are currently limited to case reports.
- We aimed to determine the reversibility of $\geq 7\%$ TAF- and/or INSTI-associated WG in virally suppressed people with HIV (PWH) of the ATHENA national observational HIV cohort, representing $>95\%$ of PWH in HIV care in the Netherlands.

METHODS

Study population

- We included ART-experienced adults, virally suppressed for ≥ 12 months, with a first switch to only TAF, only INSTI or both TAF+INSTI, who subsequently gained $\geq 7\%$ weight within 24 months after switch to TAF and/or INSTI.
- We excluded participants with hypothyroidism, Cushing's syndrome, congestive heart failure, renal failure, liver cirrhosis, use of corticosteroids, antidepressants or antipsychotics.
- We selected individuals who discontinued only TAF, only INSTI or both TAF+INSTI after first recording of $\geq 7\%$ WG, with at least 1 weight measurement ≥ 3 months after discontinuation.
- We excluded participants with $<7\%$ WG at moment of discontinuation
- For comparison, we selected individuals with $\geq 7\%$ WG within 24 months after switch to TAF and/or INSTI, but who continued this ART-regimen, with at least 1 weight measurement ≥ 3 months after first recording of $\geq 7\%$ WG.

Statistical analysis

- Absolute mean weight change in the 24 months prior to and after discontinuation or first recording of $\geq 7\%$ WG was modelled using mixed-effect linear regression; a priori adjusted for age, sex at birth, region of origin and last available weight prior to discontinuation or first recording of $\geq 7\%$ WG.
- Factors associated with mean weight change (kg/yr) after discontinuation of TAF and/or INSTI were assessed using linear regression.

TAF and/or INSTI-associated weight gain of $\geq 7\%$ appears to be **only partly reversible** after discontinuing TAF and/or INSTI, without independent associations between weight change after discontinuation and changes in NRTI backbone or anchor agent.

In contrast, weight in those continuing TAF and/or INSTI after a first recorded $\geq 7\%$ weight gain remained **relatively unchanged**.

RESULTS

Study population

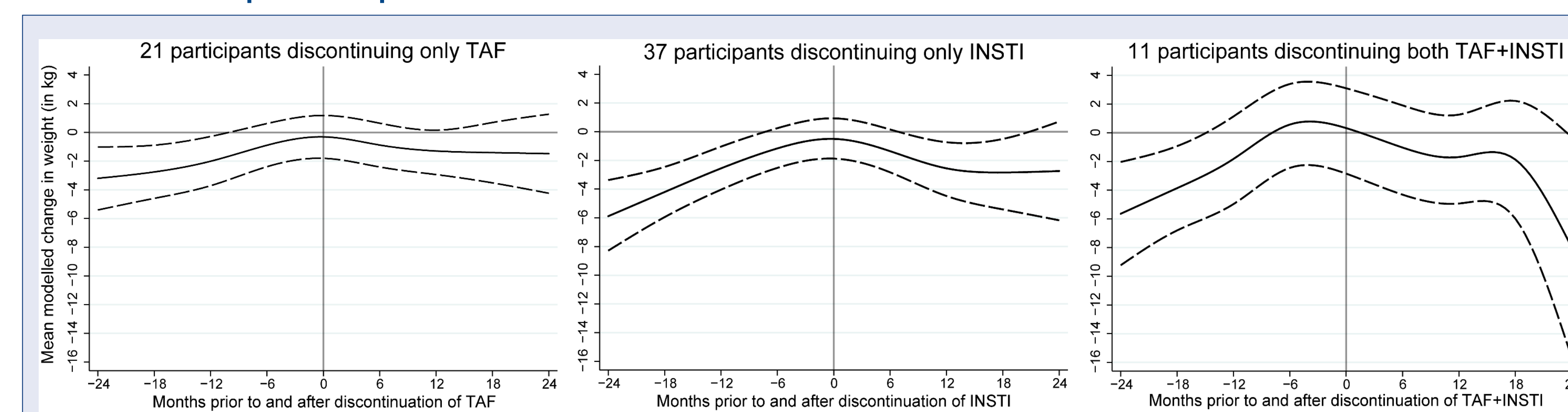
- Of 6,245 eligible participants, 1,440 participants gained $\geq 7\%$ weight within 24 months after switch to TAF and/or INSTI. Of those, 165 discontinued TAF and/or INSTI. **69** of 165 with available follow-up weight were included: 21 discontinuing only TAF, 37 only INSTI and 11 both TAF+INSTI.
- 998 of 1,440 participants continued using TAF and/or INSTI, of whom **800** with available follow-up weight were included.

Characteristics of **69 PWH** discontinuing TAF and/or INSTI

- 79.7% male; 69.6% of western origin; median age 47.8 years (IQR 41.3-58.1); known with HIV for median 12.7 years (IQR 8.3-17.2); current CD4 cell count 670 cells/mm³ (IQR 620-1100); median BMI at discontinuation of TAF and/or INSTI 25.7 kg/m² (IQR 23.7-28.0).
- Demographic and HIV-specific characteristics of 800 PWH continuing TAF and/or INSTI were not significantly different

Absolute mean weight change after discontinuation of TAF and/or INSTI (n=69)

- Within 24 months prior to discontinuation, WG on TAF and/or INSTI was +3.20kg [95%CI, 1.02-5.40] in PWH who subsequently discontinued only TAF; +5.89kg [3.37-8.29] in the only INSTI and +5.64 [2.03-9.23] in the TAF+INSTI group.
- In the first 12 months after discontinuation, weight change was -1.30kg [-2.94 to +0.15]; -2.55kg [-4.48 to -0.73] and -1.69kg [-4.93 to +1.26], respectively.
- After 12 months, weight loss stabilized. The strong decrease in weight in those discontinuing TAF+INSTI should be interpreted with caution given the small number of participants.



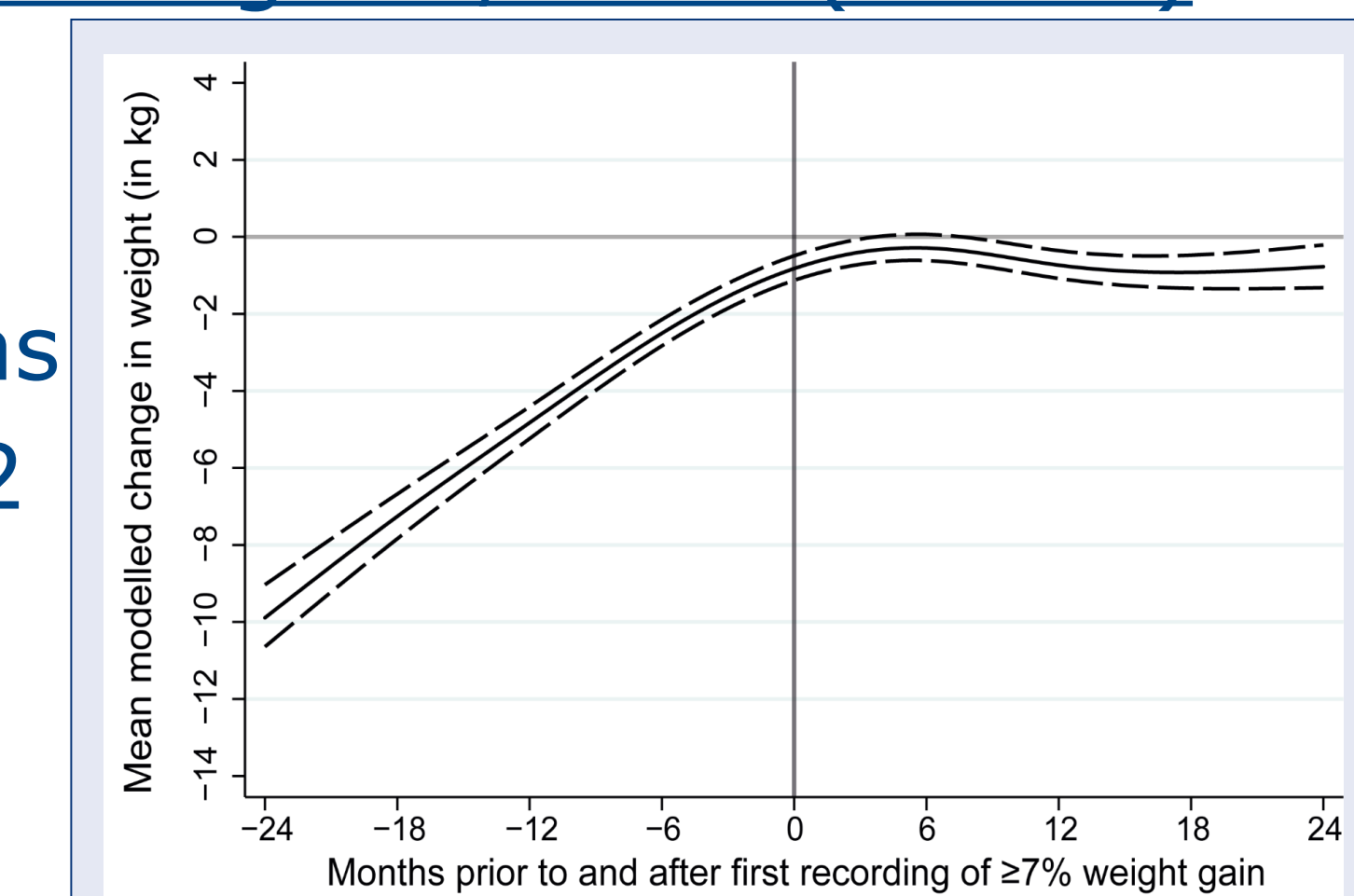
RESULTS

Factors associated with mean weight change after discontinuation of TAF and/or INSTI (n=69)

- Only BMI ≥ 30 kg/m² at moment of discontinuation of TAF and/or INSTI was independently associated with more weight loss after discontinuation (-5.42 kg/yr [95%CI, -9.19 to -1.65] more compared to those with BMI 18.5-24.9kg/m²).
- Changes in NRTI backbone or anchor agent at the moment of TAF and/or INSTI discontinuation were not independently associated with weight change.

Absolute mean weight change after first recording of $\geq 7\%$ WG in those continuing TAF/INSTI (n=800)

- At 24 months after first recording of $\geq 7\%$ WG, weight change was -0.77kg [95%CI, -1.32 to -0.21].



CONCLUSIONS

- TAF- and/or INSTI-associated WG of $\geq 7\%$ appears to be only partly reversible after discontinuation of TAF and/or INSTI.
- No independent associations were found between weight change after discontinuation of TAF and/or INSTI and concomitant changes in NRTI backbone or anchor agent at moment of discontinuation.
- Only BMI ≥ 30 kg/m² was associated with greater reversibility of WG
- A limitation is the limited sample size.
- In contrast, weight in those continuing TAF and/or INSTI after a first recorded $\geq 7\%$ WG remained relatively unchanged.

ADDITIONAL KEY INFORMATION

- **Acknowledgements:** all staff at Dutch clinical HIV centres, staff at the HIV Monitoring Foundation and all ATHENA cohort participants
- **Author contact information**
Myrthe Verburgh | MD, PhD student | ✉ m.l.verburgh@amsterdamumc.nl

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