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Association between BMI changes and risk of hypertension and dyslipidaemia in people treated with INSTI and/or TAF versus other contemporary regimens

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Introduction

- The use of INSTIs and TAF has been associated with weight gain[1].
- In PLWH weight gain is associated with hypertension[2] and dyslipidaemia[3].
- INSTIs may be associated with CVD events in the first 24 months of exposure[4].
- Analyses in selected populations and small cohorts have associated INSTI use and hypertension or dyslipidemia[1,2,3-6].
- However, the clinical impact of weight gain associated with INSTIs is not clear.

[1]Bansi-Matharu et al. Lancet HIV, 2021; [2]Brennan et al. EclinicalMedicine, 2022; [3]Galdamez, et al. OFID, 2019; [4]Neesgaard et al. Lancet HIV, 2022; [5]Saums et al. Obstetrics and Gynecology, 2019; [6]Summers et al. JAIDS, 2020.

Objective and analysis

Aim: To compare the association between BMI change and risk of incident HTN or dyslipidaemia in PLWH receiving INSTIs and/or TAF versus ART without INSTI/TAF.

Research Questions

- Does adjustment for time-updated BMI alter the association between INSTI/TAF and HTN?
- Is there an interaction between the ART and time-updated BMI?

Statistical analysis

- Multivariable Poisson regression: interaction term between time-updated BMI and ART.
- Adjustment for confounders, including exposure to ABC, NVP, IDV, d4T, LPV.
- Baseline date: latest of RESPOND baseline or date of joining local cohort.
- Performed several sensitivity analyses.

Endpoint definitions

- Primary exposures: ART regimens with or without INSTI or TAF.
  - INSTI+TAF, INSTI with no TAF, non-INSTI + TAF, vs no INSTI/TAF (*reference group*)
- If TDF or EFV was taken prior to current ART, included follow-up after 6 months.
- HTN was defined as two consecutive BP ≥140/90 mmHg or the initiation of antihypertensives.
- Dyslipidaemia was defined as total cholesterol >6.2 mmol/L, or HDL<0.9 mmol/L, or TRIGs >2.3 mmol/L, or lipid-lowering therapy[1]
- Sensitivity analysis with hypertriglyceridemia dropped from the definition

[1]Byonanebye et al. AIDS, 2021

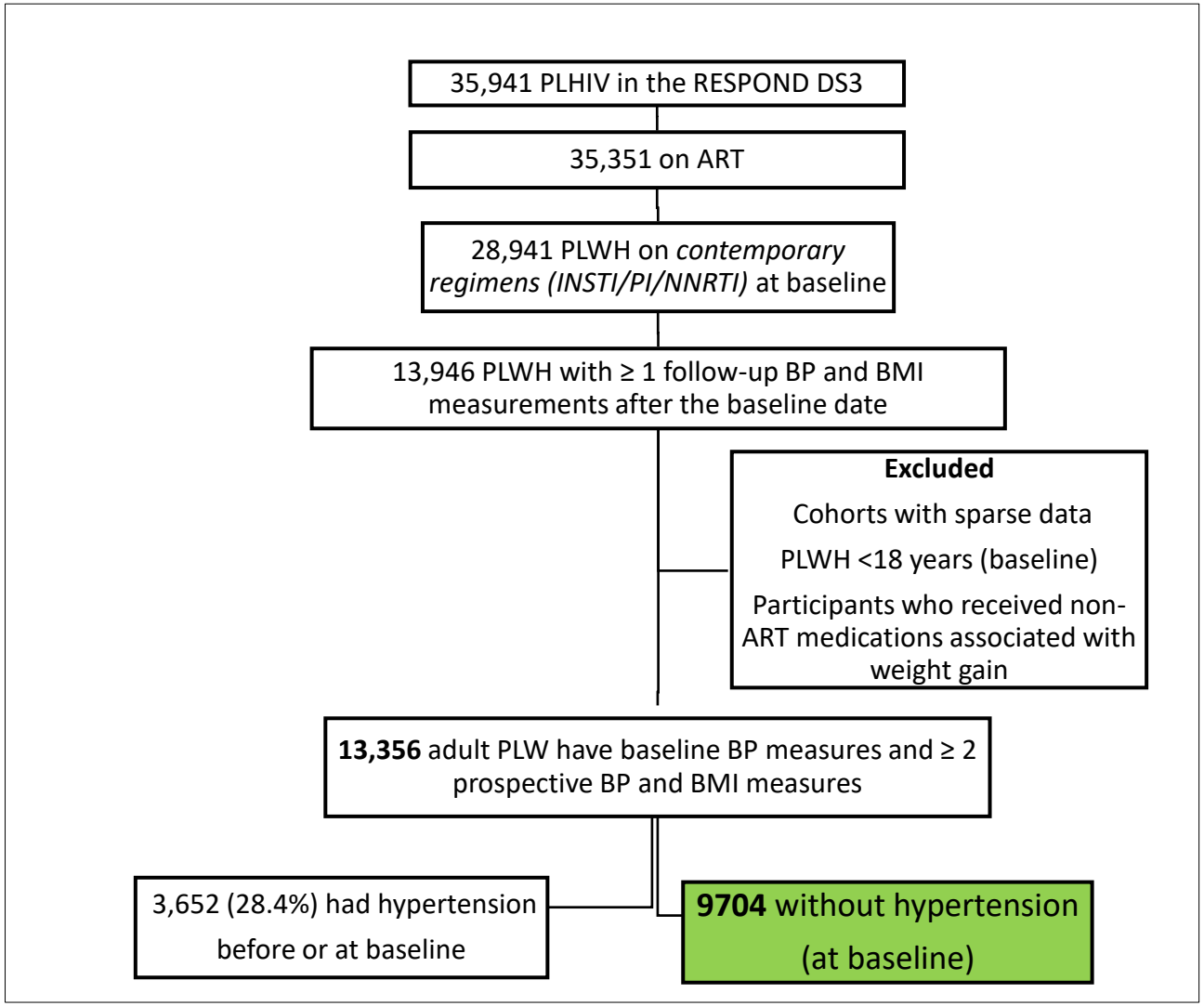
Eligibility

- Analysis within RESPOND: A consortium of 17 observational HIV cohorts in Europe and Australia
- **Inclusion**
  - Adults (≥18 years)
  - Receiving INSTIs (DTG, BIC, RAL, EVG), or bPIs (DRV, ATV), or NNRTIs (EFV, RPV).
  - Baseline BMI result (within 1 year before baseline) and ≥2 follow-up BMIs
  - >2 lipid and blood pressure measures (for the respective analyses)
- **Exclusion**
  - Subjects without baseline CD4 and HIV viral load.
  - Participants receiving non-ART medications associated with weight gain.

Wharton S et al. Diabetes Metab Syndr Obes 2018

Results : HTN analysis

- 9,704 subjects, 39,993 PYFU
  - Male:76%, White:72%
  - Median age: 44(36–51) years
  - ART duration: 10(5–16) years
- 2977 (30.7%) developed hypertension
- Overall incidence: 74 (72–77) per 1000 person



Unadjusted vs adjusted IRRs of hypertension

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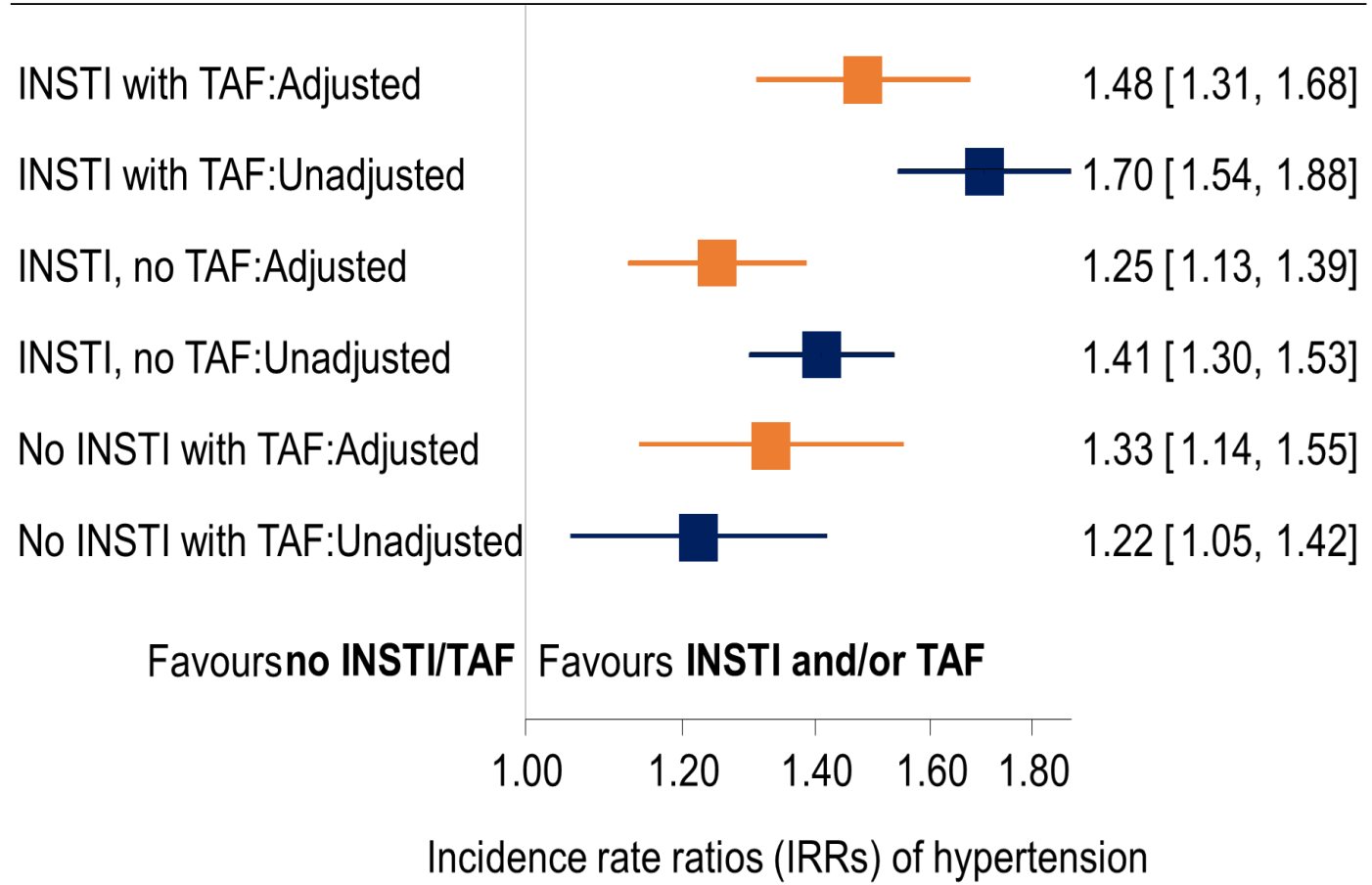
Current use of INSTI and/or TAF was associated with HTN.

Adjustment for time-updated BMI attenuated the risk.

No interaction between ART and BMI (*interaction p*=0.459).

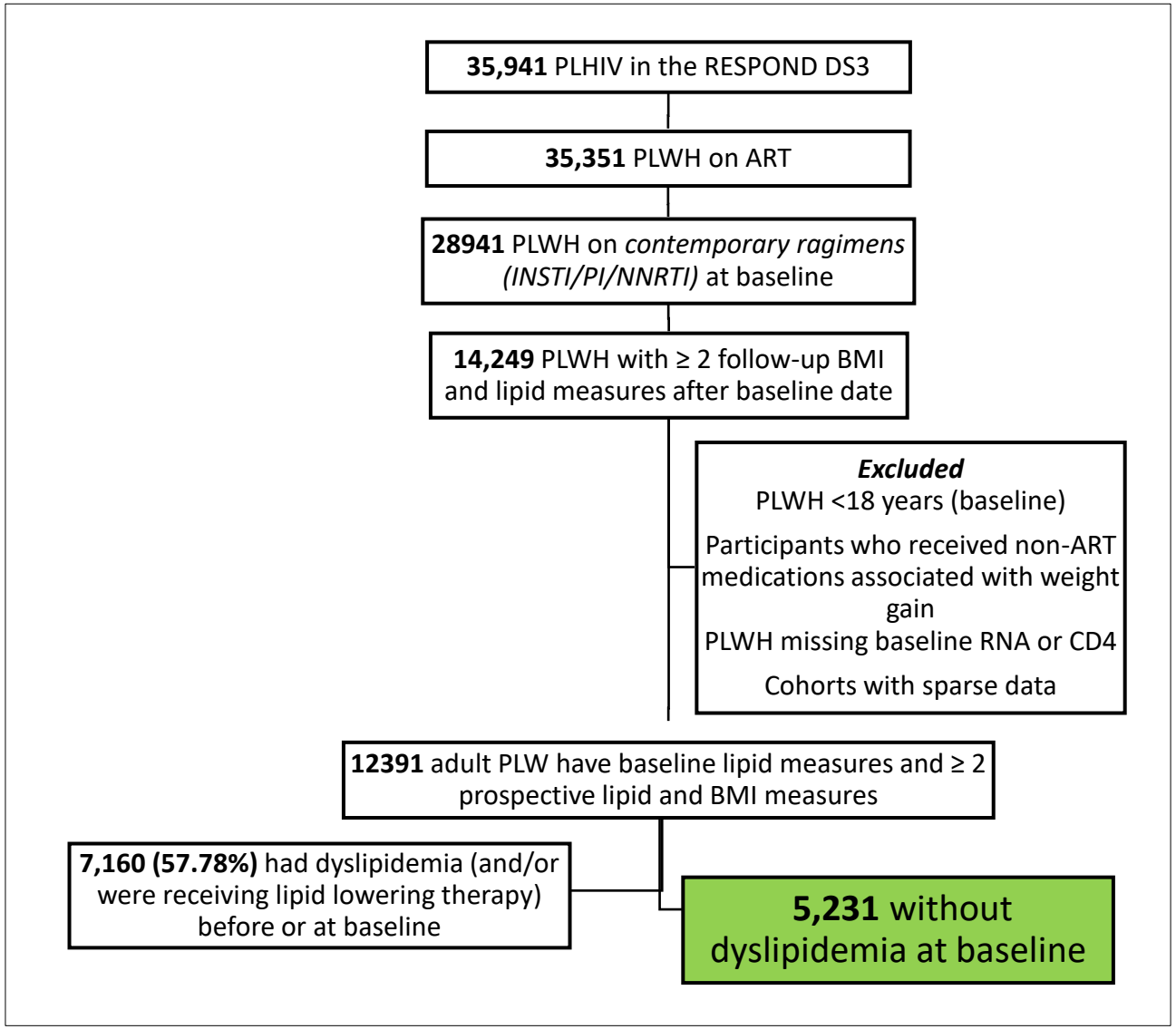
Results similar when analysis stratified by BMI quintiles.



**Note:* ART and BMI time-updated, ref group=No INSTI or TAF

Results 2: Dyslipidemia analysis

- 5,231 subjects observed over 19547 PYFU
  - Male:73%, White:71%
  - Median age:43(35–50) years
  - ART duration: 10 (5,15) years
- 2689 (51.4%) developed dyslipidaemia
- Overall incidence: 138 (133-143) per 1000 person



Unadjusted vs adjusted IRRs of dyslipidaemia

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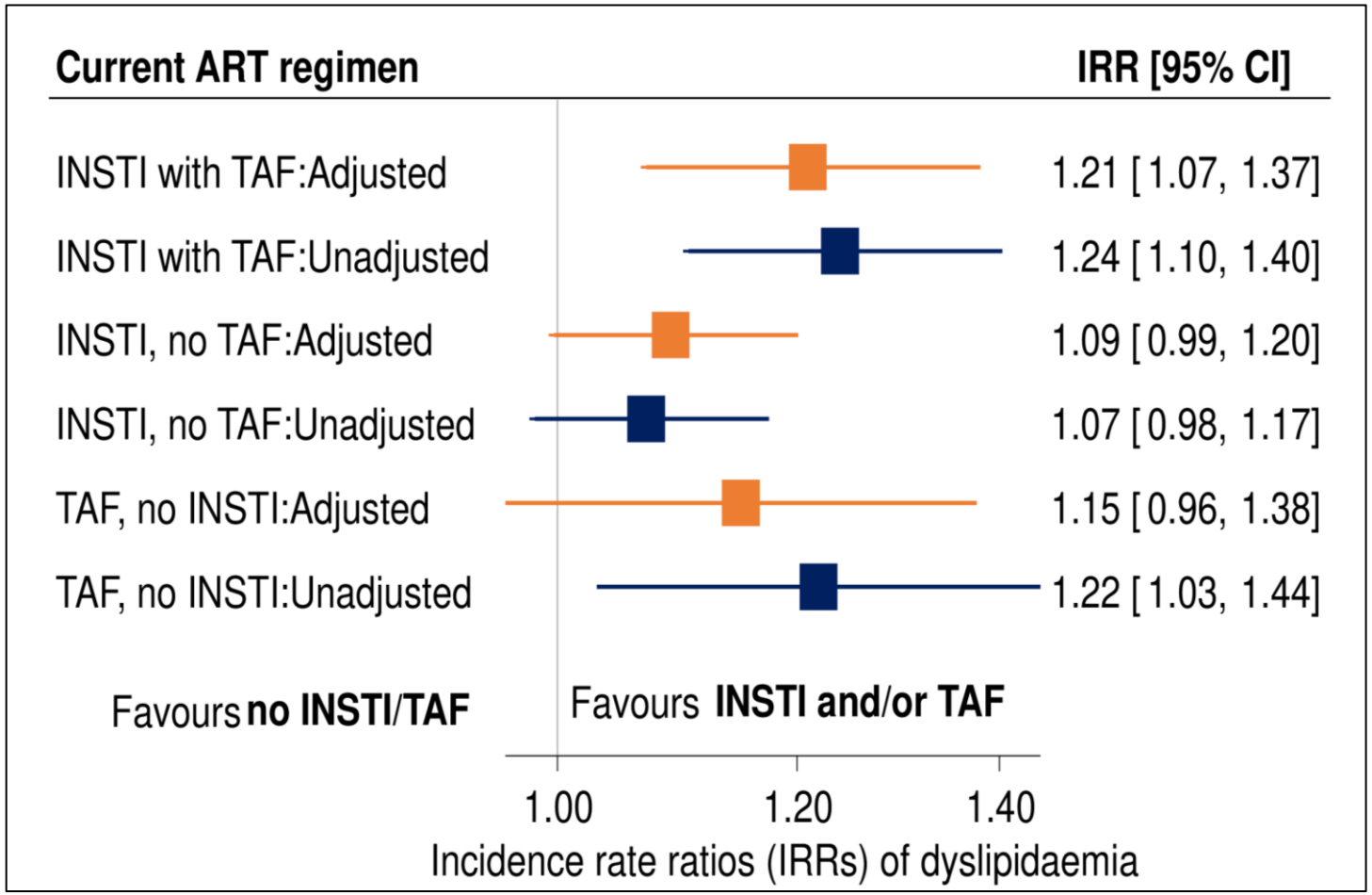
Current use of TAF with/out INSTI was associated with dyslipidaemia

Adjustment for time-updated BMI attenuated the risk.

No interaction between ART and BMI (interaction P=0.303).

Results similar in analysis stratified by BMI quintiles.



Note: ART and BMI time-updated, ref group=No INSTI or TAF

Results were consistent in all sensitivity analyses

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- Time-updated BMI (lagged by 12 months).
- BMI increase defined as a 7 % increase in BMI.
- EVG not considered INSTI.
- Analysis stratified by ART status at baseline (naïve vs ART-experienced).
- Analysis limited to individuals with suppressed HIV RNA (<200 copies/mL).
- Dyslipidaemia defined without triglycerides.
- Follow-up censored upon switch from or to TDF/EFV.
- Analysis limited to PLWH without prior exposure to PIs or ABC.

Limitations

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- Assumption that any raised risk of HTN and dyslipidaemia due to BMI increases is captured by fitting models with time-updated BMI.
- Data on BMI, BP, and lipids sparse in some cohorts (excluded).
- Data missing on diet, exercise, family history, and some comorbidities.
- Cohort differences in BP/lipid monitoring and treatment.
- LDL infrequently reported, excluded from dyslipidaemia definition.
- However, RESPOND allowed larger sample size, clinic-based data, heterogeneous cohorts

Conclusions

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- In RESPOND, current use of INSTI and TAF together increased rates of incident HTN.
- Adjustment for time-updated BMI attenuated the association with hypertension though it remained significant .
- TAF with/out INSTI, but not INSTI alone, was associated with incident dyslipidaemia.
- After adjustment for BMI the dyslipidemia association was nonsignificant.
- The relationship between BMI and hypertension or dyslipidaemia was not different in PWH on INSTI or TAF compared to ART without INSTI or TAF.
- However, residual confounding cannot be fully excluded
- Analysis exploring the association between weight gain and CVD events is underway (Bansi-Matharu et al.)

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