

Risk factors associated with adverse metabolic health in youth with perinatally acquired HIV living in the United Kingdom

Caroline FOSTER^{1,2} Alexandra BLENKINSOP³, Merle HENDERSON^{1,4}, Hermione LYALL², Sarah FIDLER^{1,4} on behalf of the BONDY study group.

Short title: Metabolic health in youth with perinatal HIV

¹900 Clinic, Imperial College Healthcare NHS Trust London W2 1NY, UK

²Department of Paediatric Infectious Diseases, Imperial College Healthcare NHS Trust London W2 1NY, UK

³Department of Mathematics Imperial College London, UK

⁴Department of Infectious Diseases, Imperial College London, Imperial College NIHR BRC, W2 1NY, UK

Corresponding author

Caroline Foster, 900 Clinic @ Imperial College Healthcare NHS Trust, Imperial College London W2 1NY, UK

Email: caroline.foster5@nhs.net, c.foster@imperial.ac.uk

Funding

This study was funded by an Investigator led grant from Gilead Sciences (Dr Caroline Foster)

Abstract

Objective: Non-AIDS-related morbidity and mortality in people with HIV are associated with adverse metabolic health, influenced by both traditional- and HIV-related risk factors. There is a paucity of data for youth with perinatal HIV (PHIV). We explored the relationship between markers of metabolic health and antiretroviral therapy (ART) in youth with PHIV.

Design: Longitudinal observational cohort study; 26 months.

Methods: 85 youth enrolled in the “Bone Density in Youth living with PHIV” (BONDY) underwent assessment of metabolic health including fasting biochemistry, body mass index (BMI), total body dual energy x-ray absorptiometry scan and hepatic transient elastography.

Results: Of 85 participants with PHIV, mean age 21.7 years, 58% were female and 82% black African. Median ART exposure was 15 years, median CD4 count 623 cells/ μ L at enrolment with 82% viral load <200 copies/ml. Median weight gain over 26 months was 3kg, with BMI category overweight/obese increasing from 37% to 50% with 48% having dyslipidaemia. Metabolic syndrome criteria were fulfilled in 7%, with 13% having hypertension, 18% hepatic steatosis and 7% fibrosis on transient elastography. Bayesian regression analyses demonstrated no association of integrase strand transfer inhibitor (INSTI) and/or tenofovir alafenamide (TAF) use, and sex at birth or prior CDC-C diagnoses or current HIV viraemia on metabolic outcomes.

Conclusion: While adverse metabolic outcomes are common in this youth cohort with PHIV, no association was observed with INSTI and/or TAF use. Given the relatively young age of this cohort, preventative interventions targeting traditional metabolic risk factors are required to avoid comorbidities in later life.

Keywords: Perinatally acquired HIV, youth, metabolic syndrome, metabolic dysfunction-associated steatotic liver disease, antiretroviral therapy.

Introduction

Metabolic syndrome (MetS), characterised by central obesity, hypertension and impaired lipid and glucose metabolism, is a predictor of future cardiovascular risk and type 2 diabetes (T2DM). Increased rates of MetS are reported in adults with horizontally acquired HIV (HHIV); associated with traditional factors including obesity, alcohol, smoking, sedentary lifestyle and genetic factors - and HIV-related risk factors including viraemia and some antiretroviral regimens [1]. People born with perinatally acquired HIV (PHIV) experience lifelong exposure to HIV-associated inflammation and increasingly antiretroviral therapy (ART), with the oldest entering their 5th decade of life; approaching the age clinical cardiovascular events and MetS-associated T2DM appear in the general population [2-5].

Emerging data suggests increased rates of MetS and cardiovascular (CVS) risk in PHIV. Cohorts from the US report incidence rates of T2DM of 19%, dyslipidaemia 50% and hypertension 22% by 30 years of age [6]. In this setting youth with PHIV (median age 26 years) had higher rates of MetS (13% vs. 4%), than aged/ethnically matched HIV negative youth, and higher rates of truncal/android fat distribution; a pattern associated with increased CVS events [7]. While two thirds were overweight/obese, rates were comparable to youth without HIV (47% vs. 51% overweight, 20% vs. 17% obese). In settings with lower rates of obesity, youth with PHIV remain at increased risk of MetS (France; 13.2% males, 10.4% females with PHIV vs. 10.6% and 1.7% youth without HIV and in 10.2% Thai PHIV youth) [8,9]. Conversely data from South Africa in youth, median age 18 years, suggested lower rates of MetS in those with PHIV (12%) when compared to youth with HHIV (34%) and HIV negative youth (23%) but with higher rates of dyslipidaemia in youth with PHIV without obesity and highlights the considerable geographic heterogeneity in obesity and metabolic health [10].

Obesity driven metabolic dysfunction-associated steatotic liver disease (MASLD) is the main driver of liver fibrosis in adults with HHIV [11]. Transient elastography (FibroScan®) controlled attenuation parameter (CAP) scores have good correlation with steatosis in adults with HHIV and in youth without HIV [12,13]. Early data in adolescents with PHIV suggests increased rates of steatosis compared to HIV negative youth, only partially explained by metabolic factors [14,15].

The potential metabolic impact of ART includes dyslipidaemia with boosted protease inhibitors (bPI), and weight gain with integrase inhibitors (INSTI) and tenofovir alafenamide (TAF) [4,16-18]. Data for PHIV is emerging; 70% of Thai adolescents receiving bPIs had dyslipidaemia, with tenofovir disoproxil fumarate (TDF) a protective factor [19]. Boosted PI use remains high for treatment experienced youth with extensive drug resistance [20,21]. Studies of INSTI-related weight change in PHIV vary from no association to weight gain in young women with increased truncal fat deposition [4,22-25]. In a meta-analysis of 4 paediatric TAF studies weight-for-age z-scores increased by 0.25 at 48 weeks, however data on the impact of INSTIs with TAF in youth is lacking [26].

The Reprieve Study demonstrated a 35% reduction in major CVS events following statin use in adults with HHIV (median 50 years) and a low/moderate CVS risk, acknowledging that cardiovascular risk scores underestimate risk in those with HIV and in younger populations [27,28]. Interventions to reduce risk factors for non-communicable diseases are required from early adult life, prior to established pathology [29]. In this study, we examined the relationship between markers of metabolic health, hepatic steatosis, HIV clinical status and ART exposure in PHIV youth in the United Kingdom, exploring the hypothesis that weight gain associated with INSTIs in conjunction with TAF would impact metabolic health.

Methods

Study Population

The “Bone Density in Youth living with perinatally acquired HIV” (BONDY) study has been described in full previously [30]. Participants aged 15-24 years were eligible for the longitudinal study arm with a second assessment after 24 months. At this visit they were invited to enrol in the sub-study (BONDY-Met) assessing metabolic health.

Study procedures BONDY-Met

Demographics, ART history, past CDC-C diagnoses, length of viral suppression, latest CD4 count, HIV viral load (VL), a family history of diabetes, cardiovascular and liver disease, concomitant medication, and substance use were recorded [30]. During the study period the NHS commissioned TAF for those <25 years, with a TDF to TAF switch offered to participants and all ART changes documented [31].

Height, weight, Tanner staging, blood pressure (BP) and waist circumference were assessed. Body mass index (BMI) was calculated as weight/height (kg/m²) and as an age-adjusted z-score if 15-19-years and classified as overweight BMI >25-29 or obese BMI >30.

Metabolic biochemistry: Participants fasted for 12 hours, and glucose, lipid profile, glycosylated haemoglobin (HbA1c), C-peptide, insulin and liver enzymes measured. Homeostatic model for assessment of insulin resistance (HOMA-IR) was calculated using $\text{insulin } (\mu\text{U/mL}) \times \text{glucose } (\text{mmol/L}) / 22.5$ [32].

Total body dual energy X-ray absorptiometry (DXA) scans measured total body fat, android (AFM) and gynoid fat mass (GFM), using Lunar Prodigy or iDXA (GE Healthcare) scanners [30]. The android:gynoid ratio (AGR) was calculated using the fat percentage in regions A and G.

Transient elastography (TE; fibroscan)

Assessed CAP (dB/m) with correlates of steatosis graded as [33].

1. 238-260 dB/m S1=11-33% liver fatty change (LFC)
2. 260-290 dB/m S2=34-66% LFC
3. > 290 dB/m S3=67+% LFC

Fibrosis scoring (F) assessed by E score (kPa) and graded as:

1. E2-7 F0-1 no/mild fibrosis
2. E7-10 F2 moderate
3. E10-14 F3 severe
4. E14+ F4 cirrhosis

Metabolic Syndrome

Rates were defined using a consensus definition adjusted for age and ethnicity [34]. Three of five criteria led to a diagnosis of MetS.

1. Waist circumference > 102cm men, >88 cm women (16+ years)
2. Triglycerides ≥ 1.7 mmol/L
3. HDL <1.04 mmol/L men, <1.29 mmol/L women,
4. Blood Pressure $\geq 130/85$ mmHg
5. Fasting glucose ≥ 5.6 mmol/L

Statistical analysis

Participant characteristics were summarised using counts and proportions for categorical variables, means and standard deviations (SD) for normally distributed continuous variables, and medians with interquartile ranges (IQR) for skewed distributions. We examined six primary outcomes: change in BMI baseline to follow-up, and five metabolic outcomes at visit 2 (FibroScan CAP, HbA1c, HOMA-IR, MetS, and meeting two criteria for MetS). Associations of INSTI-based vs. other ART, TAF- vs. non-TAF-containing regimens, INSTI + TAF versus other regimens and HIV parameters (CDC-C, HIV viraemia and CD4:8 ratio) were estimated using Bayesian generalised linear models with Gaussian link functions for continuous outcomes and logit link functions for binary outcomes. All

models were adjusted for age and sex, and models for BMI change also adjusted for baseline BMI. For each outcome, we quantified the evidence for an association by estimating the posterior probability that the corresponding regression coefficient exceeded 0 for continuous outcomes or 1 (on the odds ratio scale) for binary outcomes. The threshold for significance was set at 1% (one-sided) due to multiple hypothesis testing increasing the probability of a spurious finding, with probabilities >99% interpreted as significant. Potential interactions between treatment and sex were assessed.

Ethical considerations

All participants provided written consent with ethical approval from the London-Stanmore Research Ethics Committee (REC) (IRAS 18/LO/1474).

Results

Of 100 youth eligible for the BONDY study longitudinal arm (perinatal HIV, age 15-24 at study entry, on ART), 85 enrolled in BONDY-Met: 49 (58%) were female, 70 (82%) of black ethnicity with a mean age of 21.7 years (SD 2.7). Reasons for not enrolling included (n=15): transfer of care 5, personal choice/did not attend 5, unable to consent: pregnant 1, psychosis 1, central nervous system infection 1, travel 1, incarceration 1). The median follow up was 26 months (IQR 25,28) from study entry with a median weight gain of 3kg [IQR -1,7]. At latest follow up, median CD4 count was 623 cells/ μ L (IQR 156), with 68 (80%) having a VL <200 copies/ml. Mean ART duration was 15 years with 39 (46%) currently on INSTI-based ART, 32 (38%) on bPI (darunavir 27, atazanavir 5 [1 unboosted]) with 43 (51%) on TAF and 14 (16%) on INSTI +TAF (Table 1). Half had a prior CDC-C diagnosis, 22% were current or former smokers, 18% had a family history of cardiovascular disease, 26% a family history of DM and 32% drank alcohol. All were post pubertal and none had DM or were receiving lipid lowering or antihypertensive agents.

Median weight gain over 26 months was 3kg, with BMI category overweight/obese increasing from 37% to 50% with 28 (33%) having an A/G ratio within the 3rd tertile. Forty-one (48%) had MetS defined dyslipidaemia and 11 (13%) had hypertension [34]. Six (7%) fulfilled MetS criteria with a further 13/85 (15%) having two criteria. Insulin resistance, (HOMA-IR $\geq$ 3) was evident in 19% with none having an HbA1c above 48mmol/l (Table 1). On transient elastography, 15 (18%) had evidence of steatosis ($\geq$ S2), 7 (8%) had evidence of fibrosis ($\geq$ F2) and 8% had liver transaminases above the upper limit of normal. Mean BMI was 24.7 (5.1) with no difference in change from baseline by TAF (n=43) versus non-TAF/TDF (n=40).

Bayesian regression analyses demonstrated no association of INSTI and/or TAF containing ART on metabolic outcomes including, BMI change, MetS, hepatic steatosis, HbA1c and HOMA-IR (table 2). Further analyses showed no evidence of interactions between sex (male vs female at birth) and HIV parameters (CDC-C, current viraemia VL $\geq$ 200 and CD4:8<1) or INSTI and/or TAF containing regimens on metabolic outcomes, adjusting for age group at study entry (Supplementary Table 1, <http://links.lww.com/QAD/D872> and Figure 1).

Discussion

In this cohort of youth with PHIV (mean age 21.7 years), rates of MetS were low (7%) although half were overweight or obese, with 48% having dyslipidaemia. Rates of MetS were comparable to PHIV cohorts in France and Thailand but lower than an older cohort in the US (13% MetS; median age 30 years), with MetS prevalence increasing with age in the general population [6,8,9]. Rates of overweight/obesity in 16–24-year-olds in England are estimated at 37%, associated with female sex, black ethnicity, and deprivation; risk factors common in this study population [35]. The median weight gain over 26 months was 3kg, with BMI category overweight/obese moving from 37% to 50%. Obesity rates increase with age; however recent general population data in England suggest those currently aged 18–24 years have the highest risk of BMI gain compared to older age groups [36]. Increasing youth weight gain is associated with environmental factors (calorie rich processed food, increasingly sedentary lifestyle) and genetic heritability results in both metabolic and psychological consequences [37].

While weight gain has been reported in association with INSTIs and TAF, we found no association with adverse metabolic outcomes, including BMI change, suggesting that addressing traditional risk factors is more important for metabolic health than switching ART. Current viraemia and past CDC-C diagnosis were not associated with adverse metabolic outcomes, however, maintaining viral suppression remains a priority for youth where rates of viral suppression are lower than in adults, with uncontrolled viraemia associated with multimorbidity and potential onward transmission [5]. Rates of MetS defined dyslipidemia approached 50% in this cohort. The Reprieve study led to the recommendation of empirical statin use from 40 years in adults with HHIV [27]. However, there are no recommendations for statins in PHIV despite high rates of dyslipidaemia reported in both high and low incomes settings (34–70%) and in the context of lifelong inflammation and increased cardiovascular risk [7,10,19,22–25,38]. With the metabolic impact of lifestyle interventions for youth limited and pharmacotherapy currently targeted to older adults with established morbidity, the optimal timing and modality of intervention strategies to prevent cardiovascular disease remains a research priority for this emerging adult population with PHIV [5,10,27,38].

The limitations of this study include the relatively short duration of follow up, potential selection bias of those consenting to the sub study and variable rates of viral suppression during the study period potentially influencing the impact of ART, although reflecting real world adherence patterns in this population and the challenges of maintaining viral suppression during this period of life [5]. Major limitations include the low participant number resulting in likely underpowering to study ART interactions and lack of age and ethnically matched HIV negative youth. However, the lack of effect on outcomes by ART regimen (INSTI vs. other, TAF vs. non-TAF/TDF and INSTI with TAF vs. other) adds to the evidence base underlining the importance of addressing traditional risk factors for adverse metabolic health from early childhood and through into adult life, while maintaining sustained viral suppression.

Acknowledgements

The writing team would like to thank all the participants who took part in the BONDY-Met Study and the members of the BONDY study group Sara Ayres, Alice Walley, Rebecca Hall, Natalie Kirkhope, Fiona Brown and Wilbert Ayap.

Authors' contributions

CF conceived the study, recruited participants, collated the data and wrote the draft article. AB performed the statistical analyses and reviewed the article. HL recruited participants and reviewed the draft article. SF and MH recruited patients, reviewed the data and draft article and are supported by Imperial College NIHR BRC.

Conflict of interest

We have no conflicts of interest to declare.

References

1. Trachunthong D, Tipayamongkhogul M, Chumseng S, Darasawang W, Bundhamcharoen K. Burden of metabolic syndrome in the global adult HIV-infected population: a systematic review and meta-analysis. *BMC Public Health*. 2024 Sep 28;24(1):2657.
2. Foster C, Ayers S, McDonald S, Frize G, Chhabra S, Pasvol S, Fidler S. Clinical outcomes post transition to adult services in young adults with perinatally acquired HIV infection: mortality, retention in care and viral suppression. *AIDS* 2020 1;34(2):261-266.
3. Majonga ED, Henderson M, Ferrand RA. Cardiovascular health in people with perinatally acquired HIV - where do we stand? *Curr Opin HIV AIDS*. 2024 Jun 27. doi: 10.1097/COH.0000000000000872.
4. López E, Sainz T, Dirajlal-Fargo S, Jao J, Pinto J, Buchanan AM, et al. Cardiometabolic Health Burden in Pediatric HIV: Unmet Need in the Contemporary Antiretroviral Therapy Era. *Cureus*. 2025 Jun 4;17(6):e85329. doi: 10.7759/cureus.85329.
5. Henderson M, Fidler S, Foster C. Adults with perinatally acquired HIV; Emerging clinical outcomes and data gaps. *Trop Med Inf Dis* 2024 Apr 3;9(4):74.
6. Haw NJL, Lesko CR, Ng DK, Lam J, Lang R, Kitahata MM, et al; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Incidence of non-AIDS defining comorbidities among young adults with perinatally acquired HIV in North America. *AIDS*. 2024 Jul 15;38(9):1366-1374.
7. Sahagun SJ, Yerosu T, Purdy JB, Reynolds JC, Hadigan CM. Associations Between Central Obesity and Lifelong Antiviral Therapy in Adults Living With HIV Acquired From Early Childhood. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2022;89(2):208-14.
8. Arrive E, Viard J-P, Salanave B, Dollfus C, Matheron S, Reliquet V, et al. Metabolic risk factors in young adults infected with HIV since childhood compared with the general population. *PLOS ONE*. 2018;13(11):e0206745-e.

9. Aupibul L, Namwongprom S, Sudjaritruk T, Ounjaijean S. Metabolic syndrome, biochemical markers, and body composition in youth living with perinatal HIV infection on antiretroviral treatment. *PLoS One*. 2020 Mar 30;15(3):e0230707.
10. Dirajlal-Fargo S, Nyathi M, Sun S, Bonner LB, Kahts M, Asafu-Agyei NA, et al. Metabolic syndrome and Pathobiological Determination of Atherosclerosis in Youth risk score in adolescents with and without perinatally acquired HIV in the Cape Town Adolescent and Antiretroviral Cohort (CTAAC)-Heart study. *HIV Med*. 2025 Aug;26(8):1239-1250.
11. Gawrieh S, Vilar-Gomez E, Woreta TA, Lake JE, Wilson LA, Price JC, et al. Prevalence of steatotic liver disease, MASLD, MetALD and significant fibrosis in people with HIV in the United States. *Aliment Pharmacol Ther*. 2024 Mar;59(5):666-679.
12. Lemoine M, Assoumou L, De Wit S, Girard PM, Valantin MA, Katlama C, et al; ANRS-ECHAM Group. Diagnostic Accuracy of Noninvasive Markers of Steatosis, NASH, and Liver Fibrosis in HIV-Monoinfected Individuals at Risk of Nonalcoholic Fatty Liver Disease (NAFLD): Results from the ECHAM Study. *J Acquir Immune Defic Syndr*. 2019 Apr 1;80(4):e86-e94.
13. Chen BR, Pan CQ. Non-invasive assessment of fibrosis and steatosis in pediatric non-alcoholic fatty liver disease. *Clin Res Hepatol Gastroenterol*. 2022 Jan;46(1):101755.
14. Rose PC, Davies C, Cotton MF, Otjombe K, Browne SH, Vaida F, et al. Longitudinal controlled attenuation parameter and liver stiffness in children with and without perinatal HIV infection in South Africa. *AIDS*. 2024 Sep 1;38(11):1638-1647.
15. Carrasco I, Oliveira A, Lancharro Á, Escosa L, Mellado MJ, Busca C, et al. Prevalence of nonalcoholic fatty liver disease using noninvasive techniques among children, adolescents, and youths living with HIV. *AIDS*. 2022 May 1;36(6):805-814.
16. Hatleberg CI, Ryom L, Sabin C. Cardiovascular risks associated with protease inhibitors for the treatment of HIV. *Expert Opin Drug Saf*. 2021 Nov;20(11):1351-1366.
17. Capeau J, Lagathu C, Béréziat V. Recent data on the role of antiretroviral therapy in weight gain and obesity in persons living with HIV. *Curr Opin HIV AIDS*. 2024 Jan 1;19(1):14-20.
18. Savinelli S, Newman E, Mallon PWG. Metabolic Complications Associated with Use of Integrase Strand Transfer Inhibitors (InSTI) for the Treatment of HIV-1 Infection: Focus on Weight Changes, Lipids, Glucose and Bone Metabolism. *Curr HIV/AIDS Rep*. 2024 Dec;21(6):293-308.
19. Santiprabhob J, Tanchaweng S, Maturapat S, Maleesatharn A, Lermankul W, Sricharoenchai S, et al. Metabolic Disorders in HIV-Infected Adolescents Receiving Protease Inhibitors. *Biomed Res Int*. 2017;2017:7481597.
20. Glenn J, Bennett A, Mackie NE, Lyall EGH, Taylor GPT, Fidler S, Foster C. The Cumulative Prevalence of HIV-1 Drug Resistance in Perinatal HIV. *AIDS*. 2025 Jul 15;39(9):1161-1177.
21. Eni-Olutu A, Mackie N, Glenn J, Bailey A, Bamford A, Kenny J, et al. Emerging integrase resistance in an international perinatal virtual clinic. *AIDS*. 2025 Mar 1;39(3):276-280.
22. Belfrage E, Soeria-Atmadja S, Navér L. Growth, weight gain and BMI in virally suppressed children on antiretroviral therapy with specific reference to dolutegravir. *BMC Pediatr*. 2023 Jul 4;23(1):339.

23. Turkova A, White E, Mujuru HA, Kekitiinwa AR, Kityo CM, Violari A, et al; ODYSSEY Trial Team. Dolutegravir as First- or Second-Line Treatment for HIV-1 Infection in Children. *N Engl J Med*. 2021 Dec 30;385(27):2531-2543.
24. Yeoh DK, Campbell AJ, Bowen AC. Increase in body mass index in children with HIV, switched to tenofovir alafenamide fumarate or dolutegravir containing antiretroviral regimens. *Pediatr Infect Dis J*. 2021;40:e215–e216.
25. Thivalapill N, Simelane T, Mthethwa N, Dlamini S, Lukhele B, Okello V, et al. Transition to dolutegravir is associated with an increase in the rate of body mass index change in a cohort of virally suppressed adolescents. *Clin Infect Dis*. 2021 Aug 2;73(3):e580-e586.
26. O'Rourke J, Townsend CL, Milanzi E, Collins IJ, Castro H, Judd A, et al. Effectiveness and safety of tenofovir alafenamide in children and adolescents living with HIV: a systematic review. *J Int AIDS Soc*. 2023 Feb;26(2):e26037.
27. Grinspoon SK, Fitch KV, Zanni MV, Fichtenbaum CJ, Umbleja T, Aberg JA, et al; REPRIEVE Investigators. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. *N Engl J Med*. 2023 Aug 24;389(8):687-699.
28. Triant VA, Lyass A, Hurley LB, Borowsky LH, Ehrbar RQ, He W, et al. Cardiovascular risk estimation is suboptimal in people with HIV. *J Am Heart Assoc*. 2024 May 21;13(10):e029228.
29. Rajashekhar M, Joshi M, Mundra A, Kolhe R, Kirubakaran R, Raut AV, Nazli Khatib M. Community-based health promotion interventions to reduce risk factors in non-communicable diseases among adolescents and young adults in low- and middle-income countries: A systemic review and meta-analysis. *Public Health* 2025 Jun;243:105714.
30. Henderson M, Blenkinsop A, Ratmann O, Cheung M, Lyall H, Fidler S, Foster C; BONDY study group. Bone health in a U.K. cohort of youth living with perinatally acquired HIV-1: a longitudinal study. *J Int AIDS Soc*. 2025 Sep;28(9):e70029. doi: 10.1002/jia2.70029
31. NHS commissioning policy: Tenofovir alafenamide for treatment of HIV-1 in adults and adolescents. <https://www.england.nhs.uk/wp-content/uploads/2017/03/f03-taf-policy.pdf> (accessed 8th November 2025).
32. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β -cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; 28:412–419. doi: 10.1007/BF00280883.
33. Mikolasevic I, Orlic L, Franjic N, Hauser G, Stimac D, Milic S. Transient elastography (FibroScan®) with controlled attenuation parameter in the assessment of liver steatosis and fibrosis in patients with nonalcoholic fatty liver disease - Where do we stand? *World J Gastroenterol*. 2016 Aug 28;22(32):7236-51.
34. Anagnostis P. The metabolic syndrome. *BMJ Best practice* updated 12 December 2025. <https://bestpractice.bmj.com/topics/en-gb/212/pdf/212/Metabolic%20syndrome.pdf> (accessed 9th January 2026).
35. NHS England. The Health Survey for England 2022 Part 2. <https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2022-part-2/adult-overweight-and-obesity#:~:text=Overweight%20and%20obesity%2C%20by%20age,women%20aged%2055%20to%2074.> (accessed 6.12.25)
36. Katsoulis M, Lai AG, Diaz-Ordaz K, Gomes M, Pasea L, Banerjee A, et al. Identifying adults at high-risk for change in weight and BMI in England: a longitudinal, large-scale, population-based

cohort study using electronic health records. *Lancet Diabetes Endocrinol.* 2021 Oct;9(10):681-694.

37. Heymsfield S, Wadden TA. Mechanisms, pathophysiology and management of Obesity. *N Engl J Med* 2017;376:254-266.
38. Henderson M, Kastrup V, Ahmad S, Glenn J, Ayres S, Jadayel H, et al. Evaluation of Cardiovascular Risk Factors Among Adults With Perinatally Acquired HIV. *Open Forum Infect Dis.* 2025 Nov 6;12(11):ofaf629. doi: 10.1093/ofid/ofaf629.
39. Messina C, Albano D, Gitto S, Tofanelli L, Bazzocchi A, Ulivieri FM, et al. Body composition with dual energy X-ray absorptiometry: from basics to new tools. *Quant Imaging Med Surg.* 2020 Aug;10(8):1687-1698.

Table 1: Participant characteristics

Characteristic		Total (n=85)	Female (n=49)	Male (n=36)
Age (years)	Mean (sd)	21.7 (2.7)	21.6 (2.8)	21.9 (2.7)
Ethnicity	Black/African/Caribbean/ Black British	70 (82%)	39 (80%)	31 (86%)
	Other	15 (18%)	10 (20%)	5 (14%)
ART Duration (yr)	Mean (sd)	15.0 (6.1)	14.3 (6.8)	15.8 (5.2)
ART Anchor	INSTI-based	39 (46%)	28 (57%)	11 (31%)
	PI-based	32 (38%)	14 (29%)	18 (50%)
	NNRTI-based	14 (16%)	7 (14%)	7 (19%)
TAF/TDF	TAF	43 (51%)	28 (57%)	15 (42%)
	TDF	2 (2%)	0 (0%)	2 (6%)
	Non-TAF/TDF	40 (47%)	21 (43%)	19 (53%)
CD4	CD4, cells/ μ L (median [IQR])	623 [467, 770]	650 [524, 791]	583 [436, 736]
CD4:8 ratio	Median [IQR]	0.9 [0.6–1.3]	0.9 [0.6–1.4]	0.9 [0.6–1.1]
Viral load (c/ml)	<20	57 (67%)	30 (61%)	27 (75%)
	20-199	11 (13%)	8 (16%)	3 (8%)
	≥ 200	16 (19%)	10 (20%)	6 (17%)

Previous CDC-C	Yes	44 (52%)	26 (53%)	18 (50%)
Smoking history	Smoking never	66 (78%)	39 (80%)	27 (75%)
	Smoking current/former	19 (22%)	10 (20%)	9 (25%)
Any alcohol		27 (32%)	15 (31%)	12 (33%)
Family history of CVD		15 (18%)	9 (18%)	6 (17%)
Family history of DM		22 (26%)	11 (22%)	11 (31%)
METABOLIC PARAMETERS				
BMI (baseline)*	Underweight	1 (1%)	0 (0%)	1 (3%)
	Normal weight	53 (62%)	27 (55%)	26 (72%)
	Overweight	22 (26%)	17 (35%)	5 (14%)
	Obese	9 (11%)	5 (10%)	4 (11%)
BMI (follow-up)*	Underweight	2 (2%)	0 (0%)	2 (6%)
	Normal weight	40 (47%)	21 (43%)	19 (53%)
	Overweight	24 (28%)	16 (33%)	8 (22%)
	Obese	19 (22%)	12 (24%)	7 (19%)
Prevalence of metabolic syndrome		6 (7%)	5 (10%)	1 (3%)
Prevalence of dyslipidaemia		41 (48%)	28 (57%)	13 (36%)
Prevalence of hypertension		11 (13%)	5 (10%)	6 (17%)
Waist circ (cm)	Mean (sd)	80.6 (14.4)	80.4 (13.4)	80.8 (16.0)
Systolic BP	Mean (sd)	120.3 (12.5)	116.5 (11.0)	125.6 (12.6)
Diastolic BP	Mean (sd)	75.8 (10.5)	75.5 (9.5)	76.1 (11.8)
Triglycerides	Mean (sd)	0.8 (0.5)	0.8 (0.4)	0.9 (0.6)
	≥1.7mmol/L	6 (7%)	5 (10%)	1 (3%)
Total cholesterol	Mean (sd)	4.2 (0.9)	4.1 (0.9)	4.3 (1.0)
	≥5.18mmol/L	14 (16%)	7 (14%)	7 (19%)
HDL - cholesterol	Mean (sd)	1.4 (0.4)	1.4 (0.4)	1.3 (0.4)
	<1.29 (M), <1.04 (F)	31 (36%)	24 (49%)	7 (19%)
LDL - cholesterol	Mean (sd)	2.6 (0.7)	2.5 (0.6)	2.7 (0.7)
	≥3.4mmol/L	11 (13%)	5 (10%)	6 (17%)

Glucose	Mean (sd)	4.5 (0.5)	4.5 (0.4)	4.6 (0.5)
	≥5.6mmol/L	1 (1%)	1 (2%)	0 (0%)
HOMA-IR	Mean (sd)	2.4 (2.0)	2.5 (2.2)	2.2 (1.6)
	≥3.0	16 (19%)	9 (19%)	7 (19%)
HbA1c	Mean (sd)	33.0 (4.5)	32.2 (4.1)	34.0 (4.8)
	>48mmol/L	0 (0%)	0 (0%)	0 (0%)
C-peptide	Mean (sd)	589.6 (333.8)	588.7 (328.5)	590.8 (346.6)
	>1500pmol/L	2 (3%)	1 (2%)	1 (3%)
Insulin	Mean (sd)	11.7 (8.7)	12.1 (9.4)	11.3 (7.6)
	>15μU/mL	14 (18%)	7 (16%)	7 (22%)
ALT	Mean (sd)	25.6 (21.7)	18.5 (6.6)	35.3 (30.1)
	>45 (M), >34 (F)	7 (8%)	2 (4%)	5 (14%)
TOTAL BODY DUAL ENERGY X-RAY ABSORPTIOMETRY				
Total body fat (%)	Mean (sd)	33.9 (10.8)	39.0 (7.5)	26.5 (10.8)
Android (A) fat (%)	Mean (sd)	34.0 (14.4)	38.7 (11.9)	27.4 (15.1)
Gynoid (G) fat (%)	Mean (sd)	37.1 (12.6)	43.7 (7.7)	27.9 (12.4)
A/G ratio*	Mean (sd)	0.9 (0.2)	0.9 (0.2)	0.9 (0.2)
	Tertile 1	29 (34.5%)	18 (36.7%)	11 (31.4%)
	Tertile 2	27 (32.1%)	16 (32.7%)	11 (31.4%)
	Tertile 3	28 (33.3%)	15 (30.6%)	13 (37.1%)
TRANSIENT ELASTOGRAPHY (FIBROSCAN)				
CAP (dBm)	Mean (sd)	198.9 (52.9)	196.8 (49.9)	201.8 (57.4)
Steatosis	S1 (238 to 260)	4 (4.7%)	3 (6.1%)	1 (2.8%)
	S2 (260 to 290)	5 (5.9%)	3 (6.1%)	2 (5.6%)
	S3 (290 to 400)	6 (7.1%)	2 (4.1%)	4 (11.1%)
E-score (kPa)	Mean (sd)	5.3 (3.6)	4.9 (2.6)	5.9 (4.7)
	2-7	78 (91.8%)	45 (91.8%)	33 (91.7%)
	7-10	4 (4.7%)	3 (6.1%)	1 (2.8%)

	10-14	0 (0.0%)	0 (0.0%)	0 (0.0%)
	>=14	3 (3.5%)	1 (2.0%)	2 (5.6%)

ART; antiretroviral therapy, sd; standard deviation, IQR; interquartile range, INSTI; integrase strand transfer inhibitor, PI; protease inhibitor, NNRTI; non-nucleoside reverse transcriptase inhibitor, TAF; tenofovir alafenamide, TDF; tenofovir disoproxil fumarate, CDC-C; Centre for Disease Control category C AIDS diagnostic condition, CVD; cardiovascular disease, DM; diabetes mellitus, BMI; body mass index *z scores aged 15-19 years, BP; blood pressure, HDL; high density lipoprotein, LDL; low density lipoprotein, HbA1c; glycosylated haemoglobin, ALT; alanine aminotransferase, M; male, F; female, CAP; controlled attenuation parameter, E-score; elastography score.

*Central fat deposition assessed by DEXA as an android (abdominal) /gynoid (hip) ratio of ≥ 0.8 in women and ≥ 1.0 in men has been associated with an increased risk of adverse metabolic and cardiovascular outcomes in youth and adult populations.³⁹

Table 2: Estimated effect of INSTI-based ART regimens, TAF-containing regimens and HIV clinical markers on metabolic outcomes, obtained from Bayesian generalised linear regression models (Gaussian link for continuous outcomes; logit link for binary outcomes). Each row corresponds to a distinct model, adjusting for age and sex, and models for change in BMI also adjusted for baseline BMI.

Outcome type	Outcome	Risk factor	Estimate [95% credible interval]*	Posterior probability of positive association	Significant
Continuous outcomes	BMI change	INSTI	0.16 [-1,1.37]	0.60	No
		TAF	-0.72 [-1.94,0.5]	0.12	No
		INSTI+TAF	-0.07 [-1.7,1.58]	0.46	No
		Prior CDC-C	0.17 [-1.04,1.35]	0.61	No
		**VL ≥ 200	0.21 [-1.3,1.7]	0.60	No
		CD4:8 ratio<1	-0.47 [-1.71,0.74]	0.22	No
	Fibroscan CAP	INSTI	-2.73 [-26.74,21.02]	0.41	No

		TAF	-3.79 [-28.1,19.73]	0.38	No
		INSTI+TAF	-17.46 [-47.65,13.35]	0.13	No
		Prior CDC-C	-4.19 [-28.62,19.19]	0.36	No
		VL $\geq$ 200	-0.95 [-30.35,29.45]	0.46	No
		CD4:8 ratio<1	1.06 [-23.05,24.88]	0.54	No
	HbA1c	INSTI	1.73 [-0.28,3.76]	0.96	No
		TAF	-0.36 [-2.32,1.65]	0.35	No
		INSTI+TAF	0.19 [-2.51,2.77]	0.56	No
		Prior CDC-C	-0.34 [-2.28,1.57]	0.36	No
		VL $\geq$ 200	1.4 [-1,3.83]	0.87	No
		CD4:8 ratio<1	0.97 [-0.88,2.89]	0.84	No
	HOMA-IR	TAF	0.3 [-0.63,1.2]	0.75	No
		INSTI	0.41 [-0.45,1.26]	0.82	No
		INSTI+TAF	0.47 [-0.71,1.62]	0.80	No
		Prior CDC-C	0.29 [-0.54,1.11]	0.75	No
		VL $\geq$ 200	-0.14 [-1.21,0.88]	0.40	No
		CD4:8 ratio<1	0.19 [-0.72,1.13]	0.65	No
Binary outcomes	Hepatic steatosis	INSTI	0.58 [0.13,1.62]	0.12	No
		TAF	1.52 [0.37,4.07]	0.66	No
		INSTI+TAF	0.42 [0.02,1.68]	0.09	No
		Prior CDC-C	0.63 [0.17,1.64]	0.14	No
		VL $\geq$ 200	3.39 [0.7,9.73]	0.92	No
		CD4:8 ratio<1	1.07 [0.28,2.92]	0.42	No
	MetS	INSTI	3.97 [0.43,16.26]	0.85	No
		TAF	2.81 [0.29,12.23]	0.71	No
		INSTI+TAF	7.62 [0.83,30.85]	0.96	No

		Prior CDC-C	15.02 [0.74,82.02]	0.95	No
		VL $\geq$ 200	1.11 [0.03,5.09]	0.35	No
		CD4:8 ratio<1	3.38 [0.4,13.93]	0.79	No
	2 criteria of MetS	INSTI	1.14 [0.25,3.23]	0.44	No
		TAF	1.35 [0.27,4.06]	0.53	No
		INSTI+TAF	1.22 [0.11,4.23]	0.44	No
		Prior CDC-C	3.86 [0.71,13.9]	0.93	No
		VL $\geq$ 200	2.07 [0.29,6.75]	0.71	No
		CDC4:8 ratio<1	3.91 [0.75,13.6]	0.93	No

* Estimated coefficients and 95% credible intervals on odds ratio scale for binary outcomes.

ART; antiretroviral therapy, INSTI; integrase strand transfer inhibitor, TAF; tenofovir alafenamide, CDC-C; Acquired Immunodeficiency syndrome diagnosis, **VL; most recent viral load, BMI; body mass index, HbA1c; glycosylated haemoglobin, CAP; controlled attenuation parameter. HOMA-IR; homeostatic model for assessment of insulin resistance, MetS; metabolic syndrome.